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Source: *DI-International Diabetes Foundation, **ADA-American Diabetes Association
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TRIBUTE TO DR. AZIZUL HASAN

Dr. Azizul Hasan, renowned physician who was working with Apollo Hospitals Dhaka since its inception; passed away tragically and unexpectedly on 10th September 2015.

Dr. Azizul Hasan was born in Dhaka, Bangladesh on 1st March 1955. He graduated from Dhaka Medical College in 1979 (with honors in Community Medicine). He received Diploma in Cardiology from University of Vienna and Fellow in Cardiology from American Medical Society of Vienna. He completed his FMGEMS in 1985. He was awarded the Diploma in Tuberculosis and Chest Diseases from the University of Wales, UK. He completed his MRCP (Ireland as well as UK) in 1993.

Dr. Azizul Hasan worked in Jahurul Islam Medical College, Bajitpur in Bangladesh. He also worked in Tauhid Government Hospital in Iran, University of Vienna Hospital in Vienna, Landough Hospital in Wales, and King Khaled University Hospital & Prince Mansoor Military Hospital in KSA.

Dr Hasan joined Apollo Hospitals Dhaka in the year 2005. He served this hospital in the capacity of senior consultant and coordinator of Internal Medicine department.

He played an active role as an advisory member in many committees including credentialing committee, recruitment committee, and ethics committee.

Dr. Azizul Hasan was loved equally by patients and all staff. He was admired for his commitment, sincerity and empathetic touch for his patients. His warm touch and courteous heart supported many in their times of distress.

Dr. Hasan was a soft-spoken person with humble approach and down to earth personality. He was an inspiration for many. His charismatic nature and respect for each and every individual will always be remembered.

Dr. Hasan has left behind his wife - Dr. Parveen Akhtar and two sons - Dr. Farsheed Hasan & Tanveer Hasan.

His sad demise is a great loss to his family, his colleagues, to Apollo Hospitals Dhaka and to the nation. On behalf of the family of Apollo Hospitals Dhaka, we would like to express our deepest sorrow and solemn prayer for his departed soul.

Dr. Azizul Hasan will never be forgotten.
The Man - Made Healthcare Disaster

There has been a remarkable progress in the field of medicine, particularly in recent past. But this technological advancement has come at a price. Since past few decades, health care system worldwide has seen a steady increase in costs that have burdened nations. In this scenario, tobacco use has emerged as one of the biggest public health threats the world has ever seen.

Globally, tobacco use is increasing despite gradually declining in the developed countries. The epidemic of tobacco use is now shifting to the developing world. Currently, there are more than a billion smokers in the world, with more than 80 percent smokers living in low and middle-income countries. Tobacco use kills 5.4 million people annually accounting for about 10 percent adult deaths worldwide, thus killing up to half of all users, and becoming a leading preventable cause of death globally. The tobacco-related deaths are expected to increase to more than eight million per year by 2030, with 80 of such deaths occurring in the developing nations. It has caused an estimated 100 million deaths in 20th century, and with current trends it is expected to kill up to one billion in the current century.

Smoking harms nearly every organ of the body. It causes many diseases and reduces the health of smokers in general. It is a risk factor for six of the eight leading causes of deaths in the world. It increases risk for death from all causes in men and women. As the health consequences of tobacco use appear after many years, it seems that the epidemic of disease and death has just begun. The healthcare scenario is going to worsen in coming years, more so in developing countries.

As it is the single largest preventable cause of death and diseases, there is an urgent need to wage a war against this man-made disaster. No longer, one has to accept it as a personal choice of those who smoke, as it directly and indirectly affects almost everyone in the society including small children through passive smoking. The task at hand is really huge, but not impossible if we act collectively at all levels to control it.

Dr. Chandra P. Dokwal
Sr. Consultant & Coordinator
Department of Respiratory Medicine
Apollo Hospitals Dhaka
Surgical Outcomes of Cerebellopontine Angle Tumors in 34 Cases

Joarder MA1, Karim AKMB2, Sujon SI3, Akhter N4, Waheeduzzaman M5, Joseph V6, Jahangir SM7, Chandy MJ8

Abstract

Introduction: Cerebellopontine angle tumors are a surgical challenge to many neurosurgeons who want to operate in this space. Although most of these tumors are benign, they are a challenge because of the complex anatomy and important neurovascular structures that traverse this space. Most common cerebellopontine angle tumor is vestibular schwannoma. The management of these cases is essentially surgical. There has been a change in the surgical strategy over the years from simple intratumoral decompression to complete microsurgical excision, to radical excision with facial nerve and hearing preservation. Objectives: To study the clinical and radiological characteristics, know the pathological types and determine the surgical resectability and outcome of cerebellopontine angle tumor. Materials and Methods: It is a retrospective study done in the department of Neurosurgery, Apollo Hospitals Dhaka. 34 patients diagnosed with cerebellopontine angle tumor were recruited into the study. Results: Among 34 cases of cerebellopontine angle tumors vestibular schwannoma alone constituted 79%. Most of the tumors were large or giant tumors. Total resection was done in 25% of vestibular schwannoma and 50% of meningiomas. Anatomical preservation of facial nerve was achieved in 73% of patients. Facial nerve function as measured by the House Brackmann system. Postoperatively 61% had a score of 1 or 2; 29% had a score of 3 or 4; and 8% had a score of 5 or 6. Other complications included 2 cases of CSF leak, 3 cases of meningitis, 2 cases of lower cranial nerve palsy and 1 patient died. Conclusion: Cerebellopontine angle tumors show high incidence from 3rd to 5th decade with common symptoms being hearing loss and ataxia. Most of the patients presented at a delayed stage with large to giant tumors with no useful hearing. Sub total excision with keeping anterior part of tumor for preserving facial nerve function is the goal.

Key words
Cerebellopontine angle tumors, vestibular schwannoma, meningioma

Introduction

Cerebellopontine angle is a triangular space bounded anteromedially by pons, posteromedially by cerebellum and laterally by petrous part of temporal bone. Although most of the cerebellopontine angle tumors are benign, the complex anatomy and important neurovascular structures traversing this space makes the management of these tumors, a surgical challenge to the neurosurgeon who would like to operate in
Surgical Outcomes of Cerebellopontine Angle Tumors in 34 Cases

this space. Most (80%) of the cerebellopontine angle tumors are vestibular schwannomas. The rest of the tumors are meningiomas, epidermoids, arachnoid cysts, other rare tumors are trigeminal schwannomas, facial nerve schwannomas, exophytic brainstem gliomas, secondaries and choroid plexus papillomas. The management of these cerebellopontine angle tumors is essentially surgical except for the smaller ones (<2.5 cm) which can be managed by radiosurgery. The advancement in imaging has resulted in the detection of smaller tumors at an earlier stage, and therefore increased the ability to preserve hearing. Over the years the surgical strategy has changed from simple intratumoral decompression to complete or near complete microsurgical excision, to facial nerve preservation and hearing preservation.

Methods

Introduction

Cerebellopontine angle is a triangular space bounded anteromedially by pons, posteromedially by cerebellum and laterally by the petrous part of the temporal bone. Although most of the cerebellopontine angle tumors are benign, the complex anatomy and important neurovascular structures traversing this space makes the management of these tumors a surgical challenge to the neurosurgeon who would like to operate in this space. Most (80%) of the cerebellopontine angle tumors are vestibular schwannomas. The rest of the tumors are meningiomas, epidermoids, arachnoid cysts, other rare tumors are trigeminal schwannomas, facial nerve schwannomas, exophytic brainstem gliomas, secondaries and choroid plexus papillomas. The management of these cerebellopontine angle tumors is essentially surgical except for the smaller ones (<2.5 cm) which can be managed by radiosurgery. The advancement in imaging has resulted in the detection of smaller tumors at an earlier stage, and therefore increased the ability to preserve hearing. Over the years the surgical strategy has changed from simple intratumoral decompression to complete or near complete microsurgical excision, to facial nerve preservation and hearing preservation.

Aims and Objectives

To study the cerebellopontine angle tumors with respect to clinical characteristics, radiological, pathological types, surgical respectability and its outcome.

Materials and Method

This retrospective study was performed in the Department of Neurosurgery, Apollo Hospitals Dhaka. 34 patients of cerebellopontine angle tumors operated between January 2009 to January 2015 were included in this study. It is a retrospective study.

Methodology

All patients with cerebellopontine angle tumors were assessed with respect to age, sex, clinical presentation, imaging characteristics and resectability. Facial nerve function was graded according to House - Brackmann scorepre-operatively and at the time of discharge and follow up. Pre-operative pure tone audiometry was done to assess the degree of hearing loss. A criterion for useful hearing was taken as hearing loss <50 decibel (Gardener - Robertson modification of the Silverstein and Norell system). Postoperative hearing assessment was done only in those patients who had useful hearing pre-operatively. The tumor size was measured in MRI in two axes, i.e. diameter parallel to the petrous ridge, vertical diameter in the coronal slices. The size of the tumor was taken as the largest vertical diameter in any one of the axes. The tumors were then categorized according to the classification proposed by Jackler et al. All patients were operated via the sub-occipital retro-mastoid craniectomy using standard microsurgical techniques.

Results

A total of 34 patients with cerebellopontine angle tumors operated between January 2009 to January 2015 were assessed. Of the 34 cases of cerebellopontine angle tumors, 27 were vestibular schwannomas, meningiomas constituted 6 cases, one case of epidermoid.
### Table 1: Distribution of tumors according to age

<table>
<thead>
<tr>
<th>Age</th>
<th>Vestibular schwannoma</th>
<th>Meningioma</th>
<th>Epidermoid</th>
<th>Total No. of Patients</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 20</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>21 – 30</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>31 – 40</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>9</td>
<td>26</td>
</tr>
<tr>
<td>41 – 50</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>9</td>
<td>26</td>
</tr>
<tr>
<td>51 – 60</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>8</td>
<td>24</td>
</tr>
<tr>
<td>61 – 70</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>12</td>
</tr>
</tbody>
</table>

### Table 2: Distribution of Cases according to Sex

<table>
<thead>
<tr>
<th>Sex</th>
<th>Vestibular schwannoma</th>
<th>Meningioma</th>
<th>Epidermoid</th>
<th>Total No. of Patients</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>14</td>
<td>5</td>
<td>0</td>
<td>19</td>
<td>55</td>
</tr>
<tr>
<td>Male</td>
<td>13</td>
<td>1</td>
<td>1</td>
<td>15</td>
<td>45</td>
</tr>
</tbody>
</table>

### Table 3: Distribution of cases according to clinical presentation

<table>
<thead>
<tr>
<th>Clinical findings</th>
<th>Vestibular Schwannoma</th>
<th>Meningioma</th>
<th>Epidermoid</th>
<th>Total No. of Patients</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensorineural hearing loss</td>
<td>24</td>
<td>4</td>
<td>1</td>
<td>29</td>
<td>85</td>
</tr>
<tr>
<td>Cerebellar signs</td>
<td>16</td>
<td>2</td>
<td>0</td>
<td>18</td>
<td>53</td>
</tr>
<tr>
<td>Headache</td>
<td>14</td>
<td>3</td>
<td>1</td>
<td>17</td>
<td>50</td>
</tr>
<tr>
<td>Trigeminal dysfunction</td>
<td>14</td>
<td>2</td>
<td>0</td>
<td>16</td>
<td>47</td>
</tr>
<tr>
<td>Facial nerve dysfunction</td>
<td>16</td>
<td>2</td>
<td>0</td>
<td>18</td>
<td>53</td>
</tr>
<tr>
<td>Papilloedema</td>
<td>9</td>
<td>1</td>
<td>0</td>
<td>10</td>
<td>29</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>12</td>
<td>2</td>
<td>0</td>
<td>14</td>
<td>44</td>
</tr>
<tr>
<td>Pyramidal signs</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>9</td>
<td>26</td>
</tr>
<tr>
<td>Nerve dysfunction</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>6</td>
</tr>
</tbody>
</table>
### Table 4: Distribution of cases according to size of tumor

<table>
<thead>
<tr>
<th>Size</th>
<th>No. of Patients</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium (10-25mm)</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>Large (26-40mm)</td>
<td>20</td>
<td>58</td>
</tr>
<tr>
<td>Giant (&gt; 40mm)</td>
<td>9</td>
<td>27</td>
</tr>
</tbody>
</table>

### Table 5: Distribution of cases according to pure tone audiometry

<table>
<thead>
<tr>
<th>Class</th>
<th>No. of Patients</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I &amp; II (Serviceable)</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>III &amp; IV (Non Serviceable)</td>
<td>29</td>
<td>85</td>
</tr>
</tbody>
</table>

### Table 6: Distribution of cases according to Facial Nerve Functional Grading (n=20)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Pre OP (n=20)</th>
<th>Post OP Grade (n=20)</th>
<th>Follow up Grade (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I &amp; II</td>
<td>III &amp; IV</td>
<td>V &amp; VI</td>
</tr>
<tr>
<td>I &amp; II</td>
<td>16</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>III &amp; IV</td>
<td>4</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>V &amp; VI</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

### Table 7: Distribution of cases according to Facial Nerve Functional Grading (n = 9)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Pre OP (n=9)</th>
<th>Post OP Grade (n=9)</th>
<th>Follow up Grade (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I &amp; II</td>
<td>III &amp; IV</td>
<td>V &amp; VI</td>
</tr>
<tr>
<td>I &amp; II</td>
<td>7</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>III &amp; IV</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>V &amp; VI</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

### Table 8: Distribution of cases according to findings on Imaging

<table>
<thead>
<tr>
<th>Imaging Findings (n=34)</th>
<th>Vestibular Schwannoma (n=27)</th>
<th>Meningioma (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homogenous enhancement</td>
<td>21</td>
<td>4</td>
</tr>
<tr>
<td>Heterogenous enhancement</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Cystic component</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Centered on IAM</td>
<td>22</td>
<td>3</td>
</tr>
<tr>
<td>Hyperostosis, Broad dural base, dural tail</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>
Table 9: Distribution of cases according to surgical procedure

<table>
<thead>
<tr>
<th>Surgical procedure (n=34)</th>
<th>No. of patients</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VP Shunt + Tumor surgery</td>
<td>8</td>
<td>24</td>
</tr>
<tr>
<td>Direct Tumor surgery</td>
<td>26</td>
<td>76</td>
</tr>
</tbody>
</table>

Table 10: Distribution of cases according to resectability

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Excision</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sub total</td>
<td>Total</td>
</tr>
<tr>
<td>Vestibular Schwannoma (n=27)</td>
<td>24 (89 %)</td>
<td>3 (11 %)</td>
</tr>
<tr>
<td>Meningioma (n=6)</td>
<td>4 (66%)</td>
<td>2 (33 %)</td>
</tr>
<tr>
<td>Epidermoid (n=1)</td>
<td>1 (100%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 11: Distribution of cases according to Histopathology

<table>
<thead>
<tr>
<th>Histopathology (n=27)</th>
<th>No. of patients</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vestibular schwannoma</td>
<td>27</td>
<td>79</td>
</tr>
<tr>
<td>Meningioma</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td>Epidermoid</td>
<td>1</td>
<td>3</td>
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</table>

Table 12: Distribution of cases according to anatomical preservation of facial nerve in entire group

<table>
<thead>
<tr>
<th>Tumour size</th>
<th>No. of patients</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium</td>
<td>3</td>
<td>60</td>
</tr>
<tr>
<td>Large</td>
<td>15</td>
<td>75</td>
</tr>
<tr>
<td>Giant</td>
<td>5</td>
<td>55</td>
</tr>
</tbody>
</table>

Table 13: Distribution of cases according to complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Vestibular Schwannoma (n=27)</th>
<th>Meningioma (n=6)</th>
<th>Epidermoid (n=1)</th>
<th>Total No. of Patients (n=34)</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF Leak</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Meningitis</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Hematoma</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nerve palsy</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Mortality</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>
Surgical Outcomes of Cerebellopontine Angle Tumors in 34 Cases

Analysis
In this study vestibular schwannomas constituted 79% of cerebellopontine angle tumors. The rest comprised of meningiomas (17%), epidermoids (3%). There was predominance of these tumors in females accounting for 55% of cases. About 76% of vestibular schwannomas presented between third, fourth and fifth decades. The most common presenting complaint was sensorineural hearing loss, cerebellar dysfunction, headache and sensory trigeminal dysfunction. Pre-operatively, 85% of cerebellopontine angle tumor patients had no useful hearing (<50 decibels). Out of the five patients who had useful hearing pre-operatively (3 vestibular schwannomas, 2 meningiomas) three patients retained it post operatively also. Most of the tumors are either large or giant (85%). Few patients showed a worsening of the facial grade in the immediate postoperative period which improved by the time of discharge and follow-up. Preoperative V-P shunt was required in 24% of cases of cerebellopontine angle tumors for hydrocephalus. Total resection was possible in 26% cases of vestibular schwannomas and 66% in meningiomas. Adherence of tumour with brainstem and facial nerve were responsible for subtotal resection in remaining cases. CSF leak from wound site occurred in 6% of cases. All were managed conservatively with lumbar drain and medication. Meningitis occurred in 9% cases. All of them recovered with appropriate antibiotics. Lower cranial nerve paresis developed in 6% of patients. They were managed with nasogastric tube feeding. Two patients required temporary tracheostomy for the management of secretions and low conscious level. Mortality in this study was 3%.

Discussion
There has been a considerable evolution in the management of cerebellopontine angle tumors especially vestibular schwannoma. Initially it was Cushing who was the first to reduce mortality from 50% to 11%. Later complete excision without mortality was reported by Walter Dandy in his study. With the advent of the era of operating microscope by the efforts of House, Rand and Kurze in 1964 and 1965 and safe modern anesthesia and refinements in microsurgical techniques the goal of vestibular schwannoma surgery shifted from complete excision to preservation of facial nerve function and cochlear nerve function. In the present study 85% of patients had either large or giant sized tumors. Pre-operative V-P shunt was required in 24% of patients. The incidence of pre-operative shunt was as high as 66% in the study reported by Rama Murthi et al. In the study published by VK Jain et al 8.5% of patients required V-P shunt. Complete tumor excision was done in 32% of patients in this study. VK Jain et al reported complete tumor excision in 96.5% of patients. Anatomical preservation of facial nerve was achieved in the present study for large size tumors in 74% of the cases and for giant size tumors in 62%. In a study by Samii and Matthias preservation rate was reported to be 93% independent of tumour size. In Jain VK et al study, the preservation of facial nerve was 84.3%. In the present study 15% (5 patients) had useful hearing preoperatively. Post-operative hearing could be preserved in 3 of these patients (60%). Samii et al reported hearing preservation in 23.6% with large tumors. VK Jain et al reported hearing preservation in 29.6% of their patients who had useful pre-operative hearing. The reported incidence of cerebrospinal fluid leak ranges between 0-30% with the average approximately 12%. In the present study, 6% of the patients had cerebrospinal fluid leak which was managed conservatively. Although injury to facial and vestibulocochlear nerve are the two major cranial nerve injuries that can occur during the surgery, there are risks of injury to lower cranial nerves in large and giant sized tumors,
which can complicate the post-operative course. Judicious use of nasogastric tube feeding and planned tracheostomy can avoid major respiratory complications post operatively. The reported incidence of lower cranial nerve paresis in the literature ranges from 1.5% to 5.5%.\textsuperscript{11, 12, 13} It is 6% in the present study. In the present study, all the cases were operated by sub-occipital retromastoid approach in lateral position.

References
Detection and Antimicrobial Susceptibility Pattern of Extended Spectrum Beta Lactamases (ESBLs) Producing Gram Negative Bacteria from Different Clinical Samples

Biswas SM1, Ara N2, Huda N3, Andalib S4, Rahman MH5, Mia MRA6

Abstract

Introduction: Extended spectrum β-lactamases (ESBLs) are enzymes that mediate resistance to extended-spectrum (third generation) cephalosporins (e.g., cefazidime, cefotaxime, and ceftiraxone) and monobactams (e.g., aztreonam) but do not affect cephamycins (e.g., cefoxitin and cefotetan) or carbapenems (e.g., meropenem or imipenem). Though the no. of ESBLs producing organism has been increasing day by day, the detection methods and treatment option for them are extremely limited. Aims & Objective: The present study was undertaken to investigate the rate of ESBLs production and their antibiotic susceptibility pattern. Materials & Method: A total 110 Gram negative isolates from various clinical samples from a tertiary care hospital were studied and ESBLs production was detected by double disc synergy test. Antibiotic susceptibility test was done for commonly used antibiotics. Results: Among the total isolates 66.36% (73) were ESBLs producer, and the rate of ESBLs positivity was 80.32% for E.coli (49 out of 61), 25% for Pseudomonas spp (6 out of 24), 71.42% for Klebsiella spp (10 out of 14), 80% for Enterobacter spp (4 out of 5), 100% for Acinetobacter spp (4 out of 4) and 0% for Proteus spp (0 out of 2). ESBLs producing organisms were resistant to most of the antibiotics but 100% were sensitive to imipenem. Conclusion: Screening for ESBLs production needs to be carried out routinely in every clinical diagnostic laboratory to guide clinicians in proper selection of antibiotics.

Key words
ESBLs, multidrug resistance, double disc synergy test

Introduction

Enterobacteriaceae producing extended spectrum β-lactamases (ESBLs) cause inactivation of β-lactam antibiotics especially the newer third generation cephalosporins. ESBLs producing enterobacteriaceae are also frequently resistant to other groups of commonly used non-β-lactam antibiotics such as fluroquinolones. Majority of ESBLs producing strains are Klebsiella pneumoniae, Klebsiella oxytoca and E.coli. Other organisms reported to harbour ESBLs include Enterobacter spp, Salmonella spp, Morganella morganii, Proteus mirabilis, Serratia marcescens and Pseudomonas aeruginosa. ESBLs enzymes are mediated by plasmids and are the products of point mutations at the active site of Temoniera (TEM), Sulphhydryl variable (SHV) and Oxacillinase (OXA) enzymes. In addition these plasmids also carry resistance to
several other antimicrobial agents, an important limitation in the design of treatment alternatives. It is generally thought that patients suffering from infections caused by an ESBLs-producing organism are at an increased risk of treatment failure with an expanded-spectrum β-lactam antimicrobials as well as other commonly used antimicrobial agents.

The prevalence of ESBLs among clinical isolates varies from country to country and from institution to institution. In the United States the occurrences of ESBLs in enterobacteriaceae range from 0 to 25%. In India, the prevalence rate varies in different institutions from 28 to 84%. Elsewhere in Asia the percentage of ESBLs production in E.coli and K. pneumoniae varies from 4.8% in Korea to 8.5% in Taiwan and up to 12% in Hong kong. A comprehensive study of 2840 isolates collected between April and October 2002 from both hospital and community specimens in Pakistan revealed 40% overall ESBLs production rate.

In 2005 a study in BSMMU, Bangladesh by Alim, showed that 23.19% of the Gram negative bacteria were ESBLs producing organism. While another study in the same institution in 2007 revealed ESBLs production rate to be 30.90% among the Gram negative bacteria. A similar study from Mymensingh, Bangladesh showed among the 300 gram negative isolates 214 (71.4%) was ESBLs producers. These studies strongly suggest increasing prevalence of ESBLs producing organisms in Bangladesh.

So the present study was designed to see the rate the ESBLs production in gram negative bacteria by double disc synergy test and to analyze antimicrobial susceptibility of the ESBLs producing organisms.

**Materials and Methods**

**Settings and samples**

This study was carried out in the Microbiology & Immunology Laboratory of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka during the period of July 2008 to June 2009. Total one hundred ten clinical Gram negative isolates were studied, which were isolated from different clinical samples (urine, wound swab, pus, throat swab and sputum) submitted to Microbiology & Immunology Laboratory of BSMMU.

**Test for determination of ESBLs activity**

All 110 isolates were tested for ESBLs activity by Double Disc Synergy Test.

**Double Disc Synergy Test**

Mueller Hinton agar plates were seeded with standardized inoculum of the test organism (corresponding to 0.5 McFarland tube). Amoxycyclav (AMC, 20 µg amoxicillin and 10 µg clavulanic acid) disc was placed in the center of the inoculated plate. Three 3rd generation cephalosporin (ceftazidime CAZ 30µg, ceftriaxone CRO 30µg, cefotaxime CTX 30µg) and one monobactam (aztreonam, AZT 30µg) discs were placed at 20 mm distance from amoxycyclav disc. The plate was incubated overnight at 37°C. Extension of the edge of the inhibition zone of ceftazidime, ceftriaxone, cefotaxime and aztreonam disc on the side exposed to the amoxycyclav disc is positive for ESBLs production. This extension of edge of inhibition is due to synergy of disc of amoxycyclav with the four discs used. (Fig. 1)
Detection and Antimicrobial Susceptibility Pattern of Extended Spectrum Beta Lactamases (ESBLs) Producing Gram Negative Bacteria from Different Clinical Samples

Fig. 1: Double disc synergy test positive for ESBLs production

Antimicrobial sensitivity test: 14
All the ESBLs producing isolates were tested for antimicrobial sensitivity using disc diffusion technique by "Kirby-Bauer method" against Carbapenem and different non beta-lactam antimicrobial agents.11 These included Cotrimoxazole 1.25/23.75μg (COT), Ciprofloxacin 5μg (CIP), Nitrofurantoin 300μg (NF), Gentamicin 10μg (CN), Amikacin 30μg (Ak), Imepenem 10μg (IMP), and Netilmicin 30 μg (NET). Susceptibility and resistance was determined based on the interpretative criteria recommended by the Clinical and Laboratory Standards Institute.12 E. coli ATCC 25922 was used as the quality control strain.

Result
In the present study, a total of 110 Gram negative isolates were isolated from various clinical samples of which majority were urine 60 (54.54%), followed by wound swab 39 (35.45%), pus 5 (4.54%), throat swab 4 (3.63%) and sputum 2 (1.18%) (Fig. 2).

The distribution of different types of Gram negative bacteria among the total 110 isolates was as follows: Escherichia coli 61 (55.45%), Klebsiella spp. 14 (12.73%), Pseudomonas spp 24 (21.81%), Enterobacter 5 (4.54%), Acinetobacter spp 4 (3.64%) and Proteus spp 2 (1.82%). All of these 110 Gram negative isolates were tested for ESBLs production by double disc synergy test and it was found that total 73 (66.36%) isolates were ESBL producers. Among these ESBLs producers 49 (80.32%) were Escherichia coli, 10 (71.42%) Klebsiella spp., 6 (25%) Pseudomonas aeruginosa, 4 (80%) Enterobacter and 4 (100%) Acinetobacter spp. (Table-1).

Table 1: Frequency of different isolates and their ESBLs production rate of total isolates (n=110)

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number of isolates (%)</th>
<th>ESBLs positive isolates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E.coli</td>
<td>61 (55.45)</td>
<td>49 (80.32)</td>
</tr>
<tr>
<td>Klebsiella spp.</td>
<td>14 (12.73)</td>
<td>10 (71.42)</td>
</tr>
<tr>
<td>Pseudomonas spp.</td>
<td>24 (21.81)</td>
<td>6 (25)</td>
</tr>
<tr>
<td>Enterobacter spp.</td>
<td>5 (4.54)</td>
<td>4 (80)</td>
</tr>
<tr>
<td>Acinetobacter spp.</td>
<td>4 (3.64)</td>
<td>4 (100)</td>
</tr>
<tr>
<td>Proteus spp.</td>
<td>2 (1.82)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>110 (100)</td>
<td>73 (66.36)</td>
</tr>
</tbody>
</table>
The antimicrobial resistance pattern of the ESBLs producers showed an alarmingly high resistance to ciprofloxacin (93.15%), cotrimoxazole (79.45%), gentamicin (75.34%) and netilmicin (36.98%). Amikacin and, for urine isolates, nitrofurantoin showed fairly good sensitivity (26.02% and 25% resistance respectively). Imipenem was the only drug that was 100% sensitive (0% resistance) for all ESBLs producers. (Table 2)

**Discussion**

ESBLs producing organisms pose a major problem in clinical therapeutics. The incidence of ESBLs producing strains among clinical isolates has been steadily increasing over the past years, resulting in limitations of therapeutic options. The overall prevalence of ESBL producers was found to vary greatly in different geographical areas and in different institutes.
In the present study 66.36% of the isolates were found to be ESBLs producer out of 110 Gram negative clinical isolates from different samples. But a similar study which was carried out 2 years earlier in 2007 in the same institute, BSMMU, by Rahman revealed ESBLs in only 30.90% strains of the Gram negative isolates. However a 2012 study from Mymensingh, Bangladesh detected 71.4% ESBLs producers from 300 gram negative isolates. Higher (68%) ESBLs production rate in enterobactericeae isolates has also been reported from India. One possible reason for such variation might be varying number of samples in different studies. The clinical condition of the source patients of samples might also be a contributing factor (acute versus chronic, past exposure to antimicrobials, etc.). The probable reasons of gradual increase in ESBLs detection in various Bangladesh studies might be 1) random and inappropriate use of 3rd generation cephalosporin, which contribute to the evolution of ESBLs, 2) nonexistence of standard infection control practices in healthcare facilities and 3) Lack of national antibiotic policy.

Among the 110 isolates in the present study, 61 were E.coli, 24 Pseudomonas spp, 14 Klebsiella spp, 5 Enterobacter spp, 4 Acinetobacter spp and 2 Proteus spp and their rate of ESBLs positivity was 49 (80.32%), 6 (25%), 10 (71.42%), 4 (80%), 4 (100%) and 0 (0%) respectively. In 2007 Rahman from BSMMU, Dhaka, Bangladesh detected 35.38% ESBL producers in E. coli, in Klebsiella spp 43.47%, in Enterobacter spp 31.25%, in Proteus spp 27.11%, in Acinetobacter spp 26.32% and in Pseudomonas spp 17.07%. Another study from Bangladesh (2010) showed 57.89% ESBLs production for Klebsiella spp. followed by Proteus spp. 50.0%, E. coli 47.83% and Pseudomonas spp 31.35%. A 2012 study from Mymensingh, Bangladesh showed that among 300 gram negative isolates 80% Klebsiella spp 72% Proteus spp, 71% Enterobacter spp., 67.3 % E. coli and 88.8% Pseudomonas spp were ESBL producers. A study from Tamil Nadu, India showed ESBLs producer in E. coli 77.35%, Klebsiella spp 71.23%, Pseudomonas spp 56.75%, Salmonella spp 29.31%, Enterobacter spp 35.48%, and Proteus spp 34.61%. The reason of high rates of ESBLs production in all the strains in this study might be due to overall higher rate of ESBLs producer in the study isolates.

In the present study drug resistance of all ESBLs producer to most of the non beta-lactum antibiotics (cotrimoxazole, gentamicin, ciprofloxacin, amikacin) were found higher. This implies that ESBL producing organisms are multirig resistant as genes that code for ESBLs are linked to other resistance genes. ESBLs producing isolates showed 100% sensitivity to imipenem which conforms clearly with the CDC (1999) ESBLs definition which says ESBLs are enzymes which hydrolyze 3rd generation cephalosporins but sensitive to imipenem.

**Conclusion**

In conclusion, screening for ESBLs production needs to be carried out routinely in every clinical diagnostic laboratory to guide clinicians in proper selection of antibiotics. Continued monitoring of the susceptibility pattern of ESBLs producing bacteria will provide invaluable information in clinical management of patients and, to control and prevent the spread of these type infections.
References

Total Laparoscopic Hysterectomy: A Two-Year Experience in Apollo Hospitals Dhaka

Begum M¹, Zulfiqar N², Yasmin F³

Abstract

Objective: Aim of our study is to analyze the surgical outcome of total laparoscopic hysterectomy (TLH) in our patient perspective of Apollo Hospitals Dhaka. Methods: This is a retrospective, observational study where we have reviewed demographic data, intraoperative and postoperative outcomes, and morbidity data on 100 women who underwent TLH between January 2011 and December 2012. Results: Total 100 patients were studied. Among them five patient required conversion to laparotomy due to presence of severe adhesion. The major and minor complication rates were 2% (bladder injury-2 cases) and 0% respectively. The average operating time was 148 ± 40 minutes and the mean length of hospital stay was 3±1 day. The average uterine size was 10 ± 4 weeks. In our cases operating time and duration of hospital stay were very similar with lower procedural complications to other published data elsewhere. Conclusion: We have observed that TLH is a safe and acceptable alternative procedure to standard hysterectomy from the patients perspective at Apollo Hospital Dhaka.

Key words
Laparoscopic hysterectomy, complications, laparoscopy, hysterectomy

Introduction

Hysterectomy is the most frequently performed major gynecological surgical procedure.¹ Though there are three approaches in hysterectomy - abdominal, vaginal and laparoscopic, still there are controversies regarding the optimal route for performing it. Even though there are numerous benefits of vaginal over abdominal hysterectomy including lower morbidity and more rapid postoperative recovery,² 70 – 80% of all hysterectomies are performed abdominally.³ Since the first laparoscopic hysterectomy (LH) was described by Harry Reich,⁴ LH has become an option for women and their surgeons to consider. During the last few years considerable technical advances in this procedure have occurred.⁵⁻⁸ There are many surgical advantages to laparoscopy particularly magnification of anatomy and pathology and access to the uterine vessels. Patient advantages are multiple and are related to avoidance of a painful abdominal incision, reduced duration of hospitalization, faster recovery time and early return to the activities of daily living.⁹⁻¹² Laparoscopically assisted vaginal hysterectomy (LAVH) was introduced to overcome the technical difficulties of vaginal hysterectomy in case of large uterine size, limited vaginal capacity or presence of pelvic adhesions,¹³ but

the vaginal phase of the procedure can still be difficult occasionally in women with limited vaginal capacity or in morbidly obese women. Total laparoscopic hysterectomy (TLH), in which the entire procedure of removing the uterus is performed laparoscopically, can overcome some of the limitations of LAVH. Moreover in a study of TLH versus LAVH, it was demonstrated that TLH was associated with a shorter hospital stay.\textsuperscript{14}

**Fig: Colpo-bulger**

Since 2011, we have used the Colpo-bulger vaginal fornix delineator to facilitate the TLH procedure. The Colpo-bulger is inserted in the vagina. The device allows clear exposure of the vaginal fornices, which make the TLH procedure simpler and may reduce complication rates. This study reviews our initial two-year experience of TLH using the Colpo-bulger.

**Methods**

This is a retrospective, observational study. We reviewed the records of 100 women who underwent attempted TLH between January 2011 and December 2012 in Apollo Hospitals, Dhaka. The data were obtained from our departmental database of gynecologic patients and the information was verified via a detailed review of the medical records for each patient.

The inclusion criteria were the indication of TLH for benign disease and the uterine size did not exceed the size equivalent to 20 weeks of pregnancy. The exclusion criteria was if size of the uterus was more than 20 weeks pregnancy size and if the patient had a history of more than two cesarean sections previously. The procedures were performed by the same surgeon. Demographic data of all patients and intraoperative and postoperative outcome data were reviewed. Variables studied included age, parity, menopause, associated co-morbidity, history of previous pelvic operation and indication for operation. Other variables were uterine size and total operating time, estimated blood loss, preoperative and postoperative hemoglobin level, need for blood transfusion, quantity of analgesia use, intra- and postoperative complication rates, patient’s recovery and length of hospital stay.

Major complications were considered as haematoma requiring transfusion and (or) surgical drainage, injury to the bowel, bladder or ureter and pulmonary embolus. Minor complications were considered as any infection or temperature of more than 38\degree C on two occasions six hours apart (excluding the first 24 hours after surgery), hematoma that did not require surgical intervention, deep venous thrombosis.

**Summary of TLH Techniques**

Informed consents were obtained before surgery. Patients were admitted to the hospital one day prior to operation. Blood sugar level was well-controlled (postprandial blood sugar was within 8-10 mmol/l) in diabetic patients. All patients underwent pelvic ultrasound examination and basic blood investigations.
Patients were kept NBM 6 hours preceding surgery and received bowel preparation (lactulose and enema at night before operation). Preoperative intravenous prophylactic antibiotics (ceftriaxone 1 g or ciprofloxacin if allergic to penicillin) was given within 1 hour of incision.

All surgical procedures were performed with the patients under general and spinal anesthesia with endotracheal intubation. Patients were placed in the modified semi-lithotomy position, with knees flexed in Allen stirrups. A Foley’s catheter was placed in the bladder. The patient was placed in the deep Trendelenburg position. All laparoscopic instruments used, including the Colpo-bulger and the trocars, were reusable. Carbon dioxide pneumoperitoneum was induced using a Veres needle. The intraperitoneal pressure was maintained at 15 mm Hg throughout the surgery. Five laparoscopy ports were used: 10mm supra-umbilical, 5mm right and left lower quadrant, and 5 mm suprapubic and 5 mm left to umbilicus. Manipulation of the uterus was done with the colpo-bulger vaginally and a 5-mm myoma spiral laparoscopically. The round ligament was desiccated with bipolar and cut with harmonic. The utero-ovarian ligament was desiccated and transected. The vesico uterine peritonium at the level of the vaginal fornix was incised. As the Colpo-Probe device was being pushed into the upper vagina, the cervicovaginal tissue was put under tension, resulting in the separation of the bladder from the cervix and upper vagina. Therefore, the bladder was kept safely below the area of dissection, with clear exposure of the vaginal fornices. Posterior broad ligament was incised up to uterosacral ligament and uterine vessels were skeletonized.

The uterine vessels were then thoroughly desiccated by bipolar diathermy and cut with harmonic. The colpotomy was completed circumferentially lateral to the level of the utero-sacral ligaments and the uterus was freed from its vaginal attachments. Then if the ovary was to be removed, the infundibulo pelvic ligament was desiccated and transected. The specimen was removed vaginally. Then the vault was closed with V-loc.

The length of operating time was recorded as the time from the first surgical incision to the time at which all wounds were closed and dressed. The total blood loss is calculated from the suction apparatus deducting the irrigation fluid. The blood in the suction tube is also measured to give the accurate value.

Liquids were started after peristalsis is established and the catheter was removed when oral done. The patient was assessed for discharge from hospital on the 2nd postoperative day and was seen again in the surgeon’s office one week postoperatively.

**Result**

Of the 100 women who underwent attempted TLH during the study period, the mean age± standard deviation of patients was 46.20±8.96 years, the mean parity was 2.74±1.38, nulliparous 1 (1%), 23 women were menopausal (23%). Seventeen women (17%) had one or more previous caesarean sections. Thirty four patients (34%) had associated medical problem–diabetes and seven patients with diabetes had delayed discharge from hospital to achieve postoperative stabilization of blood sugar.
The indications of TLH are shown in Table 2. The most common indications for the procedure were fibroids (39%), followed by adenomyosis (23%) and recurrent postmenopausal bleeding (13%).

Mean operating time (from first incision to final closure suture) in each studied year is shown in Figure 2; the overall mean duration was 147.80 minutes ± SD 38.54 minutes (range 75-330 minutes). The mean uterine size (in gestational week) ± standard deviation was 9.54 weeks ± SD3.94 weeks. The largest specimen was 20 weeks & the range was 6 to 20 weeks. The mean estimated blood loss was 67.00 ml ± SD 52.15 ml. The preoperative hemoglobin concentration was compared with that observed on the first day after the operation. The postoperative hemoglobin levels in all patients were above 9 g/dL. None of them required post operative blood transfusion.

A total of 100 patients who underwent attempted TLH, the procedure were successfully completed by laparoscopy in 93 patients (93%). Five patient required conversion to laparotomy due to presence of severe adhesion. Two cases needed laparotomy due to bladder injury (2 patients). There was no bowel injury, no minor complications.

Most patients (77%) had mild post operative pain, needed only single dose narcotic on the day of operation followed by NSAIDs. The mean length of hospital stay, defined as the total number of inpatient hospital days excluding the day of admission was 2.89 days ± SD1.26 days. Forty five patients (45%) were discharged on the 2nd postoperative day. In no case redo surgery or readmission to the hospital was necessary.

Discussion

Total laparoscopic hysterectomy is currently accepted as an alternative to standard abdominal hysterectomy. Several randomized trials have shown the advantages of operative laparoscopy as compared with laparotomy. This study reports the outcomes for 100 TLH procedures carried out after the introduction of the Colpo-bulger device. Our data are similar to those reported elsewhere with respect to patient demographics, uterine size, operation time, and operative morbidity. By reducing the amount of time spent as an inpatient, patients are exposed to fewer nosocomial infections, in theory decreasing the risk of iatrogenic infections. TLH also could be performed successfully in most obese patients, and operating room times are comparable to those of abdominal hysterectomies. Some authors agree that TLH is safe and feasible in the presence of enlarged uteri. There is another potential benefit of TLH using colpo-bulger is related to the preservation of pelvic tissue. Preservation of the uterosacral ligament may maintain vaginal innervations. Moreover, laparoscopic closure of vaginal vault without inversion minimizes granulation formation, and incorporation of pubocervical fascia gives excellent vault support.

Table 1. Characteristics of 100 patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>mean value ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in year)</td>
<td>46.20±8.96</td>
</tr>
<tr>
<td>Parity</td>
<td>2.74±1.38</td>
</tr>
<tr>
<td>Uterine size (in gestational week)</td>
<td>9.54±3.94</td>
</tr>
<tr>
<td>Operating room time (in min)</td>
<td>147.80±38.54</td>
</tr>
<tr>
<td>Estimated blood loss (in ml)</td>
<td>67.00±52.15</td>
</tr>
<tr>
<td>Preoperative Hb (in gm/dl)</td>
<td>11.91±1.28</td>
</tr>
<tr>
<td>Postoperative Hb (in gm/dl)</td>
<td>11.01±1.15</td>
</tr>
<tr>
<td>Need of narcotic analgesic (in mg)</td>
<td>115.70±57.06</td>
</tr>
<tr>
<td>Length of hospital stay (in days)</td>
<td>2.89±1.26</td>
</tr>
</tbody>
</table>

Fig. 1: Number of attempted TLH performed annually between 2011 and 2012
The indications of TLH are shown in Table 2. The most common indications for the procedure were fibroids (39%), followed by adenomyosis (23%) and recurrent postmenopausal bleeding (13%).

Mean operating time (from first incision to final closure suture) in each studied year is shown in Figure 2; the overall mean duration was 147.80 minutes ± SD 38.54 minutes (range 75-330 minutes). The mean uterine size (in gestational week) ± standard deviation was 9.54 weeks ± SD 3.94 weeks. The largest specimen was 20 weeks & the range was 6 to 20 weeks. The mean estimated blood loss was 67.00 ml ± SD 52.15 ml. The preoperative hemoglobin concentration was compared with that observed on the first day after the operation. The postoperative hemoglobin levels in all patients were above 9 g/dL. None of them required post operative blood transfusion.

A total of 100 patients who underwent attempted TLH, the procedure were successfully completed by laparoscopy in 93 patients (93%). Five patient required conversion to laparotomy due to presence of severe adhesion. Two cases needed laparotomy due to bladder injury (2 patients). There was no bowel injury, no minor complications. Most patients (77%) had mild post operative

<table>
<thead>
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<tr>
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<td>Recurrent postmenopausal bleeding</td>
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<tr>
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<td>Dysfunctional uterine bleeding</td>
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<td>Cervical intraepithelial neoplasia</td>
<td>5</td>
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<tr>
<td>Ovarian tumor</td>
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<tr>
<td>Pelvic inflammatory disease</td>
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</tbody>
</table>

* TLH: Total laparoscopic hysterectomy

**Table 2. Indications of TLH***

**Fig. 2: Mean operative time for procedures performed annually between 2011 & 2012**

Mean operating time (from first incision to final closure suture) in each studied year is shown in Figure 2; the overall mean duration was 147.80 minutes ± SD 38.54 minutes (range 75-330 minutes). The mean uterine size (in gestational week) ± standard deviation was 9.54 weeks ± SD 3.94 weeks. The largest specimen was 20 weeks & the range was 6 to 20 weeks. The mean estimated blood loss was 67.00 ml ± SD 52.15 ml. The preoperative hemoglobin concentration was compared with that observed on the first day after the operation. The postoperative hemoglobin levels in all patients were above 9 g/dL. None of them required post operative blood transfusion.

A total of 100 patients who underwent attempted TLH, the procedure were successfully completed by laparoscopy in 93 patients (93%). Five patient required conversion to laparotomy due to presence of severe adhesion. Two cases needed laparotomy due to bladder injury (2 patients). There was no bowel injury, no minor complications. Most patients (77%) had mild post operative
pain, needed only single dose narcotic on the day of operation followed by NSAIDs. The mean length of hospital stay, defined as the total number of inpatient hospital days excluding the day of admission was 2.89 days ± SD1.26 days. Forty five patients (45%) were discharged on the 2nd postoperative day. In no case redo surgery or readmission to the hospital was necessary.

Table 3. Operative complications

<table>
<thead>
<tr>
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<td>Hemorrhage (requiring transfusion)</td>
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<tr>
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<td>Injury to bowel or ureter</td>
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<tr>
<td>Minor complications</td>
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<tr>
<td>Hemorrhage (attended emergency room, not requiring transfusion)</td>
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</tr>
<tr>
<td>Urinary infection</td>
<td>0</td>
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<td>Vaginal vault abscess</td>
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Discussion

Total laparoscopic hysterectomy is currently accepted as an alternative to standard abdominal hysterectomy. Several randomized trials have shown the advantages of operative laparoscopy as compared with laparotomy. This study reports the outcomes for 100 TLH procedures carried out after the introduction of the Colpo-bulger device. Our data are similar to those reported elsewhere with respect to patient demographics, uterine size, operation time, and operative morbidity. By reducing the amount of time spent as an inpatient, patients are exposed to fewer nosocomial infections, in theory decreasing the risk of iatrogenic infections. TLH also could be performed successfully in most obese patients, and operating room times are comparable to those of abdominal hysterectomies. Some authors agree that TLH is safe and feasible in the presence of enlarged uteri. There is another potential benefit of TLH using colpo-bulger is related to the preservation of pelvic tissue. Preservation of the uterosacral ligament may maintain vaginal innervations. Moreover, laparoscopic closure of vaginal vault without inversion minimizes granulation formation, and incorporation of pubocervical fascia gives excellent vault support.
Patient safety during LH has always been a major concern. Liu and Reich in 1994 assessed 518 patients undergoing LH and found that the risk of LH was no greater than either AH or VH in appropriately trained hands. The complication rate in our series compares favorably with rates reported in the literature. We had no instances of major hemorrhage, ureteric injury or bowel injury. Major complications were bladder injury (2%), rate of which were similar to those reported in other studies. A study in France, in which 29 of 416 (7%) of TLH cases were converted to laparotomy, determined that increased body mass index, uterine width more than 10 cm and adhesions from previous abdominal and pelvic surgery were predictive factors for laparotomy.

Although our data do not show an association between a history of pelvic surgery, caesarean section or increased body weight and a higher risk of conversion to laparotomy, significant conclusions cannot be made because of the retrospective nature of our study and the relatively small number of subjects. As with many other surgical procedures, proper selection of patients plays an important role in determining the success of the surgery. For TLH, the selection process depends predominantly on the experience and expertise of the surgeon; with experience, more patients can be offered TLH with confidence. Currently, in our practice about 70% to 80% of hysterectomies can be done laparoscopically. Prolonged operating and anesthesia times have always been considered to be an important drawback of LH. Although most studies have reported that LH takes longer to perform, it has been associated with shorter hospital stay and shorter recovery time than AH. LH offers reduced risk of intra-abdominal adhesions, an extremely low rate of infection and ileus. Patients who undergo LH also experience significantly less pain and require less analgesia than patients require after AH. The operating time in our series was similar to times reported in the literature. Our results are similar to those reported to date, showing that TLH can be performed safely with shorter hospitalization. LH performed on an outpatient basis has been reported to be safe, well tolerated and cost effective, and is therefore advocated by some authors.

It is well established that performing TLH involves a learning curve that, with improved skills and technique, will result in a safer procedure with improved outcomes. In a series of 1647 cases of TLH, the incidence of major complications and laparotomy conversion decreased significantly between two study periods (1989-1995 and 1996-1999). This study clearly indicate that complication rates decrease significantly as surgeons gain experience. Therefore, it is important for the surgeon to learn from his or her own experience and complications and to refine his or her own technique to lower morbidity. In our present study, we managed to shorten the operating time progressively and became capable of removing bigger uteri and performing more complicated cases. However, operating time is not always a reliable indicator of the surgeon’s technical capability; it is also influenced by the complexity of the case, the familiarity of assistants and nurses with the procedure, and the availability of equipment. Continuing review of performance and outcome data will facilitate the
learning process and help the surgeon to improve the safety of TLH.

**Conclusion**

TLH can be performed successfully in most patients with benign indications. Morbidity is comparable to that of other types of hysterectomies, and this technique may be a more reasonable approach under some circumstances. With adequate training in laparoscopic surgery, TLH can be performed in all cases with minimal blood loss and decreased operative time, irrespective of the size of the uterus. Study results in the literature continue to be encouraging and this procedure should be part of gynecologist's training, offering patients alternatives that are associated with low morbidity and rapid recovery.

**References**

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References

19. Beckmann MW. The Hohl instrument for optimizing performance and outcome data will facilitate the surgeon to learn from his or her own experience significantly less pain and require less analgesia than patients require after abdominal hysterectomy, the other comparing AH with LH, the other comparing AH with VH, both were similar. J Minim Invasive Gynecol. 2005;12:312–7.
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Cigarette Smoking, a Risk Factor for Chronic Subclinical Inflammation and a Predictor of Metabolic Syndrome in Adult Healthy Population of Bangladesh

Rehnuma B1, Eva SN2, Ibrahim M3, Nasir TA4, Ali L5

Abstract

Background and Aims: Smoking is a classical and major risk factor for cardiovascular disease. Inflammatory activators and metabolic disorders are the mediators of smoking-induced atherosclerotic progression. The aim of the present study was to investigate whether smoking alter inflammatory or metabolic status and affect subclinical atherosclerosis in apparently healthy persons. Methods: A total number of 149 adults, age 30-60 yrs, were recruited in the study. Participants were divided into sub-groups of smokers (76) and non-smokers (73). All participants were interviewed and underwent physical examinations and blood collection. High-sensitivity C reactive protein (Hs-CRP) was measured to assess degree of underlying inflammation. Fasting plasma glucose and lipid profile were measured to assess metabolic condition. Data were analyzed using statistical Package for Social Program (SPSS) for Windows version 17. Results: Hs-CRP (p=0.017), Fasting glucose (p=0.003), Triglyceride (p=0.005) was significantly high in smokers in comparison with nonsmokers. BMI (p=0.012) and BFM (%) (p= <0.001) showed significantly lower in comparison with the counterpart. HDL-c (p=.030) was also significantly lower in smoker group than non-smoker group. In Spearman’s correlation analyses Triglyceride (p=0.037) and smoking (p= 0.042) showed positive correlation with Hs-CRP. HDL-c is less in smoker subjects but not statistically up to the significant level. Conclusion: The rising Hs-CRP concentration reflects presence of chronic subclinical inflammation in middle aged Bangladeshi smokers and thus may have a risk for future cardiovascular disease.

Key words

High sensitive C-reactive protein (Hs-CRP), smoking, subclinical inflammation

Introduction

The link between smoking and increased morbidity and mortality have been long established, and current trends indicate that there are one billion smokers worldwide and 500 million will die prematurely from smoking-related diseases.1 Smoking has been shown to have harmful effects on numerous organs of the body and the list of diseases where smoking has been recognized as contributory factor is extensive.2 It has long been accepted that cigarette smoking is a classical and major risk factor in the development of cardiovascular disease (CVD) and atherosclerosis.3,4 More recently, it has been recognized that CVD contains a component of inflammation and has even been referred to as an inflammatory disease.5,6 In addition, a link has been
Cigarette smoking, a risk factor for chronic subclinical inflammation and a predictor of metabolic syndrome in adult healthy population of Bangladesh

established between several other chronic inflammatory diseases and smoking, including chronic obstructive pulmonary disease (COPD), rheumatoid arthritis, systemic lupus erythematosus and Crohn’s disease. Although the mechanisms linking smoking to these diseases are not well understood, interest in finding relationship between inflammatory markers and smoking has been gathering pace to provide explanations for smoking-mediated morbidity and mortality. One such inflammatory marker, is C-reactive protein (CRP), which may be easily and sensitively measured in a variety of clinical situations to monitor disease progression.

C-reactive protein (CRP) is an inflammatory marker whose expression is markedly up regulated during inflammation. It is the acute phase protein synthesized in the liver and regulated to a large extent by pro inflammatory cytokine interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α). Furthermore, new, highly sensitive assays for CRP (Hs-CRP assays) measure levels within the "normal" range i.e., low grade inflammation or subclinical inflammation thus enabling careful evaluation of underlying systemic inflammation in apparently healthy people as well as those with established cardiac and metabolic diseases. Moreover, Hs-CRP assay is the inflammatory marker with improved precision, standardization and other characteristics. Recent prospective studies have demonstrated that subjects with low grade inflammation have a higher risk of cardiovascular diseases. Evidence suggests that elevation of CRP reflect not only local inflammation at atherosclerotic lesions but also systemic abnormalities related to insulin resistance, such as increase in fasting insulin, body mass index (BMI), systolic blood pressure and triglyceride (TG) as well as decrease in high density lipoprotein cholesterol (HDL-c). Unhealthy lifestyle might increase the risk of CVDs. These habits include physical inactivity, calorie dense diets, alcohol drinking, smoking and psychosocial stress. Previous studies have demonstrated the adverse effect of smoking on CVDs, e.g., tobacco use increases triglycerides (TG) and decreases HDL-c levels. It has also been shown that total cholesterol (TC), low density lipoprotein cholesterol (LDL-c), and Total Cholesterol/HDL-c ratio are strongly related to smoking. There are significant improvements in LDL-c, HDL-c and the HDL-c to LDL-c ratio 8 weeks after cutting down on smoking.

Globally, tobacco use accounts for about 10% of all CVD related mortality, with the highest occurrences being in low to mid-income countries. Yet awareness about the cardiovascular implications of cigarette smoking is still unacceptably low considering that smoking is a completely preventable cause of CVD. Previous studies have demonstrated the adverse effect of smoking on serum lipid profile. We set out to examine lifestyle factors such as smoking, and levels of CRP, focusing on the use of CRP measurement to predict long-term outcome in smokers.

Subjects and Methods
An invitation was made to the volunteers of the study through personal contact to report in the department of Biochemistry and Physiology, BIRDEM in fasting condition. Subjects reported were examined for their wellbeing. Purpose and nature of the study were
explained to them. Consented respondents were given appointment for blood sampling. Detailed medical and personal history was recorded on the day of blood sampling in a pre-designed case record form.

**Anthropometric measurements and blood pressure recording**

Volunteer’s height (in meter) and weight (kg), waist and hip (cm) circumference were taken following standard procedure. Cut-off values for BMI (normal 22.9 Kg/m2; over weight 23-27.5 and obese 27.5) and WHR (male-0.90 and female-0.80) were used as per WHO, 2004 guidelines for Asian population. Blood pressure (average of two independent measurements) was recorded using barometric Sphygmomanometer.

Five milliliter of venous blood was drawn from each subject by vein puncture at fasting and drawn blood was allowed to clot. After 20 minutes samples were centrifuged at 3000 rpm for 10 minutes. Separated serum was aliquoted in micro centrifuge tubes, labeled and preserved at (-30°C) for biochemical analyses.

**Biochemical methods**

Glucose was measured by (glucose-oxidase) and Total Cholesterol, Triglyceride and HDL-c were measured (by enzymatic colorimetric) method using in the Biochemistry Auto-analyzer ‘Hitachi 704’ reagents of RANDOX Laboratories Ltd., UK. LDL- c was calculated using Fried wald formula. The method was not applied when triglyceride level exceeded 400 mg/dL. Serum Hs-CRP was estimated by enzyme linked immunosorbant assay (ELISA) method.

**Statistical methods**

Data were expressed as mean ± SD and number (percent). Statistical analyses were performed using Statistical Package for Social Science (SPSS) for Windows Version 17. Two tailed P value <0.05 was taken as significant level.

**Recruitment criteria**

A total number of 149 volunteers aged 30-60 yrs were finally recruited in this study. Subjects suffered from acute illness in the last three months, subjects with secondary obesity, pregnancy, known primary hyperlipidemias, hereditary or systemic inflammatory diseases, on any regular medications or significant physical training program were excluded.

**Ethical Consideration**

The Helsinki Declaration on medical ethics was respected in the surveys. The protocol was approved by the Ethical Committee of Diabetic Association of Bangladesh.

**Results**

Of the total subjects 73 (48.9%) were nonsmoker and 76 (51%) were smokers. Table I showed Hs-CRP was significantly high (2.89±2.2) in smokers in comparison with nonsmokers (2.3±1.8; p=0.017). Fasting glucose (p=0.003) and Triglyceride (p=0.005) was also significantly high in smokers (5.25±0.45, 187.8±90.04) compared with nonsmokers (5.02±0.46, 134.0±69.0). BMI (p=0.012) and BFM (%) (p= <0.001) and showed significantly lower (22.4±2.9 and 20.9±4.2 respectively) in comparison with the counterpart (24.1±3.3 and 26.8±6.9 respectively). HDL-c (p=.030) also showed significantly lower levels in smoker group (34.8±7.0) than nonsmoker group (39.9±8.5).
Table I: Clinical and biochemical variables between smokers and non-smokers
study subjects, n =92

Table:<br>
<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-Smoker (63)</th>
<th>Smoker (29)</th>
<th>t/p values</th>
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<tr>
<td>Age</td>
<td>39.72±7.5</td>
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<td>BMI (kg/m²)</td>
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<td>SBP (mmHg)</td>
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<td>DBP (mmHg)</td>
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<td>Fasting glucose (mmol/l)</td>
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<td>Triglyceride (mg/dl)</td>
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<td>Total cholesterol (mg/dl)</td>
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<tr>
<td>HDL-c (mg/dl)</td>
<td>39.9±8.5</td>
<td>34.8±7.0</td>
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<td>LDL-c (mg/dl)</td>
<td>117.8±31.8</td>
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<tr>
<td>hsCRP (mg/L)</td>
<td>2.3±1.8</td>
<td>2.89±2.2</td>
<td>0.017</td>
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</table>

Results were expressed as mean±SD. Unpaired Student's t test was performed to compare between groups.

Note: BMI (Body mass index), hsCRP (High sensitive C-reactive protein), WHR (waist hip ratio), SBP (systolic blood pressure), DBP (diastolic blood pressure), HDL-c (High density lipoprotein cholesterol), LDL-c (Low density lipoprotein cholesterol).

Correlation analyses
Bivariate correlation analyses
Spearman’s correlation analyses were performed for variable Age, BMI, WHR, fasting glucose, TG, Total Cholesterol, HDL-c and LDL-c and smoking habit.

Age (r = -0.028 p = 0.733), BMI (r = 0.026 p = 0.757), WHR (r = 0.132 p = 0.110) did not show any significant correlation with Hs-CRP. Triglyceride (r = 0.171, p = 0.037) and smoking (r = 0.168, p = 0.042) showed positive correlation with Hs-CRP and Fasting glucose (r = 0.030 p = 0.716), Total cholesterol (r = 0.016 p=0.842), and LDL-c (r = 0.150 p = 0.067) did not show any significant correlation with Hs-CRP. HDL-c (r = -0.157 p = 0.056) showed negative correlation but did not reach up to the significant level (Table II).
Table II: Spearman’s correlation analysis for Hs-CRP with independent variables (n=149)

<table>
<thead>
<tr>
<th>Variables</th>
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<td>BMI</td>
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<td>LDL-c</td>
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<td>Smoking</td>
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Discussion

Low grade inflammation may be part of the 'common soil' underlying the metabolic syndrome, Type 2 Diabetes Mellitus and cardiovascular diseases. CRP is a nonspecific marker widely used to monitor treatment of cardiovascular diseases (high serum CRP levels indicate poor outcome of heart disease). A healthy lifestyle decreases serum CRP levels, while obesity, physical inactivity, and smoking increase them.20,21,22

Our findings support the hypothesis that lifestyle factors such as smoking adversely affect inflammatory and metabolic processes. Our results showed an association between smoking and elevated Fasting Serum Glucose, Triglyceride, Hs-CRP as well as low HDL-c. The Hs-CRP concentration found to be elevated by smoking17,25 which can be explained by three possible mechanisms: (i) smokers have chronic airway inflammation because cigarettes contain potent airway irritants. 26 Indeed, smokers have a higher prevalence of chronic bronchitis, bronchial asthma and pulmonary emphysema than nonsmokers.27 (ii) Smokers are likely to have a tendency to have dyslipidemia, coronary vasomotor reactivity, platelet aggregation, and a prothrombotic state.28,29 Accumulation of these risk factors promotes the initiation and progression of atherosclerosis. This hypothesis is supported by reports that smokers have elevated concentrations of soluble intercellular adhesion molecule type 1, E-selectin, interleukin-5, and P-selectin30; and (iii) smoking deteriorates insulin resistance, resulting in an increase in Hs-CRP.31 Insulin resistance in smokers could be caused by an increase in counter regulatory hormones,
Cigarette smoking, a risk factor for chronic subclinical inflammation and a predictor of metabolic syndrome in adult healthy population of Bangladesh

such as, Growth hormone, Cortisol, Glucagon and Catecholamines, all of which raise blood glucose level.\textsuperscript{32} A case control study based on this showed that smokers had higher levels of Hs-CRP, FPG and TG but lower levels of HDL-c than nonsmokers.\textsuperscript{17} Smoking had a dyslipidaemic effect and can increase Total Cholesterol, LDL-c and Triglyceride; furthermore, it can decrease serum HDL-c level.\textsuperscript{17} In agreement with Oh et al,\textsuperscript{33} we find that chronic smoking is associated with higher Triglycerides and lower HDL-c.

In our study, BMI, body fat and WHR in smokers were lower than in non-smokers. Some other studies have demonstrated lower BMI in current smokers. Numerous cross-sectional studies indicate that body weight, or body mass index (BMI; in kg/m\textsuperscript{2}), is lower in cigarette smokers than in nonsmokers.\textsuperscript{34-37} In the World Health Organization Monitoring Cardiac Disease (WHO MONICA) surveys, BMI was lower in smokers than in smokers, and there was no population in which smokers had a higher BMI than did nonsmokers.\textsuperscript{38} In the second National Health and Nutrition Examination Survey (NHANES II) study (1976–1980), smokers weighed less than nonsmokers, and body leanness increased with the duration (but not with the intensity) of smoking.\textsuperscript{39} The effect of smoking on body weight could lead to weight loss by increasing the metabolic rate, decreasing metabolic efficiency, or decreasing caloric absorption (reduction in appetite), all of which are associated with tobacco use. The metabolic effect of smoking could explain the lower body weight found in smokers. Smoking a single cigarette has been shown to induce a 3% rise in Energy Expenditure within 30 min.\textsuperscript{40} And could reduce appetite, which likely explains why smokers tend to have lower body weight than do nonsmokers.

**Conclusion**

Elevated Hs-CRP has been closely linked with the development of atherosclerosis and is associated with the development of and mortality from CVD. Though not proven here, our study suggests that aggravation of systemic inflammation by cigarette smoking may account for the increased risk of CVD in smokers. Finally, we can conclude that subclinical atherosclerosis is independently accelerated via continuous smoking and that the smoking-induced promotion of atherosclerotic change is closely associated with inflammatory reactions.

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Cigarette smoking, a risk factor for chronic subclinical inflammation and a predictor of metabolic syndrome in adult healthy population of Bangladesh


Decompressive Hemicraniectomy in Hypertensive Basal Ganglia Hemorrhages

Joarder MA¹, Karim AKMB², Sujon SI³, Akhter N⁴, Waheeduzzaman M⁵, Shankar DR⁶, Jahangir SM⁷, Chandy MJ⁸

Abstract
Objectives: The aim of this study was to analyze efficacy and safety of decompressive hemicraniectomy (DHC) in hypertensive basal ganglia hemorrhage (HBGH). Neurosurgical management of HBGH is still a controversial issue. Surgical techniques are diverse, from the open large craniotomy, to the minimally invasive techniques like stereotactic aspiration of the HBGH, endoscopic evacuation and stereotactic catheter drainage after instillation of thrombolytic agents. Decompressive hemicraniectomy lowers intracranial pressure and improves outcome in patients with HBGH. Methods: 8 patients with HBGH who underwent decompressive craniectomy in the last 2 years were analyzed. Parameters investigated included clinical presentations, radiologic profile, time interval from ictus to surgery, and modified Rankin Scale score at 6 months. Results: The patients mean age 55 years, the mean Glasgow Coma Scale (GCS) score was 7 (range 5–13), the mean ICH volume was 58 ml (range 40–70 ml), and the mean midline shift was 10.62 mm (range 6-16 mm). The outcome after 6 months was appreciated as good (modified Rankin Scale 0–4) or poor (modified Rankin Scale 5-6). Five patients had good and three had poor outcomes (including two deaths). Conclusion: We conclude, based on this small cohort, that DC can reduce mortality in some cases. Larger prospective studies are needed to assess safety and efficacy of this method.

Introduction
The neurosurgical management of hypertensive basal ganglionic hemorrhage (HBGH) is still a controversial issue. The aim of this study was to analyze efficacy and safety of decompressive craniectomy (DHC) in deep HBGH. Hypertensive basal ganglionic hemorrhage (HBGH) is defined as a bleeding into the brain parenchyma which occurs in the absence of trauma or surgery. Surgical techniques are diverse, from the open craniotomy, to the minimally invasive techniques like stereotactic aspiration of the HBGH and endoscopic evacuation. Decompressive hemicraniectomy lowers intracranial pressure and improves outcome in patients with intracerebral hemorrhage. The idea of applying it in spontaneous intracerebral hematoma comes from results obtained by applying this method in massive ischemic stroke, in sinus thrombosis or in traumatic pathology. The toxic effects of hematoma degradation and the complications of mass effect are the main reasons for surgery.¹,²

Material and method
We identified 8 patients with hypertensive basal ganglionic hemorrhage (HBGH) who had

Decompressive Hemicraniectomy in Hypertensive Basal Ganglia Hemorrhages

undergone DHC between February 2012 and February 2014. Review of medical records and CT images provided preoperative and intraoperative clinical data and postoperative outcome data. To determine the hematoma volume and maximal midline shift, we reviewed radiologists’ reports, when the midline shift was not specified in a report, it was measured at the foramen of Monroe by using digital measuring tools available on our viewing software.

**Surgical Procedure**

DHCs were generally trauma-type flap intended to maximize decompression of the cerebral hemisphere. The opening of the dura was performed in a stellate fashion, and the exposed brain was covered by augmentive duraplasty with galea aponeurotica.
Results
During the study period, 8 patients were treated with DHC without clot evacuation for hypertensive basal ganglionic hemorrhage (HBGH). Mean age was 58 years, and 6 patients were male and 2 patients were female. The hemorrhage lateralized to the left in 6 patients and to the right in 2 patients. On admission mean GCS score was 7 (range 5-13), mean hematoma volume was 58 ml (range 40-70 ml), mean midline shift was 10.62 mm (range 6-16mm).

Table I: Outcome table

<table>
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<tr>
<th>mRS</th>
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<td>0-4</td>
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<tr>
<td>5-6</td>
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<tr>
<td>Total</td>
<td>8</td>
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Table II: Summary of literature on hematoma evacuation and DHC in SICH.

<table>
<thead>
<tr>
<th>Authors &amp; year</th>
<th>No. of cases</th>
<th>Dominant side</th>
<th>&gt;60ml</th>
<th>Mortality</th>
<th>Term</th>
<th>Good outcome</th>
<th>Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decompressive craniectomy with clot evacuation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dierssen et al., 1983</td>
<td>73</td>
<td>53%</td>
<td>unknown</td>
<td>33%</td>
<td>2 yrs</td>
<td>45%</td>
<td>2yrs</td>
</tr>
<tr>
<td>Ma et al., 2010</td>
<td>38</td>
<td>unknown</td>
<td>unknown</td>
<td>32%</td>
<td>1 month</td>
<td>55%</td>
<td>6 months</td>
</tr>
<tr>
<td>Maira et al., 2002</td>
<td>15</td>
<td>unknown</td>
<td>unknown</td>
<td>20%</td>
<td>1 yr</td>
<td>73%</td>
<td>1 yr</td>
</tr>
<tr>
<td>Murthy et al., 2005</td>
<td>12</td>
<td>8%</td>
<td>67%</td>
<td>8%</td>
<td>discharge</td>
<td>50%</td>
<td>17 months</td>
</tr>
<tr>
<td>Total</td>
<td>138</td>
<td></td>
<td>29%</td>
<td></td>
<td>51%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DHC without clot evacuation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ramnarayan et al., 2009</td>
<td>23</td>
<td>43%</td>
<td>30%</td>
<td>13%</td>
<td>3 months</td>
<td>56%</td>
<td>3 months</td>
</tr>
<tr>
<td>Fung et al., 2012</td>
<td>12</td>
<td>58%</td>
<td>50%</td>
<td>25%</td>
<td>6 months</td>
<td>50%</td>
<td>6 months</td>
</tr>
<tr>
<td>present series</td>
<td>08</td>
<td>75%</td>
<td>50%</td>
<td>25%</td>
<td>6 months</td>
<td>62%</td>
<td>6 months</td>
</tr>
<tr>
<td>Total</td>
<td>43</td>
<td></td>
<td>19%</td>
<td></td>
<td>56%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Outcome
Outcome was assessed by the modified Rankin Scale score, when patients returned to our outpatient clinic after 6 months. Good outcome was defined as modified Rankin Scale of 0-4 and bad outcome as modified Rankin Scale of 5-6. Five patients (62%) had good and three patients (38%) had poor outcome.

Discussion
Intracerebral hemorrhage incites ICP elevation by several distinct mechanisms. Initially, the hematoma volume itself, which can expand for up to 24 hours after the ictus, impacts the intracranial volume buffer capacity. Subsequently, osmotically active proteins in the hematoma cause edema formation in the surrounding tissue, with approximately 75% of patients experiencing an increase in perihematomal edema within the first 24 hours. Rather counter intuitively, surgical clot evacuation may in some cases also contribute to ICP elevation, as it bears the potential to induce edema formation through tissue manipulation and/or venous interruption. Although the topic of clot evacuation in ICH has gained increased attention in recent years following a relatively silent period after the 1961 landmark paper by McKissock et al., the role of decompressive craniectomy in large ICHs has only scarcely been explored. The majority of the reports on decompressive craniectomy following ICH involve a combination of decompression with concurrent clot evacuation. The mortality rates for patients undergoing such intervention in these studies were considerably better than the natural history, as the mortality of the latter approaches 86%. Moreover, the results for concurrent DHC and clot evacuation were favorable compared with results for patients managed with craniotomy and clot evacuation, suggesting a therapeutic effect of decompression.

Clinical outcomes for decompressive hemicraniectomy with clot evacuation have been reported for a total of 138 patients in the literature, rendering an overall 29% mortality rate and 51% favorable outcome rate, with follow-up duration ranging from discharge to 2 years (Table II). In light of the negative conclusions of the STICH trial and studies implicating an exacerbation of tissue damage from clot evacuation, decompression alone, without attempts at concurrent hematoma removal, may prove a better option than others for the management of medically refractory large ICH. Ramnarayan were the first to explore the impact of DHC without clot evacuation and reported on a series of 23 patients with putamen ICH. At 3-month follow-up, 56% had a favorable outcome and only 13% had died. Fung likewise reported results of DHC without clot evacuation in ICH. Of their 12 patients, of whom half had an ICH volume greater than 60 cm³, 25% died and 50% gained functional independence at 6 months. A summary of the literature on DHC without clot evacuation in ICH, including the results of the present study, yields 43 cases, with an 19% mortality rate and 56% good outcome rate after a follow-up ranging from 3 to 6 months (Table II).

This finding suggests that the harm caused by the surgery outweighs the benefit of the clot removal and that decompression with preservation of brain integrity may prove a
better therapeutic technique in ICH. Advantages of DHC include no trauma to brain, ease and speed of the procedure and no issues of brain parenchymal hemostasis. The presented data, combined with data from the literature, suggest that DHC is feasible in patients with large HBGH. Nonetheless many additional factors are involved in driving outcome following ICH, and therefore large, multicenter, randomized trials are needed to accurately assess the role of DHC in optimal ICH management.

Conclusions
Our data indicate that DHC with preservation of brain integrity in patients with spontaneous dominant ICH and medically refractory ICP elevation is feasible. Large randomized controlled trials are needed to further investigate the therapeutic value of DHC in ICH.

References
Role of Kisspeptin in Female Infertility
Bhuuiyan MRI, Khaliduzzaman SM, Priti KN

Abstract
Background: Kiss1, a noble G protein coupled receptor designated as GPR54, was first identified in rat brain in 1999 and orthologue gene identified in human in 2001. The original niche for the function of kisspeptin was restricted to cancer biology for their ability to suppress tumor metastasis. However, kisspeptin has recently emerged as a key player in the field of reproductive endocrinology. Method: A systematic literature review was done by using PUBMED. Though there is lack of human data, used animal data also hold translational potential for human. Results: Inactivating mutation of GPR54 gene is linked with absence of puberty onset and idiopathic hypogonadotrophic hypogonadism. Furthermore, recent studies support critical role of kisspeptin/GPR54 system on regulation of GnRH neurons, involvement of puberty onset and gonadal steroid feedback. Conclusion: This review will briefly discuss on cellular and molecular level of kisspeptin, their potential effects on human and clinical application of kisspeptin on human reproductive disorder.

Introduction
Procreation is an indispensable part of every species. To initiate and control reproduction, coordination of neuronal networks play complex role and finally make a common pathway, which is well known as Hypothalamic Pituitary Gonadal (HPG) axis that synthesize gonadotrophic releasing hormone. Since its discovery, adequate pulsatile hypothalamic gonadotrophic releasing hormone (GnRH) secretion has been considered as key element for maintaining reproductive function.1-4 During puberty, hypothalamus start synthesis and release of GnRH, which acts on anterior pituitary to secrete FSH and LH, as a result gonads begin to produce sex steroid and peptide hormone.5-7 Only a decade ago in 2003, discovery of kisspeptin and its role on regulation of the HPG axis, revolutionized our current understanding on control of human reproduction.8 It is believed that, kisspeptin and functional neural network KNDY (kisspeptin / neurokinin / dynorphin) system modulate GnRH pulse. Therefore, Kisspeptin is considered as a key regulator of gonadotropin secretion and responsible for many physiological phenomenons. Moreover, manipulation of KNDY neural network and regulation of LH pulse, subsequently control of gonadal hormonal secretion may open a new horizon in treatment of infertility. Recently reproductive scientists are working for future application of KNDY system by increasing LH pulse, like wise hypothalamic amenorrhea, hypogonadotrophic hypogonadism or reduce LH secretion, such as in polycystic ovary syndrome.9

In this review, briefly discussed on cellular and molecular level biology of kisspeptin and its potential effect on human, more precisely on female reproduction, and how future clinical application of kisspeptin may resolve neural reproductive disorder. A systematic literature review was done by using PUBMED. Though there is lack of human data, used animal data also hold translational potential for human.

**Discovery of Kiss1 Gene and Receptor**
Kiss1, a noble G protein coupled receptor designated as *GPR54*, was first identified in rat brain in 1999. This newly identified molecule catalogued as a suppressor of metastasis in melanoma cell line, therefore it is widely known as metastin. Hershey, (PA, USA) which was famous for Hershey kisses chocolate and birthplace of kiss I gene, also named as kiss after this exclusive sweets. However, 2 years later, in 2001, orthologue gene *AXOR12* and *hOT7T175* identified in human and termed as KISSIR. Three independent research groups explore endogenous ligand of GPCR named as *GPR54*, *AXOR12*, *hOT7T175* by using different model, CHO K1, HEK 293 and B16-B26 consecutively. Therefore, international pharmacology association displaced metastin to kisspeptin considering structural similarities and origin of kiss1 derivative peptides.

**Biology of Kisspeptin**
Kisspeptin, a noble neuromodulator, which is peptide in nature and encoded by the kiss 1 gene that activate G protein coupled receptor and upstream GnRH secretion. Kisspeptins are generated from a single precursor through various proteolytic processing. In human, kisspeptin precursor encodes 145 amino acid including a 54 amino acid region, named as kisspeptin 54 (formerly termed as metastin). This segment can be further divided into low molecular weight forms which are termed as KP 54, KP13, KP 10 for 14, and 13 and 10 amino acid peptide respectively. In addition, all peptide fragment share c terminal sequence of kisspeptin 54, which is the characteristics feature of RF amide group of peptide, collectively known as kisspeptin. Kiss 1R, upon binding its ligand activates phospholipase C and convert secondary intracellular messengers, inositol 1,4, 5 triphosphate (IP3) and diacyl glycerol, that induce calcium release and finally activation of protein kinase C to proceed kisspeptins function.

**Distribution of Kisspeptin**
In 2001, different independent study group isolated kiss1 mRNA from placenta, spinal cord, pancreas, and pituitary gland by using reverse transcriptase polymerase chain reaction. In addition, northern blotting test has revealed kiss1 and *GPR54* genes in peripheral area, such as heart, liver, kidney, placenta and Immune Reactivity (IR) found in different areas of the brain. Thus in 2005, specific population of kiss1 neuron has been recognized in hypothalamus. Infundibulum as source of kiss1 neuron has been isolated from autopsy samples of premenopausal and post-menopausal women. Furthermore another study done in 2010 including both male and female autopsy sample support the location of most dense Kisspeptin neuron area as infundibulum and...
second most dense as pre-optic area.\textsuperscript{21} As highlighted above, Kisspeptin neuron has been detected in the Infundibular / Arcuate Nucleus in all species. However, availability of Kisspeptin neuron in rostral pre-optic area varies from species to species.\textsuperscript{21-25} For example, in rat model Kisspeptin is located in rostral periventricular region of the third ventricle of its brain whereas, it is absent in human brain.\textsuperscript{26-27} Only infundibulum in human, homologous to arcuate in rodent express all three KNDY neuron.\textsuperscript{36}

**Physiological Action of KNDY Neuron**

GnRH pulse is mainly mediated by gonadal steroid, (steroid sensitive receptor).\textsuperscript{30} In a study by Goodman et al revealed that Kisspeptin / Neurokinin / Dynorphin are in same functional neuronal network, collectively known as KNDY network which is steroid sensitive and play as a crucial regulator for GnRH pulse.\textsuperscript{29} In a schematic overview published by Skoroupskate et al 2014 to correlate KNDY-GnRH pathway and sex steroid feedback system\textsuperscript{9} which is adapted in this article. (Fig:1) It was not until 2003, that \textit{GPR54} mutation in men was identified to be associated factor for hypogonadotrophic hypogonadism and subsequently absent/delayed puberty, made a revolutionary understanding in role of Kisspeptin and KNDY neuron GnRH pulse. Furthermore, subsequent research has revealed that KNDY subpopulation in various species range from rodent to human play a key role in GnRH secretion by controlling neuro activity of KNDY cells.\textsuperscript{30-32} These reciprocally inter connected KNDY cells are very sensitive to steroid and act by direct contact with GnRH cell bodies and neuro secretory terminal (in human)

on to the median eminence (in rodent, sheep & monkey).\textsuperscript{22,23,25,33} In 2009, Navarro et al discovered that LH secretion was inhibited by dynorphin and neurokinin B, which act auto synaptically on pulsatile release of Kisspeptin and drive pulsatile release of GnRH and LH.\textsuperscript{34}

**Role of steroid on Kisspeptin**

Studies with human and various animal models suggest that pulsatile GnRH secretion followed by LH secretions is controlled by steroid feedback.\textsuperscript{35} However, GnRH neuron located in hypothalamus are devoid of estrogen receptor that suggests another group of neuron is essential to convey message of ovulation induction to GnRH neuron.\textsuperscript{9} After discovery of physiological role of KNDY it is suggested as <missing link> of gonadal steroid feedback.

Various animal data collection suggests that estrogen derived negative feedback has been mediated by Kisspeptin neuron and neurokinin B of arcuate nucleus. In ovariectomised animal model (rodents, sheep, monkey etc.)\textsuperscript{32} express high level of kiss1 mRNA in arcuate nucleus, which supports high level of kiss1 mRNA and neurokinin B in infundibulum of post menopausal women than in premenopausal women.\textsuperscript{20}

In the late follicular phase estrogen feedback switches to positive, ultimately induce LH surge for ovulation. Though arcuate Kisspeptin (widely known as KNDY) mediates negative feedback, the positive steroid feedback mediated Kisspeptins are species specific (figure). Apart from Kisspeptin, other KNDY neuron originating from arcuate nucleus do not participate in positive feedback.\textsuperscript{31,34}
Kisspeptin neurons send impulse directly to the GnRH neurons of kisspeptin receptor (Fig. 1). Kisspeptin neurons located in the anteroventral periventricular nucleus (AVPV) and the arcuate nucleus in rodents, and within the preoptic area (POA) and the infundibular nucleus in humans. KNDY neuron regulates kisspeptin pulse through their reciprocal connection via neurokinin B receptor and kappa opioid peptide receptor where neurokinin B acts as stimulatory and dynorphin inhibitory. Negative (red) and positive (green) sex steroid feedback is mediated via distinct kisspeptin populations in rodents, via the AVPV and the arcuate nucleus, respectively. In humans KNDY neurons in the infundibular nucleus relay both negative (red) and positive (green) feedback. The role of the POA kisspeptin population in mediating sex steroid feedback in humans is incompletely explored.

(ME, median eminence; +, stimulatory; −, inhibitory; ERα, estrogen receptor alpha; PR, progesterone receptor; Kiss1/KISS1, kisspeptin; NKB, neurokinin B; dynorphin)

**Slight modified and adapted from: The kisspeptin-GnRH pathway in human reproductive health and disease.
Clinical Aspects of Kisspeptin in Reproductive Health

Since discovery of inactivating point mutation in gene GPR54 is associated with impaired puberty and idiopathic hypo gonadotropic hypogonadism in 2003 \(^8,37\) it is believed that dysfunction in Kisspeptin neuronal network may be associated with many other clinical disorders. In addition, Teles et al identified activating mutation \((\text{Arg} \ 386 \ \text{Pro})\) in 2008, which is associated with precocious puberty.\(^{38,42}\) Furthermore missense mutation of Kisspeptin has been identified as precocious puberty in three individual cases, which suggests that mutation gene resist in vitro degradation followed by high bio-availability, ultimately causing precocious puberty.\(^{39}\)

One neuro endocrine disorder is hypothalamic amenorrhea, which is characterized by low GnRH pulse and subsequently declined LH, FSH and failure in follicular development. In this disease, sustained gonadotrophic secretion at normal physiological level was achieved with Kisspeptin inject in subcutaneous twice daily \((6.4 \ \text{mmol/kg})\) for 8 weeks.\(^{40}\) Though folliculogenesis was not restored in initial studies, the ability of Kisspeptin to increase GnRH secretion and subsequent effect on FSH and LH to restore menstrual cycle will play a major role in the therapeutic approach of Kisspeptin.\(^{42}\)

Another common disorder in women is PCOS, which is characterized by high level of LH due to neuro endocrine feedback defect and relative high insulin lead to metabolic defect.\(^{43}\) KNDY neurons are believed to be potential regulator of steroid mediated negative feedback. In 2003, Meneilly et al also suggested that GnRH secretion mainly depends on LH level, therefore, reduction of GnRH pulses may restore normal LH secretion. Therefore therapeutic manipulation can be achieved by using Kisspeptin and neurokinin B receptor antagonist or dynorphin agonist through stimulating/inhibitory action of dynorphin. Moreover, ovarian hyper stimulation syndrome (OHSS) in PCO cases can be significantly reduced by kisspeptin.\(^9\)

Kisspeptin may be a good therapeutic option in certain gynecological disorder, for example: endometriosis, uterine fibroid, where partial suppression of gonadotropin secretion is more useful than marked suppression, and significantly reduce side effect of complete suppression.\(^{44}\) Data obtained from animal model revealed that kisspeptin antagonist /agonist reduce LH pulse without affecting basal LH secretion (Fig. 2). In contrast, repeated administration of GnRH agonist/antagonist results in marked suppression of gonadotropins, more precisely LH response. Therefore, kisspeptin may be a key player in treatment of reproductive endocrine diseases and In vitro fertilization (IVF).
**Fig 2: Schematic figure of tentative LH secretion pattern after continuous administration of kisspeptin agonist (A), antagonist (B), GnRH agonist (C) and GnRH antagonist (D).**

Data obtained from animal model revealed that kisspeptin antagonist/agonist reduce LH pulse without affecting basal LH secretion. In contrast, repeated administration of GnRH agonist/antagonist results marked suppression of gonadotropins, more precisely LH response. Therefore, kisspeptin may be key player in treatment of reproductive endocrine diseases and In vitro fertilization (IVF).


**Conclusion**

In the last couple of years, kisspeptin is considered as key regulator of HPG axis and coordinator of GnRH secretions. Recent understanding on regulation of LH pulse by kisspeptin creates a new opportunity in treatment modalities of reproductive endocrinology and infertility. Now it is believed that consequent effect of complete GnRH suppression may minimize by ensuring basal LH secretion through kisspeptin analogue. Therefore, it will play a master role in the treatment of future female infertility.

**Reference**

Role of Kisspeptin In Female Infertility

1986;7:11–23.
Molecular Diagnostic Tests in Bangladesh: Opportunities and Challenges
Sultana TA¹, Rahman MM²*, Rahim R³, Nasir TA⁴ Sultana GS⁵, Alam MS⁶, Hasan R⁷

Abstract
Molecular diagnosis is rapidly becoming an inseparable part of disease diagnosis. This cutting edge technology can be used to diagnose both infectious and malignant diseases as well as to help in determining drug dosage, tissue types for organ transplant and risk of inherent disorders. An added advantage is that it provides an indication of therapeutic choice, therapy response and disease prognosis. A survey was conducted among diagnostic laboratories and research institutes of Bangladesh to observe the existing range of molecular diagnostic tests in Bangladesh. It is found that though molecular tests started in diagnostics about 15 years before, range of tests is still very limited in the country. Challenges faced in establishing as well as sustaining these tests were noted and opinions recorded from stakeholders regarding further opportunities to improve this area. We found that challenges are limited knowledge on molecular tests among physicians, unfavorable custom regulations and inadequate after-sale support from suppliers, cost of the tests and strong advocacy and marketing strategies of neighboring countries. To overcome these challenges our recommendations are inclusion of molecular medicine in medical curriculum, dissemination of information about molecular tests to existing physician community, minimum custom duty and minimum profit margin by the stakeholders to reduce test price. In addition, review of policies regarding import and support of cutting edge technology in diagnostic sector with involvement of available experts in this field is essential to make this valuable sector viable.

Key words
Molecular diagnostics, Bangladesh, challenges, opportunities

Introduction
An essential component of improving global health is the use of appropriate diagnostic tools. Molecular diagnostic tests are becoming increasingly popular all over the world and are gradually replacing the conventional diagnostic algorithms. Despite their high performance levels, these tests usually require greater levels of infrastructure and technological capabilities that are generally beyond the resources of developing countries. Though it is a fast-growing business in developed countries, molecular diagnostics is therefore somewhat new in Bangladesh. This paper outlines an approach to realize the benefits of molecular diagnostic tests as a health diagnostic tool in the face of the existing challenges.
Molecular diagnostics is one of the most dynamic and transformative areas of diagnostics, revolutionizing health care across a wide range of
diseases and health conditions. This branch of medicine is mainly the study of nucleic acid. Its application cannot be limited within the arena of disease diagnosis as molecular diagnosis can be used to determine disease prognosis, selection of drugs and drug response, tissue types for organ transplant and risk of inherent disorders.

**World wide appeal of molecular diagnostic tests**

All over the world molecular diagnosis is flourishing swiftly. Food and Drug Administration (FDA) in USA has approved human genetic tests for various malignancies, inherent disorders, tissue typing for transplant and microbial genetic tests for certain viral, bacterial infections.

The global molecular diagnostic market is witnessing a period of profound growth. The overall global market for diagnostics was valued at $45.6 billion in 2012 and is expected to grow at about 7% annually over the next five years to reach a market size of $64.6 billion in 2017. The Frost and Sullivan report has also shown the molecular diagnostics segment to represent 11% of total global IVD sales (Fig 1). Other reports state steady growth rate of the global molecular diagnostics and is expected to grow at a CAGR of 11.1% from 2013 and double its market size in 2017 from the market of 2012 to reach an estimated value of USD 8.7 billion in 2019.

![Global in Vitro Diagnostics Market (2012)](image1)

**Fig. 1: Molecular diagnostics market in the world as compared to other in vitro diagnostic tests as observed in the year 2012 and market growth from 2007-2011.**

**Molecular Test for the sensitive detection of the clinically most important bacteria with their resistance genes and viruses**

Rapid and reliable results are the basis for an adequate drug treatment. Especially in the field of sepsis diagnostics, but also for other bacterial born infections, rapid and sensitive detection methods are required. Molecular genetic test systems offer crucial advantages in contrast to conventional culture methods: Direct tests are independent from problems such as growth inhibition due to prior antibiotic treatment or inadequate culture conditions.

A single test can provide a sensitive detection of the most common gram-positive and gram-negative bacteria (Fig.2). Simultaneously,
the resistance to methicillin and vancomycin is identified by analysis of the mecA, vanA and vanB genes in approx six hours. The technology is simple, rapid and can be adaptable in our country. This type of test can be done either in real time format or in conventional format followed by strip hybridization. This test can reduce time of patient stay in ICU and hospitals and patient can get ultimate financial benefit.

A single patient suffering from active TB may infect up to 15 other individuals every year via airborne transmission. Furthermore, co-infections with HIV and the development of drug resistances of the TB bacilli lead to even higher rates of mortality.

The emergence and spread of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) are a major medical and public problem threatening the global health. MDR-TB is caused by mycobacteria which are at least resistant to the two most powerful first-line anti-TB drugs rifampicin and isoniazid. Conventional methods for mycobacteria culture and drug susceptibility testing are slow and elaborate, requiring sequential procedures for the diagnosis. During this time patients may be treated inappropriately, drug resistant strains may continue to spread, and amplification of resistance may occur. Therefore rapid diagnosis and identification of MDR-TB strains are prerequisites for the worldwide fight against TB. Genotype MTBDR has been developed that can be performed from pulmonary patient specimen and from culture material. The results are obtained in 5hrs compared to 1 to 2 months with conventional culture methods.

Detection of atypical mycobacterium is also undergoing in developed countries because they can produce similar infections to mycobacterium tuberculosis and cause a great health problem. Nosocomial respiratory tract infections are major cause of excessive morbidity and mortality. Patients with serious underlying diseases have an especially high risk of acquiring these infections and that risk is magnified by exposure to respiratory therapy.

Beta-lactams remain a cornerstone for antimicrobial chemotherapy of a large number of bacterial infections, but their efficacy has been increasingly thwarted by dissemination of acquired resistance determinants among pathogenic bacteria. The exposure of bacterial strains to a multitude of β-lactams has induced a dynamic and continuous production and mutation of β-lactamase in many bacteria, expanding their activity even against later generation cephalosporins and carbapenems by the production of extended-spectrum beta-lactamase (ESBL) and metallo-beta-lactamase (MBL) respectively. Since the genes that code for the production of ESBL are often linked to other
resistance genes causing extended spectrum of drug resistance, this will result into fewer therapeutic alternatives. Phenotypic methods (antibiotic susceptibility) are used routinely in clinical laboratories. The accuracy of semi-automated microbiology systems is not optimal. Genotypic methods (PCR-based amplification) are used in reference laboratories which can discriminate between specific types of ESBLs and need shorter time to detection (culture not required) and have ability to detect low level resistance.

Other respiratory pathogens those that can be diagnosed by PCR easily but not by the conventional cultures due to its slowness of growth includes mycoplasma pneumoniae, chlamydia pneumoniae, legionella pneumoniae, Bordetella pertussis and Bordetella parapertussis. PCR can also detect viruses those that cause respiratory infections include influenza, human respiratory syncytial virus (hRSV), coronaviruses, etc.

Infectious viral disease testing is the largest molecular diagnostics market encompassing some of today’s most challenging diseases such as HIV and Hepatitis. Molecular technology continues to evolve with the goal of providing more accurate means of disease detection and monitoring.

PCR kits already are being used in developed countries for the detection of sexually transmitted diseases (STD), helicobacter pylori, clostridium difficile, enterohaemorrhagic E. coli (EHEC), vancomycin-resistant enterococci.

**Use of molecular tests in organ transplantation**

HLA typing by PCR is indispensable to know the HLA status of transplant recipient and organ donor. Antibody detection products have been developed to monitor transplant patients, both pre- and post-transplant. They are used to detect HLA antibodies that may cause graft rejection. Biomarkers in body fluids or tissues are important indicators of biological states that can provide measurable characteristics of normal or pathogenic processes, and their progression or response to therapy. Testing for biomarkers such as complement (C1q) binding antibodies, AT1R antibodies and Cytokine, KIR or HNA polymorphisms allows Transplant Clinics to better define profiles of their patients. CMV PCR, BKV PCR is used to rule out CMV infection and BK virus infection, respectively. BK virus infection is responsible for about 10% graft loss.

**Molecular tests in Oncology**

For the fast and sensitive detection of chromosomal translocations associated with leukemia Europe standard CE-IVD marked test kits are being used in developed countries. The tests are fast one-day RT-PCR or 4 hours RT-qPCR screening tests, capable of analyzing for up to 28 translocations and more than 145 clinical relevant translocation breakpoints in a single test. Single translocation PCR kit for t(9,22) minor, major, and micro; t(1,19); t(12,21); inv16; t(15,17) S, V and L; t(8,21) and t(4,11) are also available which is useful for screening, therapy response and for minimal residual disease (MRD) monitoring. For risk stratification FLT3-ITD c-KIT and NPM mutation detection PCR are needed. JAK-2 mutation PCR can aid in the distinction between a reactive cytosis and a
chronic myeloproliferative disorder (CMPD).

**Mutation detection PCR in solid tumor**

**EGFR Mutation:** Lung cancer is the leading cause of cancer-related deaths in the world. Non-small cell lung cancer (NSCLC) represents 70% to 85% of all lung cancer diagnoses. Small molecular agents that target the tyrosine kinase domain of the epidermal growth factor receptor (EGFR) protein are approved for the treatment of locally advanced or metastatic NSCLC as a second- or third-line regimen. Subsequently, randomized trials have suggested that targeted agents alone or combined with chemotherapy may be beneficial in maintenance and first-line settings. Because the combination of targeted therapy and standard chemotherapy leads to an increase in toxicity and cost, strategies that help to identify the individuals most likely to benefit from targeted therapies are desirable. EGFR gene 29 mutation panels can identify non-small cell lung cancers that may respond to epidermal growth factor receptor-tyrosine kinase inhibitor therapies.

**KRAS Mutation:** One of the most common somatic alterations in colon cancer is the presence of activating mutations in the proto-oncogene KRAS. KRAS is recruited by ligand-bound (active) EGFR to initiate the signaling cascade induced by the RAS/MAPK pathway. Because mutant KRAS constitutively activates the RAS/MAPK pathway downstream of EGFR, agents such as cetuximab and panitumumab, which prevent ligand-binding to EGFR, do not appear to have any meaningful inhibitor activity on cell proliferation in the presence of mutant KRAS. Current data suggest that the efficacy of EGFR-targeted therapies in colon cancer is confined to patients with tumors lacking KRAS mutations. As a result, the mutation status of KRAS can be a useful marker by which patients are selected for EGFR-targeted therapy. The test can be used for noncolorectal tumors as well.

**Genetic Testing:** Mutations in the CFTR gene may cause Cystic Fibrosis (CF). One in 25 people of European descent carries a mutated CFTR allele and 1 in 2000–3000 newborns is found to be affected by CF. CFTR mutation testing can be used as an aid in newborn screening, CF diagnosis, and reproductive decisions, allowing clinicians to determine if an abnormal diagnostic result is due to a mutation within the CFTR gene. Thrombophilia is an abnormality of blood coagulation, leading to increased risk for thrombosis. Thrombophilia can be identified in 50% of people who have an episode of thrombosis that was not provoked by other causes. Venous thrombosis is one of the most common thrombotic disorders affecting up to 2 in 1000 individuals every year and is associated with life-threatening conditions such as pulmonary embolism (PE). The predisposition to form blood clots can arise from mutations, acquired changes in the clotting mechanism or, more commonly, an interaction between genetic and acquired factors. The risk of thrombosis increases with the number of genetic and acquired risk factors present so that individuals with multiple risk factors are at greater risk than those with just a few. Factor V Leiden, Factor V R2, Prothrombin / Factor II, MTHFR, Plasminogen Activator Inhibitor 1 can be detected by a single multiplex PCR test that allows testing of relevant risk factors for thrombophilia.

Analysis of the Y chromosome in men with azoospermia or severe oligozoospermia has
resulted in the identification of three regions in the euchromatic part of the long arm of the human Y chromosome (Yq11) that are frequently deleted in men with otherwise unexplained spermatogenic failure. PCR analysis of microdeletions in the AZFa, AZFb and AZFc (AZF: Azoospermia Factor) regions of the human Y chromosome is an important screening tool in the work-up of infertile males opting for assisted reproductive techniques.

**Prenatal Diagnostics:** Rapid diagnosis of aneuploidy using quantitative fluorescence-PCR (QF-PCR) has improved prenatal care for many tens of thousands of women in the past decade. Pregnancies identified as being at increased risk of chromosome abnormality by prenatal screening programs are given a rapid and accurate result.

**The Bangladesh scenario of molecular diagnostics; birth to present**

The journey of molecular medicine per se started in Bangladesh at the end of the twentieth century and was focused mainly towards various diarrheal diseases, a public health concern in this region. Molecular research was predominantly restricted to sophisticated laboratories like ICDDR,B until the dawn of the twenty-first century when the country experienced a series outbreak of Dengue viral infection. The first diagnostic laboratory to engage in molecular research was BIRDEM where the genotype of dengue virus was exposed. These studies were yet however, not used as diagnostic or prognostic tools; they rather served the academic interest. The first diagnostic molecular test available commercially in the country was in the form of viral marker assays for hepatitis. The only instance of a government supported molecular diagnostic service is in the area of tuberculosis, one of the most prevalent diseases as well as a major health concern of the country. The idea of utilizing molecular methods for the diagnosis of tuberculosis was harbored at BIRDEM in the early years of the last decade. Finally in 2012, these early research activities were endorsed by Government of Bangladesh and a real time PCR-based fully automated nucleic acid amplification test (NAAT), namely GeneXpert technology was launched under the National TB Program supported TB CARE II Project of United States Agency for International Development (USAID). This is the only molecular diagnostic service available at present outside the capital (Fig. 3). According to the annual report published by Directorate General of Health Services (DGHS) in 2013, this service that was initiated at the National TB Referral Laboratory (NTRL) at Mohakhali, presently encompasses two regional TB referral labs (RTRL), 21 chest disease clinics, other government hospitals and stretches to even tertiary level private organizations and autonomous institutes like BIRDEM and BSMMU respectively. Researchers of Bangladesh are continuing to search for potential opportunities to develop a more tailored approach suitable for our community. Molecular diagnostics in oncology has an even younger history and is yet available mainly for haematological malignancies, namely detection and quantification of BCR-ABL gene, the fusion gene present in chronic myeloid leukemia and PML-RARα gene, another fusion gene
Molecular Diagnostic Tests in Bangladesh: Opportunities and Challenges

pathognomonic for acute promyelocytic leukemia, a potentially curable class of leukemia. The last decade has brought forth an inspiring bloom in the molecular diagnostics trade in the country, and various medical laboratories and diagnostic centers have picked up the option of molecular tests to enrich their services. A dedicated private laboratory named DNA SOLUTION has also been established in the capital, offering solely molecular diagnostic services.

Certain institutes, corporate hospitals and diagnostic laboratories presently offer molecular diagnostic services in Bangladesh. However, range of molecular diagnostics tests (Table.1) is still very limited in the country and centered in capital though 15 years since its inception already has passed.

![Fig. 3: Distribution of molecular diagnostic services in Bangladesh](image)

- Government supported test for TB
- All other molecular tests
Table 1: List of molecular diagnostic services in Bangladesh.

<table>
<thead>
<tr>
<th>Name of the Lab/Institution</th>
<th>Location</th>
<th>Type of Organization</th>
<th>Services Provided</th>
<th>Virology</th>
<th>Oncology</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIRDEM</td>
<td>Dhaka</td>
<td>Private</td>
<td></td>
<td>HBV, HCV, HPV</td>
<td>BCR-ABL, PML-RARA</td>
<td>TB</td>
</tr>
<tr>
<td>BSMMU</td>
<td>Dhaka</td>
<td>Autonomous</td>
<td></td>
<td>HBV, HCV, HPV</td>
<td>BCR-ABL</td>
<td>TB</td>
</tr>
<tr>
<td>ICDDR,B</td>
<td>Dhaka</td>
<td>International</td>
<td></td>
<td>HBV, HCV, HPV</td>
<td>BCR-ABL, PML-RARA</td>
<td>E Coli</td>
</tr>
<tr>
<td>Popular Diagnostics</td>
<td>Dhaka</td>
<td>Private</td>
<td></td>
<td>HBV, HCV, HPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medinova Diagnostics</td>
<td>Dhaka</td>
<td>Private</td>
<td></td>
<td>HBV, HCV, HPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lab-Aid Diagnostics</td>
<td>Dhaka</td>
<td>Private</td>
<td></td>
<td>HBV, HCV, HPV</td>
<td>BCR-ABL1</td>
<td></td>
</tr>
<tr>
<td>CARE Hospital</td>
<td>Dhaka</td>
<td>Private</td>
<td></td>
<td>HBV, HCV, HPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AFIP</td>
<td>Dhaka</td>
<td>Government</td>
<td></td>
<td>HBV, HCV, HPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IBN-SINA Diagnostics</td>
<td>Dhaka</td>
<td>Private</td>
<td></td>
<td>HBV, HCV HPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NTP (31 centres)</td>
<td>All over the country</td>
<td>Government</td>
<td></td>
<td></td>
<td></td>
<td>MDR-TB</td>
</tr>
<tr>
<td>Square Hospitals</td>
<td>Dhaka</td>
<td>Corporate</td>
<td></td>
<td>HBV, HCV, HPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shishu Hospital</td>
<td>Dhaka</td>
<td>Autonomous</td>
<td></td>
<td>HBV, HCV, HPV</td>
<td></td>
<td>Thalassemia</td>
</tr>
<tr>
<td>DNA Solutions Ltd</td>
<td>Dhaka</td>
<td>Private</td>
<td></td>
<td>HBV, HCV, HPV</td>
<td></td>
<td>Chromosome aneuploidies, Male infertility test</td>
</tr>
<tr>
<td>Apollo Hospitals Dhaka</td>
<td>Dhaka</td>
<td>Corporate</td>
<td></td>
<td>HBV, HCV, HIV, HPV (high risk) HPV 16/18, HPV 6/11, HSV I, II CMV, EBV, HHV-6</td>
<td>Screening for BCR-ABL1, PML-RARA t(1,19); t(12,21); inv16; t(8,21); t(4,11) JAK2mutation</td>
<td>MTB/NTM, Mycoplasma/ Chlamydia Pneumoniae, Chlamydia Trachomatis/ N. Gonorrhoeae/ T. Vaginilis</td>
</tr>
</tbody>
</table>

Note: Services provided in various locations may vary, so it is advisable to contact each laboratory directly for the most accurate information.
Molecular Diagnostic Tests in Bangladesh: Opportunities and Challenges

Challenges in the area of molecular diagnostic services

Molecular diagnostic services all over the world are constantly challenged by various factors. There are some universal factors that affect any country as well as some specific challenges faced by low resource settings like in developing countries. In the developed world, the challenges include regulatory hurdles, coverage and reimbursement issues, and practical and ethical (privacy) issues associated with generating and storing large volumes of highly detailed and personal health information. In countries that are at the other end of the line like Bangladesh, the burden of cost falls on the individual. Lack of strong guidelines regarding utility of the tests, poses a threat of abuse of these investigational facilities where they are not clinically indicated. At the end of the story, it is the treatment of the patient that is always at stake.

The undergraduate and postgraduate medical education curriculum of the country does not impart sufficient and updated information regarding molecular diagnostic tests. As a result, most of our physicians do not have ample opportunity to utilize this technology optimally. The strong advocacy and ease of sending samples to foreign labs tips the balance towards an efflux of the samples to laboratories abroad to neighboring countries like India, Singapore etc. However, World Health Organization (WHO) have categorized all diagnostic samples as Category B\(^1\) under the substances identified as dangerous goods or hazardous material (HAZMAT) by International Air Transport Association (IATA)\(^1\)\(^6\) and they impose stringent conditions like appropriate labeling and packaging before any air freight is ready to carry them. Most sample collecting vendors avoid such complications and send the samples by road to the neighboring countries. This raises the concern whether proper temperature is maintained throughout the duration of transportation of the sample from the patient to the lab. There is a general ignorance among the physicians about limitations of tests done abroad.

Expertise in this field is sparse in the country. The limited expertise is also inappropriately distributed or utilized due to various bureaucratic reasons. The situation is made tougher by the lack of patronization from institutional or government policymakers regarding this new branch of laboratory medicine. Institutions can promote these molecular tests at no-profit or minimum profit margin to reduce the cost of the test for certain time. Similarly, government can take policy to decide minimum custom duty, set up cold chain at airport and quick dispatching of molecular products from airport.

Prospects for molecular diagnostics in Bangladesh

The prospect for molecular diagnostic tests in a highly-populated country like Bangladesh is immense. The emergence of ultra high-end tests is in general accompanied by consumer concerns of high cost. The initial introduction of such tests therefore must often be targeted to the economic sector that can afford such tests. The recent years have perceived a striking increase in purchasing power among the middle- to upper-tier economic
groups. Along with the increasing wealth of Bangladeshi people is the emergence of a more Westernized attitude. Thus, although diagnostic testing and disease-screening programs are largely at an embryonic stage compared to the West, the shift in economics and attitude provides for a more encouraging outlook in terms of the success of such efforts in the future. The benefit to the overall medical community in Bangladesh will be perceived once market penetration has been achieved. The combined factors of financial return from investment coupled with advancing technology are then likely to lead to cost reduction, allowing greater economic segments of the Bangladesh society to afford these tests. Efficient communication among the various sectors may help alleviate the problems faced today and help to groom this nascent technology in the country.

Conclusion

In this densely populated country, where doctor to population ratio is 1:4,719 it is of paramount importance that quality infrastructure and manpower is developed to ensure proper diagnosis. Effective communication between laboratory physicians and clinicians, dissemination of utility of molecular tests to the existing clinicians are needed. Inclusion of molecular medicine in the medical undergraduate and post-graduate curriculum should be considered for the future doctors and clinicians. A BSTI equivalent establishment in this regard is necessary to maintain and improve the quality. If institutional and government policy makers strongly held their focus on this field, Bangladesh has the potential to flourish in future.

Reference


Quality Assurance and Quality Control in Clinical Laboratories

Rehnuma B¹, Ibrahim M², Nasir TA³

Abstract
Health care delivery is no longer a simple process of examining the patient and giving him a prescription. Over the years there has been rapid expansion in the various branches of health care services. As part of this expansion process and explosion of scientific medical knowledge, laboratory diagnosis has gained tremendous importance in today’s practice. Especially in our country since the beginning of 80’s we have been witnessing significant growth in laboratory services. Through quality management process the laboratory can ensure that the result being issued by the laboratory is reliable to allow decisions to be taken with confidence. Quality control and quality assurance are parts of quality management. Quality control is focused on fulfilling quality requirements, whereas quality assurance is focused on providing confidence that quality requirements are fulfilled. By utilizing quality control practices, a laboratory is able to find and correct flaws in the analytical processes of a lab before potentially incorrect patient results are released.

Key words
Quality assurance, quality control, quality management

“Quality is never an accident; it is always the result of high intention, sincere effort, intelligent direction and skillful execution; it represents the wise choice of many alternatives.”

The issue of Laboratory quality has evolved over more than 4 decades since the 1¹st recommendation for quality control was published in 1965.¹ Now Quality Control is seen as only one part of a total laboratory program. Government of Bangladesh has recently approved a draft on National Health Policy with an aim to reach the minimum Health care facility (MDG) by 2015.²

The purpose of the health care system in a country is to correctly diagnose the disease, identify the factors responsible for the disease and take appropriate preventive and curative measures to control the disease. The pathologists and laboratory people are very much involved in the correct diagnosis, effective treatment and follow up of the patients. For correct diagnosis quality assurance and quality control are very important. Laboratory quality control is designed to detect, reduce and correct deficiencies in laboratories analytical process to release patient results and improve the quality of test result.³

Quality assurance (QA) is aimed at ensuring quality test results. The purpose of quality assurance is to give relevant, reliable, timely test

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¹ Registrar, Clinical Biochemistry, Dept. of Lab Medicine, Apollo Hospitals Dhaka; ² Consultant, Clinical Biochemistry, Dept. of Lab Medicine, Apollo Hospitals Dhaka; ³ Sr. Consultant and Coordinator, Dept. of Lab Medicine, Apollo Hospitals Dhaka.
It has been summarized as the

• right result, at the
• right time, on the
• right specimen, from the
• right patient, with result/interpretation based on correct reference date, and at the
• right place

Quality control (QC) on the other hand covers the part of quality assurance which primarily concerns the control of errors in the performance of tests and verification of test results. Quality control must be practical, achievable and affordable. The primary aim of quality control is to do the test reliably. The broad aim of quality control is that results from one lab should be comparable with that from any lab in the world provided the same method is followed.³

The fundamentals of Quality control include:

i. Total quality management of clinical laboratory
ii. Control of pre-analytical variable
iii. Control of analytical variable
iv. External quality assessment and proficiency testing programs

Many international agencies supervise quality assurance namely ISO, ioQA, intertek and Quality assurance program run by different

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**Quality Control Process**

- **Vendor quality management**
- **Incoming quality control**
  - Statistic process control (SPC)
  - Training
  - Calibration
  - Preventive Maintenance
  - Document and data control
  - Reliability test
  - Reject analysis
  - Corrective & Preventive Actions
  - Engineering Changes

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**Fig. 1: Quality control process**
For biochemistry quality control involves optimum condition variance (OCV), routine condition variance known value (RCVK), composite and long term assay, and computer aided check, accuracy and precision tests. Accuracy is defined as closeness of the test result and accepted true value, whereas precision is a measure of reproducibility. Daily QC chart preparation is mandatory. Control value within ± 2SD is good sign and patient’s results obtained are reliable and can be reported. If control value is beyond ± 2SD the result must not be reported and fresh control serum should be measured together with few patients sample. If the result is now within ± 2SD, the result can be reported. The type of material used for QC is frozen, pooled serum; commercially available lyophilized freeze dried pool serum; commercially available low temperature liquid serum pools.7

For histo and cytopathology, quality control involves intra departmental consultation, random case review, intra departmental and inter departmental conference, inter institutional review, specimen adequacy record, lost specimen record, turn around times, techniques i.e staining, proper sectioning, embedding, fixation, re and dehydration of samples, clearing, mounting, labelling etc.8,9

For microbiology, quality control involves use of ATCC strains of organisms for standardization, measuring the disc potency, MIC, media contamination, standardization of staining procedures, autoclaving and sterilization of media, safe disposal of infected materials is also an important procedure to maintain standard lab practice.

For hematology, standardization of staining procedures, preparation of proper blood film, bone marrow smear, special staining techniques flow cytometry, chromosome analysis are the mainstay of quality control.

Wrong test results are caused by faults on the part of the clinicians like sending sample without identification number and name of the test, collection date, appropriate container, sending specimens divided in several parts to different labs; without clinical history, provisional diagnosis, other relevant test results, radiology/imaging reports/etc.

Wrong results are also caused by the faults of laboratory and the pathologists which can be divided into pre-analytical stage faults, analytical stage faults and post analytical stage faults. In the pre-analytical stage the faults are misidentification of patients due to incomplete ID, incorrectly labeled specimen container, partly erased or illegible label and disparity between request form and specimen.

Faults may also be with the specimen. A faulty specimen is one which is inadequate, collected at incorrect time in dirty and contaminated container, in a container without proper anticoagulant and stored incorrectly or in hemolysed status. These are known as pre analytical faults. In the analytical stage the faults resulting in wrong findings if the principle and procedure of the test is not strictly followed; reagents, standards, QC materials are not prepared, mixed, processed properly and performance standards are not followed strictly.
In the post analytical stage the faults may occur if reporting, checking and verifications are not done properly, interpretation of test results are not considered seriously, and abnormal/unexpected result is not taken seriously and not reviewed and or performed again.

**Fig. 2: Factors influencing Quality Control Process**

Quality control is a part of total laboratory control program which can be achieved through proper documented and validated interventions at pre-analytical, analytical and post-analytical stages. Implementing quality does not guarantee an error free laboratory but it detects errors that may occur and prevents them from recurring.

To monitor QA and QC, minimize errors establishment of a Central Reference Laboratory and Institute of Pathology is a must and need of the hour. The sooner the Government, people’s representatives, Medical professionals, Social workers, Journalists, Patients and their relative understand this, the better is the outcome. Bangladesh Society of Pathologists should come up with concrete proposals for this and talk to the Government and other appropriate agencies for its early implementation. The good news is that Government has accepted in principle the concept of a Central reference laboratory, allocated budget for this project and preliminary baseline work has been done. Now the society of Pathologists should work shoulder to shoulder with Ministry of Health for quick implementation of the project.

It is very important to maintain QA and QC for reliable, quick and dependable results in shortest possible time. This will help the clinicians to come to a correct diagnosis and treat the patient early. This will lead to early recovery and save working time, money for the patient and the nation.

**Reference**

Atypical Pituitary Adenoma: A Case Report

Khaled A¹, Joarder MA², Karim B³, Chandy MJ⁴, Nasir TA⁵

Abstract
A 56 years old diabetic hypertensive male was admitted through neurosurgery OPD with the complaint of vision problems in the right eye for the last 1 and 1/2 years. Peri-metry reveals bilateral temporal field defects and MRI examination showed a sellar and suprasellar mass infiltrating the surrounding structures including cavernous sinus. Histomorphologically and immunohistochemically, a diagnosis of atypical pituitary adenoma was made.

Introduction
Tumors of the pituitary gland and sellar region represent approximately 10% to 15% of all brain tumors. Numerous types of tumors may involve the sellar region, by far; the pituitary adenomas, benign epithelial tumors derived from cells of the adenohypophysis is the commonest one. In the past, numerous classifications have been proposed to classify pituitary adenoma. The recommended WHO classification, which is now used by most laboratories, incorporates the clinical and radiological presentation of the tumour with its morphologic features, immunohistochemical profile and ultrastructural appearance. The WHO classification introduced the concept of atypical adenomas for tumors that show histologic features suggestive of aggressive clinical behavior. These adenomas are characterized by elevated mitosis index a Ki-67 labelling index greater than 3% and overexpression of P53 by immunohistochemistry.¹

As these variety of pituitary adenoma carries unfavorable prognosis, needs close follow up, it is essential that surgical pathologist, and neuropathologist should accurately diagnose these cases. Besides, there is no published report of atypical pituitary adenomas in this country so far. With this background knowledge in this case report we describe a case of atypical pituitary adenoma in Apollo Hospital Dhaka.

Case History
A 56 years old diabetic, hypertensive Bangladeshi male was admitted through neurosurgery OPD with the complaints of vision problem for last 1 and 1/2 years in the right eye. He did not have any complaints regarding hearing, walking, hand problem, any loss of consciousness or convulsions. On examination, his vitals were stable and Glasgow coma scale was 15/15. Examination of eye revealed both pupils were 2 mm and equally responsive to light, normal anterior segment of both eye, visual...
Acuity of right eye 1/60 and left 6/9, perimetry shows temporal field defect: Right > left. Fundus examination reveals pallor of disc in both eyes. Intraocular pressure of both eyes was 20 mm of Hg. His hormonal level was serum cortisol 10µg/dl, FT\(_3\) 3.6 pg/ml, FT\(_4\) 1 ng/dl and serum prolactin 3.9 ng/ml. MRI examination of brain and peroperatively, a sellar, suprasellar and parasellar mass grade D and E infiltrating the left cavernous sinus was seen. Transnasal transsphenoidal tumour decompression was done and tissue was sent for histopathology. Microscopically, the tumour tissue shows proliferation of uniform polygonal cells with round nuclei arranged in nests, trabeculae and sinusoidal pattern. In focal area, these cells show moderate pleomorphism with increased mitosis (Fig.1). Immunohistochemistry reveals strong positivity for P53 and a diagnosis of atypical pituitary adenoma was made.

**Discussion**

The aim of the current study was to present a case with clinical, imaging, and histopathological characteristics satisfying the 2004 WHO criteria for atypical pituitary adenomas. Atypical pituitary adenomas were found to have a poorer prognosis due to decreased operability by a higher degree of invasiveness, larger size, and accelerated growth. It differs from pituitary carcinoma only in the lack of metastases. Expression of p53 has been shown to correlate with the aggressiveness of pituitary adenomas and numerous other neoplastic lesions in selected studies. Another study by Thapar et al. Analyzed p53 expression in pituitary adenomas and carcinomas, reporting the proportion p53 in noninvasive adenomas, invasive adenomas, and carcinomas to be 0%, 15.2%, and 100%, respectively.

In 2007, Saeger et al. reported their series of 4122 cases from the German Pituitary Tumour Registry. In 2005, this registry reported 12 of 451 cases of atypical pituitary tumors for an overall incidence of 2.7%. In a study by Scheithauer et al., which had available follow up on 78 patients with

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**Fig. 1: Proliferation of tumor cells with moderate pleomorphism and increased mitosis.**
adenomas, the criteria for atypical lesions were met in 6 cases (14.7%), of which 5 were recurrent tumours.6

In a large study comprising 121 cases of pituitary adenoma, Zada G and colleagues found that 15% of the tumour met the WHO criteria for atypical adenoma. These cases has mean age of fifth decades, a feature similar to other cases studied in large numbers.7

The prognosis of atypical pituitary adenoma is generally poor, although patients with long-term survival have been described. Due to the small number of cases, comparative studies of different treatment options are lacking.8

Reference
CASE REPORT

A Phalangeal Osteoid Osteoma: A Case Report

Khalequezzaman S¹, Saha BK², Khan BS³, Kumar P⁴

Abstract

Osteoid osteoma is a benign bone forming tumor of the growing skeleton that is most often seen in young men. It represents by pain and radiologic appearance of a nidus surrounded by osteosclerosis that occurs mostly in long bones of the lower extremity. Occurrence of this tumor in the hand is an uncommon condition. A 35 year old right-hand-dominant man presented to our orthopedic and trauma OPD with an approximately 2 year history of right middle finger pain without any history of trauma. He consulted previously with a local doctor and had undergone x-ray of the hand with no definitive diagnosis. Computed tomography at our institution was consistent with the diagnosis of osteoid osteoma. The patient was treated with surgical excision of the lesion without bone grafting. The diagnosis of osteoid osteoma was confirmed by histopathology. Follow up visit showed complete resolution of pain. In this case demonstrating that osteoid osteoma is an important differential diagnosis in patients with finger pain.

Key words

Osteoid osteoma, phalanx, tumor

Introduction

Osteoid osteoma is a benign osteoblastic tumor that Bergstrand first described in 1930. Jaffe described it in 1935 and was the first to recognize it as a unique entity. It is characterized by nocturnal pain and local tenderness. Osteoid osteoma is a benign disease process of bone that usually affects children, adolescents, and young adults with the majority of patients being between the ages of 10 and 25 years.¹ It is the third most common benign tumor, comprising 12% of benign tumors and 3% of all tumors, and has a male to female ratio of 2:1.² Pain, worse at night and relieved by oral non-steroidal anti-inflammatory medications is the most typical symptom.³ Since osteoid osteoma is a vascular tumor, substances that cause vasodilatation, such as alcohol, may precipitate acute pain.

This tumor is most frequently seen in the metaphysis or diaphysis of long bones with half the cases involving the femur or tibia but it can affect the posterior element of the spine (10%), hands or feet (12%).³ Radiograph of the affected long bone shows a lucent area less than 1.5 cm in diameter called nidus surrounded by a zone of reactive bone formation in the cortical or medullary canal.⁴ Osteoid osteomas of the hand are uncommon, most commonly seen in the phalanges and often result in atypical clinical and radiologic findings. So, long delay in diagnosis is common since clinical findings may

¹. Specialist, Dept. of Radiology & Imaging, Apollo Hospitals Dhaka; 2. Sr. Consultant, Dept. of Radiology & Imaging, Apollo Hospitals Dhaka; 3. Consultant, Dept. of Radiology & Imaging, Apollo Hospitals Dhaka; 4. Consultant, Dept. of Orthopedics & Trauma, Apollo Hospitals
mimic a variety of diseases in differential diagnosis.

Case Report
A 33 year-old right hand dominant man presented to Orthopedic and Trauma OPD with pain in the middle finger of right hand for about 2 years. There is no history of trauma to the area. The pain had progressively increased in severity for the last couple of months and became unbearable especially at night. However, it usually relieved with oral NSAID. At the time of presentation, there was restricted movement of the affected finger. Radiographs done at the local area reported as normal. Physical examination demonstrated slight swelling and tenderness on the ulnar aspect of the proximal phalanx of the right middle finger. There was no erythema or induration. Neurovascular exam of the left upper extremity was normal.

He was ordered computed tomography (CT) scan of the right hand. This showed a focal lucent lesion at the ulnar aspect near the head of the proximal phalanx. The lesion measured 5.2 to 6.5 mm in diameter with no periosteal bone formation. A central nidus was present and surrounding sclerosis in the adjacent bone (Fig 1). These features are in consistence of an osteoid osteoma.

Fig.1 (a) Fig. 1 (b)

Fig.1: CT scan of hand in (a) coronal and (b) sagittal plan demonstrate focal lytic area with sclerotic dot at the ulnar aspect of proximal phalanx near head (white arrow in a), associated surrounding sclerosis. The epicenter of the lesion could be periosteal. No periosteal new bone formation. Fusiform soft tissue swelling at the proximal phalanx noted.
General condition and blood examination was normal. After a discussion with the patient and by consideration of his persistent pain and difficulty, it was decided to admit the patient and proceed with surgery.

The lesion was approached dorsally and exposed the pathology. Drill hole was made at the site of nidus and curettage was done. Tissue was sent for histopathology. Histopathology examination confirmed it as being an osteoid osteoma.

The patient was discharged the following day in a stable hemodynamic condition. On follow up visit, the patient had no obvious pain which he was experiencing before the surgery.

**Discussion**

Occurrence of osteoid osteoma in the hand is unusual and in order of frequency, proximal, distal and middle phalanx is the most frequent site. Therefore, patients with this entity are often resumed to have other disorders more common to the region, delaying accurate diagnosis for an extended period of time. While the patient mentioned above did demonstrate the classic symptoms of osteoid osteoma, namely localized pain that is worse at night and relieved by NSAIDs, there have been reports of other patients with this bone lesion in the hand that had atypical symptoms. These include vague, diffuse as opposed to localized pain, fusiform as opposed to localized swelling of the digit, and decreased range of motion with periarticular lesions. Other authors have also reported presentations of profuse digital tip perspiration and intense autonomic phenomena, which may mimic peripheral nerve compression or reflex sympathetic dystrophy.

Meng et al. reported the most common appearance of osteoid osteoma of the hand is of an eccentric lesion with soft tissue swelling and a relative absence of sclerosis, suggesting osteomyelitis. Most of the hand osteoid osteoma is diagnosed late because of atypical radiologic or clinical findings. This tumor may be misdiagnosed with conditions such as subacute osteomelitis, Brodie’s abscess, tuberculosis, tenosynovitis.

Osteoid osteomas produce excruciating pain that is disproportionate to their size; there are two postulated reasons for this. Within the nidus, nerve fibers are intimately associated with the blood vessels, and these fibers are larger and more numerous in the reactive zone. An excess of cyclooxygenases and prostaglandins within the lesion leads to vasodilation and also decreased nociceptive threshold of nerve endings resulting in sensations of pain. With the pharmacologic decrease in prostaglandin production, NSAIDs often provide predictable pain relief.

Patients with osteoid osteoma in the small bones of hand may present without pain or without a nidus or bone forming reaction and this is the reason for delay in diagnosis. Although this tumor may regress spontaneously after a long time, but surgery is usually indicated in symptomatic patients not responsive to medical treatment. A variety of treatment options including medication, wide excision of the nidus and curettage of the lesion, CT-guided core drill excision, radionuclide-guided excision, percutaneous radiofrequency ablation, injection of ethanol or interstitial laser photocoagulation (ILP) have been used for this tumor. Percutaneous CT-guided ablations with laser or
radiofrequency have now widely replaced surgery as the treatment of choice for osteoid osteoma. However, surgical excision still plays a major role for the lesions in the hands and feet owing to the close relationship of the small bones with the neurovascular structures.

Conclusion
Osteoid osteoma should always be considered in cases with phalangeal pain especially if the pain is worse at night time and subsides with NSAIDS. Computed tomography not only has the highest specificity but also allows for accurate preoperative planning.

References
Case Report of a Child with Developmental Delay

Rahman T

Abstract
The cerebral palsies are a group of conditions due to non progressive damage to the brain before, during or after birth. There are many causes. Although the brain damage itself doesn’t change nor is it curable, the symptoms may change with time. Classifications vary in different clinics and countries. usually there is the spastic, the athetoid and the ataxic type. The diagnostic classification may not play a direct role in the therapy plans. Diagnostic types are based on the predominant symptoms and there may be symptoms of the other types.

Although the motor delay and dysfunctions are the main problems in the cerebral palsies there is the possibility of other handicaps. The brain damage itself can be diffuse enough to affect speech and hearing, vision, perceptual function, mental ability and general behaviour. Epilepsy may occur. There may also be other associated handicaps which are due to lack of motor experiences in physically disabled children. Lack of motor exploration affects development of sensation perceptions, mental abilities and speech, emotional and social skills are also hampered. Parent-Child interaction is not always easy and may create emotional problems. Early therapy is advisable to minimize the degree of motor handicap and of the secondary development handicaps.

Key words
Cerebral Palsy, Developmental Therapy, Rapid Neurodevelopment Assessment

Introduction
Acquired brain injuries, such as hypoxic-ischemic lesions up to the age of three, are among the ten main causes of spastic hemiplegic cerebral palsy (CP). Although it does not severely impair functionality in children, hemiplegic motor impairment produces neuromotor alterations that cause precision deficits in movement performance and deficits in postural control, which is responsible for the stability and alignment between the body segments during the performance of activities. Thus, the rehabilitation of children with mild motor impairment of the hemiplegic type may prove to be especially challenging to therapists, requiring profound technical knowledge and creativity.

The progression of the therapy in these children is often compromised by the difficulty in finding tasks that motivate them, while at the same time showing therapeutic efficacy. Developmental therapy allows the child with
mild motor impairment and high levels of functionality to perform tasks close to those performed in their daily routine, facilitating the transposition of the motor learning generated during therapy and leading to measurable functional gains, increasing the social integration to the environment that surrounds them.

Case History
A 9 months old male child came to the Child development center of Apollo Hospitals Dhaka with complaints of unable to sit from lying positions and less interaction with surroundings. Child was delivered at full term by caesarean section with appropriate birth weight. Child was admitted in NICU up to his seven days of age due to peri natal asphyxia stage- II. There was history of delayed milestone and difficulties in deglutition of semi-solid food without drooling. On examination by Rapid neurodevelopmental assessment-Gross Motor: Couldn’t sideline in right and left side from lying position, Fine Motor-No reaching and digital grasp with left and right hand, Vision- Only could fix and follow adults face, couldn’t fix and follow spinning bright ball from 12.5cm. Hearing-Could locate voice at ear level with minimum sound. Speech- Only had vocalization (ghh, ooh, eeh), Cognition- He had no social smile.

Nervous system examination- Tone was increased in right side, Deep tendon reflexes were exaggerated on the right side. EEG was suggestive of abnormal record due to presence of sharp transients over both anterior temporal, posterior temporal and occipital regions. MRI of brain was advised.

Developmental Therapy (motor therapy, stimulation program, visual stimulation) is continue with regular follow up for 14 days interval and psychological assessment (BSID-III) is done. These assessment was carried out based on observation during administering BSID-III edition. Bayley Scales of Infant Development third Edition is a standardized psychometric test for measuring children’s cognitive, receptive communication, expressive communication, fine motor, gross motor, socio emotional, and adaptive behaviour ability. Throughout this assessment we found his Cognitive domain: Significantly delayed intellectual functioning level, Language (receptive and expressive) domain: Significantly delayed, Motor (Fine and gross) domain: Significantly delayed.

After 4th follow up in 14 days interval Rapid Neurodevelopmental assessment was done whereas Gross Motor - could sit from lying without support, Fine Motor- could transfer object in both hands but radial digital grasp in right hand and digital grasp in left hand, Cognition- could shake rattle and had pat-a-cake. Vision - could fix and follow shiny bright object, Speech - babbling was started.

Discussion
The cerebral palsies are a group of conditions due to non-progressive damage to the brain before, during or after birth. Although the brain damage itself does not change nor is it curable, the symptoms may change with time. The brain
and nervous system are maturing in the presence of the damage and this cannot take place in a vacuum. The way the baby is handled and the attitudes that surround the baby influence how the maturation expresses itself in the subsequent child’s and adult’s ultimate function.

Although the motor delay and dysfunctions are the main problems in the cerebral palsies there is the possibility of other handicaps. The brain damage itself can be diffuse enough to affect speech and hearing, vision, perceptual function, mental ability and general behavior. Epilepsy may occur. There may also be other associated handicaps which are due to lack of motor experiences in physically disabled children. Lack of motor exploration affects development of sensations, perceptions, mental abilities and speech. Emotional and social skills are also hampered. Patients-child’s interaction is not always easy and may create emotional problems.

Early therapy is advisable to minimize the degree of motor handicap and of the secondary development handicaps.

There are still medical practitioners who hesitate about the referral of cerebral palsied babies for therapy. This may be due to the fact that some babies improve and even become normal without any treatment. Unfortunately we do not yet know definitely which neurologically damaged babies will become cerebral palsied and which will not. It is best to give each child the benefit of developmental therapy, and his parents practical guidance in his daily care, by a therapist who can also detect motor patterns of cerebral palsy. Every chance for the baby’s damaged nervous system to develop is offered by early treatment of this kind. We know that the human nervous system when damaged has powers of compensation. In addition, the baby and young child are still maturing and dormant abilities can be activated. In cerebral palsy there is a potential for abnormal patterns of movement and posture to become habitual and deformities can occur and become fixed. Prevention of deformities is possible to a large degree and often completely with early treatment. If deformities are allowed to develop, then secondary deformities may also be promoted in other parts of the child’s body. This handicaps him even more.

Early treatment also decreases the associated handicaps which need specific therapy. The associated handicaps have also been known to become more severe than the motor problems. Handicaps interact with one another and the cerebral palsied child must be considered as a multiple handicapped child. Not all cerebral palsied children have multiple handicaps, but today there seem to be increasing numbers referred for therapy who are mentally and in multiple ways handicapped.

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CASE REPORT

A Case of Multiple Myeloma with Unusual Serum Protein Electrophoresis

Nargis W\textsuperscript{1}, Ibrahim M\textsuperscript{2}

Abstract
Monoclonal gammopathy is a group of B-cell disorders resulting in the secretion of a specific and unique monoclonal immunoglobulin (M-component); best detecting with high resolution agarose gel electrophoresis. An M-protein is usually visible as a localized band on agarose gel electrophoretic peak in the beta, gamma, or rarely in the alpha-2-globulin region of the densitometer tracing. Here, we presented a multiple myeloma patient with IgA kappa paraprotein showing an M spike in the alpha-2 globulin region in agarose gel electrophoresis.

Key words
Multiple myeloma, protein electrophoresis

Introduction
Among the methods of protein electrophoresis; agarose gel electrophoresis is much more sensitive than cellulose acetate method. In order to determine the immunoglobulin subtype and ensure the presence of M-protein in all patients with local M band detected in protein electrophoresis, serum and urine immunofixation procedure must surely be performed as further investigation. M-protein is generally observed as a localized band which is frequently seen on gamma or beta region, it may also be seen on alpha-2 globulin region but this situation is very rare.\textsuperscript{1,2} Sometimes, IgG multiple myeloma may extend to the alpha-2 globulin area, because IgG M-protein may range from the slow gamma to the alpha-2 globulin region.\textsuperscript{3} Here, we presented an adult patient diagnosed as IgA kappa type multiple myeloma, who had an M band on alpha-2 globulin region on the protein electrophoresis performed by agarose gel electrophoresis.

Case Report
A sixty one year old woman was referred to the hematology clinic of Apollo Hospitals Dhaka with symptoms of fatigue and back pain in November 2011. On physical examination, there was no pathological finding other than paleness of the skin and conjunctiva. In the laboratory examinations performed, the following values were found; erythrocyte sedimentation rate: 130 mm/hour, Hb- 6.2 g/dl, TLC-4.4 x10\textsuperscript{9}/L, PLT (plateletcount)-160x10\textsuperscript{9}/L. S. protein electrophoresis showed monoclonal gammopathy (Fig.1). Serum Immunofixation revealed IgA, Kappa monoclonal gammopathy with raised Beta 2 microglobulin (7369 ug/L). Creatinine clearance was found to be 18.1 ml/hour. Urinary system ultrasonography was normal. The bone marrow aspirate showed infiltration with plasma.
cells by 57%. In the bidirectional cranial X-ray graphy, five lytic lesions, the biggest one being 5 mm in diameter were detected. In dorsal and lumber vertebra direct X-ray graphs, collapse fractures were seen on L2-L3 and L4-L5. The patient was diagnosed as Stage-IIIB multiple myeloma according to Salmon-Durie staging criteria and was planned to be treated accordingly.

**Discussion**

Multiple myeloma is the second most-common hematologic cancer, representing 1% of all cancer diagnoses and 2% of all cancer deaths. Multiple myeloma affects men slightly more than women. African Americans have the highest reported incidence of this disease and Asians have the lowest. The case presented here was of a 61 year old Bangladeshi female.

In multiple myeloma patients, mutated plasma cells - otherwise known as myeloma cells - grow unregulated by the processes that normally control cell division and death. By the time the disease is diagnosed, most patients have myeloma cells in multiple sites throughout the bone marrow. There are often no symptoms in the early stages of myeloma. In some cases, myeloma may be discovered by accident during routine blood testing. When present, symptoms may be vague and similar to those of other conditions. Our case presented with fatigue and back pain for 2 years.

A myeloma diagnosis is often based on the presence of an increased number of plasma cells in the bone marrow and, in most cases, the presence of excess protein (M protein) in the blood or urine. Serum electrophoresis can be routinely used for the diagnosis of multiple myeloma and is well correlated with biochemical, radiological and pathological findings. In our patient most of the biochemical results were suggestive of the pattern found in multiple myeloma. The patient was having normal serum calcium level at time of diagnosis. Hypercalcemia is found initially in 22–30% patient with multiple myeloma, the exact cause...
of which is unknown. The patient was not in renal failure as evident from GFR and renal function test. Renal failure, defined as a serum creatinine ≥2 mg/dl at the time of diagnosis, is seen in 21% of patients.\textsuperscript{9,10} In the patient, the M band on the α2 region and β region was shown to be bound to IgA. The conventional technique serum electrophoresis is still widely used for the demonstration of M-Protein in the myeloma patient and it remains a gold standard. Multiple myeloma arises from plasma cell dyscrasia. These malignant plasma cells synthesize monoclonal antibody and release it to the circulation. As a result high concentration of monoclonal antibodies is present in bone marrow as well as in serum.\textsuperscript{4} The circulating M-protein may consist of an intact immunoglobulin, the light chain only, or (rarely) the heavy chain only. The heavy chain is from one of the five immunoglobulin classes G, A, M, D or E, while the light chain is either κ (kappa) or λ (lambda) in type. It occurs as intense, narrow band most often found with the gamma-globulins, then in a diminishing frequency between γ and the β-globulin and rarely in the β and α2 regions. Generally IgA, IgG and IgM proteins are not observed on the α2 fractions. These proteins compose β-1, β-2, and γ fractions.\textsuperscript{5} However, in IgG multiple myeloma immunoglobulins may rarely migrate from γ fraction to α2 fraction.\textsuperscript{6} M-protein that is seen on the α2 band is just reported in a few numbers of IgA multiple myeloma cases. Very rarely, biclonal gammopathies (accounts for 1% of all monoclonal gammopathies) or triclonal gammopathy can be observed in multiple myeloma.

Ceruloplasmin, alpha-2 macroglobulin and haptoglobin constitute the alpha-2 fraction of the protein electrophoresis and the alpha-2 component increases as an acute phase reactant. Generally IgA, IgG and IgM proteins are not observed on the alpha-2 fractions. These proteins compose beta-1, beta-2, and gamma fractions.\textsuperscript{4} However, in IgG multiple myeloma immunoglobulins may rarely migrate from gamma fraction to alpha-2 fraction.\textsuperscript{3} M-protein that is seen on the alpha-2 band is just reported in a few numbers of IgA multiple myeloma cases in literature. Mseddi-Hdiji et al.\textsuperscript{7} reported that in electrophoresis that is performed by agarose gel method 78% of the 242 monoclonal gammopathy cases had M band on gamma region whereas 22% of the cases had band on beta region and none of the cases had it on alpha-2 region. Bakta and Sutarka\textsuperscript{8} observed two separate M bands on the beta-2 and alpha-2 regions in the serum protein electrophoresis of a patient that they considered to have multiple myeloma. From the serum immunofixations, these were reported to be IgM and IgA immunoglobulins. In our patient, the M band on the alpha-2 region was shown to be bound to IgA like a few others.\textsuperscript{9,10} So, this case reminds that, M band on alpha-2 region in serum protein electrophoresis can rarely be seen in IgA myeloma patients.

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CASE REPORT

Chondroma of the Cerebellopontine Angle: A Case Report

Khaled A1, Ahsan S2, Joarder MA3, Karim B4, Chandy MJ5, Nasir TA6

Abstract

A 41 year old non-diabetic, non hypertensive male was admitted in AHD through neurosurgery OPD with the complaints of left eye watering and left sided weakness for 1 month. MRI examination revealed a mass / lesion in the left preptontine cistern, left CP angle with extension to left middle cranial fossa which was histologically found to be chondroma, an extremely rare tumour in the above mentioned location.

Introduction

The (Cerebellopontine Angle) CPA is a triangular area bounded by the temporal bone anterolaterally, pons medially, cerebellar hemisphere posteriorly, tentorium cerebelli superiorly and lower cranial nerves inferiorly. Its contents include the anterior inferior cerebellar artery (AICA) and 7th and 8th cranial nerves. These nerves emerge from junction of pons and midbrain and course, through the CPA to reach the internal acoustic meatus (IAM). Cerebellopontine angle (CPA) tumours can be divided into extra-axial tumours, intraaxial tumours, extradural tumours and petrous apex lesions. Extra-axial tumours can be divided into those common and rare. Acoustic tumours or more precisely vestibular schwannomas (VS) are by far the most common extra-axial tumour. Other common extra-axial tumours include meningiomas and cysts of the posterior fossa (epidermoid, arachnoid, etc.). Rare extra-axial tumours include other cranial nerve neuromas (V, VII, IX, X, XI, XII) and vascular malformations (aneurysms, A-V malformations). Intra-axial tumours include parenchymal lesions such as astrocytomas, ependymomas, papillomas, haemangioblastomas and metastases. Extradural tumours include glomus tumours and bone lesions. Petrous apex lesions include cholesterol granulomas, epidermoid cysts, mucoceles and aneurysms of the carotid artery.1

Among all these lesions, intracranial chondromas are rare, comprising roughly 01% to 02% percent of the intracranial tumours in several large series studies 2,3,4 and are most common in the second through fifth decades with a female predominance.4 They arise in bones formed by enchondral ossification. Since the bones of the vault are formed by membraneous ossification, these tumours are rarely found there. More common sites for these tumours are the skull base and the paransal sinuses. Rarely they occur below the tentorium in the cerebellopontine angle.5 Only very few cases of CPA chondroma have been reported. We present a new case of cerebellopontine angle chondroma and report the histological, CT and MRI appearance of the tumour.

Case History
A 41 year old nondiabetic, non hypertensive male was admitted in AHD hospital through neurosurgery OPD with the complaints of double vision for 10-15 years, occasional headache for 2-3 months, left eye watering with inability to open left eye, left sided weakness with disorientation for 1 month with no history of loss of consciousness (LOC), vomiting or convulsion. On examination, he was conscious with GCS of 15/15 both pupil equally reactive to light, bilateral planter reflex, pulse (100/min), BP-160/110, SPO2-99%, left eye watering and left sided weakness 3+/5. Left sided 5th motor cranial nerve weakness with bilateral Hoffman sign positive and exaggerated DTRs (Deep tendon reflex). His ophthalmology examination reveals, Visual acuity (B/E)-6/6, anterior segment (B/E): normal, Fundus (B/E): right eye-normal, left eye-hyperaemic disc. Schirmer’s test (B/E): O MM, 10P-12, perimetry- not significant.

Neuroradiological Findings
MRI shows a mass lesion occupying prepontine cistern, left CP angle with extension to left middle cranial fossa. Lesion was T1 hypo, T2 and FLAIR hyper intense (Fig. 1 and 2). The lesion was not restricted in diffusion weighted sequence and did not demonstrate susceptibility artifacts. There was no enhancement of the lesion in post contrast CT (Fig. 4) or MRI done outside. Nerve sheath tumour was unlikely. MRI in AHD showed the lesion was separate from Meckel’s cave. CT demonstrated erosion of left petrous apex and greater wing of sphenoid bone (Fig.3) MRI Spectroscopy showed no evidence of neuronal element. Provisional diagnosis was epidermoid vs neuro enteric cyst. Patient underwent left retromastoid sub-occipital craniotomy and removal of tumour was done.

Fig. 1: MRI coronal view(T2). A large hyperintense mass

Fig. 2: MRI axial FLAIR reveal hyperintense masss
Treatment of choice. The total surgical removal of the tumour is the epidermoid cyst. Meningioma with chondroid metaplasia and differential diagnoses include chordoma or chondroma is schwannoma. The other main differential diagnosis for CP angle MRI Spectroscopy showed no evidence of apex and greater wing of sphenoid bone (Fig. 3). CT demonstrated erosion of left petrous cave. MRI in AHD in post contrast CT (Fig. 4) or MRI done outside. Artifacts. There was no enhancement of the lesion sequence and did not demonstrate susceptibility was not restricted in diffusion weighted FLAIR hyper intense (Fig. 1 and 2). The lesion cistern, left CP angle with extension to left MRI shows a mass lesion occupying prepontine nerve complex, above 9th, 10th & 11th nerve complex. Tumour was epidermoid with vessel incised. Tumour partially excised, after haemostasis, duroplasty done and closed in layers.

Tumour tissue was sent for histopathology. Grossly, the specimen composed of multiple small grey white pieces of tissue. Microscopically, it reveal lobulated clusters of regular chondrocytes which was strongly immunoreactive for S-100 (4+) and non-immunoreactive for EMA (Fig. 5). Based on both histomorphologically and immuno histochemistry a diagnosis of CP angle chondroma was made.

**Operation note**

After craniotomy, dura was incised to 'K' shape. After CSF drainage from cerebello-medullary cistern, tumour was found anterior to 7th & 8th nerve complex, above 9th nerve complex. Tumour was epidermoid with vessel incised. Tumour partially excised, after haemostasis, duroplasty done and closed in layers.

Tumour tissue was sent for histopathology. Grossly, the specimen composed of multiple small grey white pieces of tissue. Microscopically, it reveal lobulated clusters of regular chondrocytes which was strongly immunoreactive for S-100 (4+) and non-immunoreactive for EMA (Fig. 5). Based on both histomorphologically and immuno histochemistry a diagnosis of CP angle chondroma was made.

**Discussion**

Intracranial chondromas usually arise at the skull base from embryonic chondrocytic cell remnants or from meninges from metaplastic meningeal fibroblasts. Less commonly they originate from the cerebral parenchyma. Only a few reports describe a chondroma at the CP angle.
Histogenesis of these lesions at the CP angle or within the brain parenchyma is not clear. Possible theories include cartilaginous metaplasia of mesenchymal perivascular cells, heterotopic chondrocytes, and cartilaginous displacement by trauma. Intracranial chondromas may be solitary or multiple, as a component of Ollier’s disease and Maffucci’s syndrome.

Our case possibly originated in the petrous bone and involved the CP – angle by direct extension. Neuroimaging reveals typical, but not characteristic features. In many cases calcification within the tumour is demonstrable. However calcification is rarely seen in cerebellopontine angle chondromas. Erosion and destruction of surrounding bone, hyperostosis of the inner table of the skull, cystic change, variable tumour density and patchy, delayed contrast enhancement are other features. The main differential diagnosis for CP angle chondroma is schwannoma. The other differential diagnoses include chordoma or menigioma with chondroid metaplasia and epidermoid cyst.

The total surgical removal of the tumour is the treatment of choice.

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Adult Patient Presenting Rare Brain Tumour-Gliosarcoma

Khalequezzaman S¹, Alam J², Ahsan S³, Khan BS⁴

Abstract
Gliosarcoma is a rare primary malignancy of the central nervous system, classified by the World Health Organization as a high-grade glioma and a variant of glioblastoma multiforme. A 57-year-old gentleman presented with a history of left-sided weakness and loss of appetite. Brain MRI was suggestive of right frontal and thalamic mass lesion with contrast enhancement at the periphery. Open biopsy examination revealed a malignant brain tumour presenting a biphasic tissue pattern with gliomatous and mesenchymal components suggestive of gliosarcoma. Although the treatment of gliosarcomas is almost similar to glioblastomas (surgical resection and, depending on clinical status, radiotherapy and/or chemotherapy) the prognosis of gliosarcomas remains poor.

Key words
Brain tumor, gliosarcoma

Introduction
Gliosarcoma is a rare primary malignancy of the central nervous system, classified by the World Health Organization (WHO) as a high-grade glioma and a variant of glioblastoma multiforme.¹ Gliosarcoma accounts for <2% of all gliomas and 5% of all astrocytomas. The tumour has a clinical presentation, natural history, and radiological profile similar to glioblastoma multiforme.

Case Report
A 57 years old right handed gentleman admitted in Apollo Hospitals Dhaka with the complains of difficulty in moving left lower limb for 1 month and loss of appetite for 2 months duration. He gave the history of fall 2 months back. He was hypertensive and non diabetic. No history of loss of consciousness or convulsion. At admission, his GCS scores were E4V5M6, muscle power was 3/5 on left side, 5/5 on right side.

Investigations at admission were normal for blood CBC, S. Creatinine, S. electrolytes, liver function tests and lipid profile.

He underwent MRI of brain which revealed 3.3 x 3.1 x 3.9 cm well defined lesion in right thalamic region with mild perifocal edema. The mass is hypointense on T1 WI and hyperintense

on T2 WI with hypointense rim (Fig.1-a,b). After contrast, which showed irregular rim enhancement and an enhancing thin septation (Fig.1-d). The mass causes mass effect as evidenced by compression on body of right lateral and 3rd ventricles with mild obstructive triventriculomegaly. Another smaller similar lesion was noted in right frontal lobe. InDiffusion weighted (DW) and Apparent Diffusion Co-efficient (ADC) sequences, cystic area was similar to CSF signal intensity (Fig. 2-a,b).

The conclusion of MRI examination was drawn as multi focal gliomas, however, other possibility of metastases could not be ruled out.

Fig.1: (a) T1 WI (b) T2 WI and (c) FLAIR sequences showing two similar rounded lesions in right thalamic region and frontal region. The mass is hypointense on T1WI and hyperintense on T2WI and FLAIR sequence. After contrast (d), it shows rim enhancement and enhancing thin septa within
Patient underwent CT scan of abdomen to search for any primary cause or metastases, but revealed no abnormality. His chest X-ray was unremarkable. PSA was within normal limit (1.3 ng/ml).

For uncertain diagnostic dilemma, patient underwent right fronto-parietal craniotomy and open biopsy of the right thalamic lesion was taken under GA. The material was grey brown. At biopsy, the section showed proliferation of anaplastic tumor cells displaying gliomatous as well as sarcomatous differentiation along with transition area. The spindle cells were forming fascicles and at places adenoid arrangement. The cells showed hyperchromatic nuclei with frequent mitoses and focal areas of necrosis. Gliosarcoma, WHO grade - IV, was diagnosed. The patient was discharged in a hemodynamically stable condition and advised to consult with radiotherapist as patient needs radiotherapy.

**Discussion**

According to the new WHO classification, gliosarcoma is defined as a glioblastoma variant, characterized by a biphasic tissue pattern with alternating areas displaying glial and mesenchymal differentiation. Gliosarcoma is a relatively rare malignant neoplasm accounting for approximately 2% of glioblastomas. Gliosarcoma occurs most commonly in adults in the fourth to sixth decades of life and men are more commonly affected than women (ratio 1.8:1). Anatomically, gliosarcomas are usually located in the cerebral cortex, and involve the temporal, frontal, parietal, and occipital lobes in decreasing frequency. The presenting symptoms depend on the location of the tumour. The aetiology of gliosarcoma remains uncertain, although it is recognized that gliomas can induce sarcomatous transformation in the supporting mesenchymal elements and irradiation of the central nervous system can induce malignant transformation of the brain parenchyma and the meninges, predominantly to fibrosarcoma. The appearance of gross gliosarcoma may be a poorly delineated...
peripheral greyish tumour mass with central yellowish necrosis stippled with red and brown from hemorrhage, and with the sarcomatous component producing a firm discrete mass. Histologically, the diagnosis of gliosarcoma is based on a biphasic tissue pattern comprising 2 distinct malignant cell populations, one component being gliomatous (fulfilling the criteria for glioblastoma) and the other with malignant mesenchymal differentiation (fulfilling the criteria for sarcoma). The glioblastoma part of the tumour forms heterogeneous infiltrative areas with hemorrhage and necrosis. The sarcomatous portion produces a firm discrete mass. At microscopy, the glial portions show the typical features of glioblastoma multiforme. Interestingly, the sarcomatous component can have varied histological features, ranging from the herringbone pattern of fibro-sarcoma to the malignant bone of an osteosarcoma and cartilaginous differentiate of chondrosarcoma. Single institutional data from Germany published in 2009 revealed only 16 patients treated over a period of 10 years (1997-2006). Another audit from an institute of India published in 2008 presents only 24 patients of gliosarcoma as compared to 251 cases of GBM treated over a period of 15 years (1990-2004). 16 cases of gliosarcoma was reported from pathology department of Aga Khan University hospital, Karachi, Pakistan in 2004. There are fewer than 20 reported cases of extracranial metastases of gliosarcoma with majority of them reflecting a tendency for haematogenous dissemination.

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The editorial board has decided to comply with “Uniform Requirements for Manuscripts Submitted to Biomedical Journals” published by the International Committee of Medical Journal Editors in Vancouver, British Columbia in 1979 (the widely accepted “Vancouver style”) published in the Annals of Internal Medicine 1982;96:766-71. All scientific units should be expressed in System International (SI) units. Authors are referred to Annals of Internal Medicine 1987; 106:114-29 for guidance in the use of SI units. All drugs should be mentioned in their generic form.
- Original articles, reviews, special articles, case reports and any other articles of medical interest are welcome.
- Should be typed in English and on one side of A4 (290 x 210cm) size white paper, using Times New Roman font, size 12, with double space.
- There should be one original and two paper copies and one IBM compatible electronic copy.
- There should be a margin of 2.5 cm at top and bottom and remainder.
- Pages should be numbered in English numerical at the upper right hand, consecutively, beginning with the title page.

Manuscripts should be submitted in the following order:
- Title page
- Abstract (should include background, objective, methodology, results, conclusion in short) with key words
- Text (Introduction, Materials & Methods, Results, Discussion, Conclusion).
- Acknowledgements
- References
Photographs:
- Unmounted glossy paper, 12.7x17.3 size
- Should be clipped to a white paper with appropriate labeling (number in English numerical, title of photographs and title of manuscripts.)

Illustrations:
- All illustrations should be cited in the text
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- Should not duplicate the text.
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Placement:
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References:
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Manuscripts Submission: the manuscripts should be submitted to the editor/ executive editors with a covering letter, mentioning that the work has not been published or submitted for publication anywhere else. (Both soft and hard copies). We are also going to open a new pulse email address.

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10 Years Achievements of Apollo Hospitals Dhaka

Apollo Hospitals Dhaka celebrated its amazing journey which started 10 years back as the first corporate Hospital in Bangladesh in 2005. As you read these lines we have stepped into a very successful 11th year of operation.

We have created entire spectrum of clinical services starting from Accident & Emergency, top end surgical specialties like Neuro and Cardiac Surgeries, Organ Transplant to just name the few clinical services.

We also boast of being the only hospital in Bangladesh to have achieved standardization by getting JCI accreditation three times in a row for last 7 years. This has gone long way in serving quality health care to the community.

This organization has left indelible mark on Health Care in Bangladesh. The reason is sheer dedication and compassion of our highly skilled care givers and vision and commitment of our Board of Directors. Their continuous strive to invest in state of the art technology; standardized care through highly skilled and qualified doctors and to manage the hospital through professionals has given this hospital the edge over other health care setting.

Since its inception 4,484,507 patients have registered with us and over 1,602,827 patients have availed out-patients consultation across all the specialties.

Our organization has pioneered the preventive health check program, in Bangladesh, which is now developed into very successful program and is providing robust screening services to the people of the country.

Over 48,553 successful surgeries have been carried out in the hospital till date, with excellent, outcomes due to stringent infection control practices in place and we are striving hard to stay on course.

As a responsible health care organization we also have designed and executed programs like Apollo Priyojan which is training program for volunteers to teach Basic Life Support – First Aid. Till date we have created close to 1000 volunteers.

Continuous investment in creating skilled manpower and capability enhancement is mantra of our organization. In this quest we have sent hundreds of staff for training programs - home and abroad. At the same time, we are enhancing our academic environment by bringing in more and more post-graduation programs recognized by the Bangladesh College of Physicians and Surgeon (BCPS).

Currently we have 11 specialties which have been approved for post-graduate training. This facilitates our future generation doctors to develop their careers as well as foster the culture of practicing evidence based medicine.

Some of our future expansion plan includes setting up of comprehensive Cancer Center by adding Radiation Oncology and PET CT. Also, we are expanding our dialysis and gastro units. Our Chittagong Hospital Project is underway and progressing very fast.

We are committed to the transparency and patient centric approach and produce comparable clinical outcomes to international bench marks. We will continue to service our patients and try to make a positive impact in their lives.
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Office of the Editorial in Chief : Department of Paediatric Surgery & Paediatric Urology
OPD Level – 5; Apollo Hospitals Dhaka
Phone: 880-2-8431661; Ext. 2525
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