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ORIGINAL ARTICLES

Estimation of Serum Trace Elements (Copper, Zinc, Magnesium) in Patients with Epilepsy Taking Antepileptic Drugs

AKM ANWAR ULLAH[1], SOHELA AKTHER[2], MD REZAUL KARIM KHAN[3], SHAMSHAD QURAISHI[4], MD NASIER UDDIN[5], ABDUL KADER SHAIKH[6], MD RAFIQUL ISLAM[7], SHAMSUN NAHAR[8]

Abstract

The objective of this cross-sectional comparative study was to determine the levels of copper (Cu), zinc (Zn) and magnesium (Mg) in serum from patients with epilepsy taking antiepileptic drugs. For this purpose, levels of these elements were measured in 30 patients with epilepsy and 30 healthy subjects. Element analyses were carried out by atomic absorption spectrophotometer (AAS).Decreased Cu^{++} levels were detected in serum of patients with epilepsy taking antiepileptic drugs compared to healthy controls (P<.001). The mean serum Zn^{++} and Mg levels were found to be unchanged in epileptic patients compared to control subjects. Our results demonstrate that some trace element levels may be altered in epilepsy patients taking antiepileptic drugs which may be an etiological factor or may play a role as precipitating factor or as aggravating factor or may be altered by antiepileptic drug or drugs used by the particular patient.

Introduction

Epilepsy is a one of the commonest serious neurological condition. It is a global problem and largest health economic burden in the world[1]. Epilepsy accounts for 1% of the world's burden of disease, the same as breast cancer in woman, or lung cancer in man[2]. The annual incidence of new cases of epilepsy is 20-70/1,00,000[3] population. Over two-thirds of all epileptic seizures begin in childhood (most in the first year of life), and this is the age when seizures assume the most array of forms[4]. Five percent of the population suffers a single seizure at sometime in life and 0.5% of the population has recurrent seizures and of which 70% are well controlled with drugs and 30% are at least partially resistant to drug treatment[5]. Epilepsy is more likely to occur in economically deprived groups, possibly because of pre-term birth, and of subsequent cranial trauma[6]. With appropriate treatment, three-quarters can be seizure free[7]. In Bangladesh there are

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deeply rooted prejudicial attitudes towards epilepsy. We do not have any national statistical data but hospital records[8,9] and our observations reveal that there are at least 12-15 million epileptics in Bangladesh.

Trace elements (e.g., Copper, Zinc and Manganese) are minor building components in tissues including the nervous system. The very complex balance of trace elements is crucial for all areas of maintaining human health, preventing as well as overcoming health problems[10]. The brain barrier system, that is, the blood-brain and blood cerebrospinal fluid (CSF) barriers, are important for trace element homeostasis in the brain[11]. The concentration of trace elements in cerebral tissue is not equal in all parts of the brain[12]. Trace elements play important functional roles in peripheral and central nervous systems[13-18]. Zinc, selenium, and copper are indispensable components for certain enzymes responsible for various metabolic processes in different tissues including the brain[19, 20].

Copper (Cu^{++}) is involved in a large number of enzymes which catalizes and oxidizes many reactions. Some studies reported relationship between the serum levels of Cu^{++} and Zn^{++} and CuZn-SOD activity and the serum concentration of Se2+ and GSH-Px activity in the group of healthy subjects[21]. Crl (a copper-binding protein) appears to have two antioxidant properties: firstly, it binds Cu^{++} and therefore prevents this transition metal from catalyzing hydroperoxide decomposition to radicals. Secondly, Crl oxidizes ferrous iron to ferric and concomitantly converts O2 to H2O, thereby inhibiting iron-dependent lipid peroxidation[22].

In the brain, Zinc (Zn^{++}) is abundant, after iron, the highest concentrations among all transition metals. Most of this brain zinc (approximately 90%) is bound up in metal-protein complexes. Many neurons in addition contain a significant amount of reactive ionic zinc. Within the telencephalon, zinc-containing fiber systems form vast association networks that reciprocally interconnects isocortical, allocortical, and limbic structures. Large amounts of chelatable Zn^{++} are concentrated also in the limbic region, notably in the hippocampus formation[23]. Approximately 10% of the total Zn^{++} in the brain, probably ionic Zn^{++} exists in the synaptic vesicles of what is known as zinc-containing neurons (a subclass of glutaminergic neurons) and is released in a calcium and impulse-dependent manner[18]. Because the hippocampal, amygdalar, and perirhinal regions are prominent nodes in this glutaminergic network, it is presumed that vesicular Zn^{++} is involved in modulation of neuronal excitability and in the synaptic plasticity of developmental and experimental learning[18]. Zn^{++} is a potent modulator of amino acid receptors (especially the NMDA receptor) and co-release of zinc along with glutamate would provide a mechanism for modulating postsynaptic excitability with little or no effect at physiological firing rates, but selectively depressing excitability (by NMDA-receptor depression) when firing rates reach dangerous, paroxysmal levels[18].

Manganese (Mn^{++}) is a component of the antioxidant enzyme manganese superoxide dismutase (MnSOD). Antioxidants scavenge damaging particles in the body

known as free radicals. These particles occur naturally in the body but can damage cell membranes, interact with genetic material, and possibly contribute to the aging process as well as the development of a number of health conditions. Antioxidants such as MnSOD can neutralize free radicals and may reduce or even help prevent some of the damage they cause.

Deficiency and excess amount of these trace elements play an important role in several well recognized diseases[24], studies are going on to establish their role in epilepsy. Antiepileptic drugs alter metabolism and distribution of blood trace elements like Zinc, Copper and Magnesium[25].

With a view to the above facts and controversies regarding the role of trace elements in pathogenesis of epilepsy we have conducted a case control study to observe the role of trace elements Zn^{++}, Mg^{++} & Cu^{++} among Bangladeshi population as no such study was carried out previously in Bangladesh.

Materials and Methods

This is a cross sectional comparative study which was carried out in Neurology Department of' Bangahandhu Sheikh Mujib Medical University (BSMMU), Dhaka and Atomic Energy Commission (AEC), Dhaka during 01-07-2003 to 31-12-2003, 30 epileptic patients of idiopathic in nature and 30 age and sex matched apparently healthy volunteers having no history of fit were selected as controls from Neurology Out Patient Department of BSMMU, Dhaka and blood samples for trace elements were analyzed at AEC, Dhaka.

The detailed clinical history was taken and proper physical examination was done for each and every subject initially by a medical research officer and this was checked by principal investigator. Blood for TC, DC, Hb% & ESR; Urine RME; Blood sugar; Blood urea and other necessary investigations were done whenever indicated. EEG was done in each subject. CT scan/MRI of brain was done if indicated to exclude structural brain lesion. The cases were recorded in a printed proforma.

Under all aseptic procedure 5 ml of venous blood was collected from antecubital vein in a heparinised test tube and estimation of trace elements was done by atomic absorption spectrophotometer.

Appropriate statistical analysis like mean, SD was done. The statistical analysis was done by software program SPSS version 12 and unpaired t test was used to compare between group means and $p<0.05$ were taken as minimum level of significance.

Results

This study included sixty patients. Thirty epilepsy patients were recruited from the out-patient epilepsy clinic of the Neurology Department of Bangahandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Thirty age and sex matched apparently healthy volunteers having no history of fit had been selected as controls from Neurology out Patient Department of BSMMU.

Mean (±SD) age of control group was 16.97(±5.75) and that of case group was 16.23(±5.47).

Table-I

Age distributions (in years) of the patients both in case and control groups

Groups	Minimum	Maximum	Mean	Std. Deviation
Control	8.00	27.00	16.9667	5.75046
Case	7.00	27.00	16.2333	5.47523
Total	7.00	27.00	16.6000	5.57902

In control group, 19 patients were male and 11 were female and in case group 20 patients were male and 10 were female.

Table-II

Sex distribution of the patients both in case and control groups

Groups	Sex		Total
	Male (%)	Female (%)	
Control	19(63.3%)	11(36.7%)	30(100.0%)
Case	20(66.7%)	10(33.3%)	30(100.0%)
Total	39(65.0%)	21(35.0%)	60(100.0%)

The control group exhibited significantly higher levels of Cu^{++} compared to case group (P<0.001) (Table-III). No difference was observed in the levels of Zn^{++} and Mg^{++} in the two groups (P<0.001) (Table IV and V).

Table-III

Distribution of cupper in case and control groups

Groups	Mean	Std. Deviation	P-value
Control	1.15	0.34	<0.001
Case	0.84	0.25	

Table-IV

Distribution of zinc in case and control groups

Groups	Mean	Std. Deviation	P-value
Control	0.98	0.35	
Case	0.97	0.35	>0.05

Table V

Distribution of magnesium in case and control groups

Groups	Mean	Std. Deviation	P-value
Control	19.28	4.84	<0.001
Case	17.29	4.50	

Discussion

In this study, the epileptics exhibited very significantly lower level of serum Cu^{++} than non-epileptic subjects (P<0.001).

Olatunbosum et al[26] recorded an increase in serum copper level in epileptics. Liu et al[27] and Shah *et al.*[28], reported normal serum Cu++ levels in different groups of epileptics included in their study. Our finding is not consistent with these findings.

Brunia and *Buyze* found the concentration of copper (Cu^{++}) in the serum was significantly higher in the patients than in the controls ($p < 0.01$)[30]. Our finding is not similar with this finding.

Tutor-Crespo[30] found that chronic administration of antiepileptic drugs (phenobarbital, phenytoin, carbamazepine or valproic acid) does not produce marginal or moderate copper deficiency.

Abdullah *et al.* and Pippenger *et al* reported lower levels of serum Cu^{++} in untreated epileptics[31,32]. Kaji *et al.*[33] and Hurd *et al.*[34] reported low serum Cu++ levels in sodium valprote (VPA) treated epileptics. In contrast, Kuzuya *et al.*[35], Sozuer *et al.*[36], and Motta *et al.*[37] reported significant increased levels of Cu^{++} in patients who were treated with single antiepileptic drug (AED) carbamazepine (CBZ), phenobarbitone (PB) and VPA and this was attributed to the influence of AEDs on the serum Cu^{++} and Crl concentrations by hepatic enzymes induction. This finding is not consistent with our finding.

In our study, the epileptics did not differ significantly in serum Zn^{++} level with non-epileptic subjects (P>0.05).

No relation was observed among $Zinc^{++}$ and epilepsy with AEDs monotherapy by some authors[36]. This finding is consistent with our study.

In Sherifa *et al.*[38] series the untreated epileptics exhibited normal Zn^{++} levels and the VPA treated epileptics showed significantly higher level of Zn^{++}. This finding is dissimilar with our study.

Kuzuya *et al.*[39] reported lower levels of Zn^{++} in patients who were treated with mono-AEDs (CBZ and VPA) with no dose related changes. Yuen *et al.*[40] reported normal levels of Zn^{++} in white blood cells of epileptic patients on VPA or CBZ. They suggested that AEDs might affect the intracellular Zn^{++} level concentrations. Steidl *et al.*[41] reported significant lowering of serum Zn^{++} in patients treated with AEDs for <5 years. Lerman-Sagie *et al.*[42] reported reduced erythrocyte Zn^{++} content in their epileptics. In the prospective study done by Altunbasak *et al.*[43] the serum and hair levels of Zn^{++} were found to be higher in untreated epileptic patients than those treated with VPA and controls and returned to normal level after VPA treatment.

Kürekçi *et al.*[36] reported higher levels of Zn^{++} in treated groups of patients that remained within the normal range and attributed this to the normal physiological variation in serum Zn^{++} concentrations (circadian variation) and is unlikely related to the anticonvulsant drugs or epilepsy[44, 45]. Others attributed the increased serum Zn^{++} levels to measuring such levels at least 2 hour later than VPA intake, that is, at the peak of VPA concentration[46].

In our study, the epileptics did not differ significantly in serum Mg^{++} level with non-epileptic subjects (P>0.05).

Hoffman found the same result as our study, he stated that there is no statistically significant difference between the Mn^{++} serum levels for epileptic and non-epileptic children as well as for epileptic adults and non-epileptic adults[47]. No relation was also observed in Manganese and epilepsy with AEDs monotherapy[37].

In other study, plasma Mn^{++} level in patients receiving AEDs were unchanged[32, 42, 48,49].

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Psychiatric Morbidity in Hansen's Disease

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Summary

The primary aim of this study was to investigate psychiatric morbidity among the patients with Hansen's disease or leprosy. A total of 100 leprosy patients were examined at Leprosy Hospital, Mohakhali, Dhaka from March 2005 to September 2005. They sought medical treatment voluntarily and were selected consecutively on the basis of defined criteria. Research instruments were interviewer-administered questionnaire and BDI, and other standard mental state examination criteria. Of the 100 leprosy patients, 58.0% were literate and 42.0% were illiterate. Regarding current profession, most of the female leprosy patients had no occupation except household works. Among the male leprosy patients, majority of them have had particular occupation in which 15.8% were service -holders, 18.4% were students, 18.4% were cultivators, 15.8% were businessmen, 13.2% were day-labourer and rest were unemployed. Fifty percent of the leprosy patients were the members of low economic class, 48.0% were of middle economic class and rest were high economic class of population. Majority of the leprosy patients were adolescent and young adults, age ranging from 16-35 years. Regarding marital status, 72.0% of them were married and 28.0% were found to be unmarried. Fifty-four percent of them were living in rural communities and 46.0% in urban areas. In the assessment of co-morbid mental problems, results showed that they were living with leprosy patients for 2-18 years. Most of them (79.0%) have been suffering from major depressive disorders (MDD). Twelve percent were suffering from generalized anxiety disorders and 6.0% from dysthima. Only 3.0% have had no psychiatric problems. In conclusion, in combination with medicines, motivational enhancement therapies can be the only applicable way to perform better management of the leprosy patients in Bangladesh.

Introduction

Hansen's disease is a public health hazard all over the world, particularly in developing countries it becomes a critical national health crisis[1]. Worldwide, nearly 4 million people have or are permanently disabled as a result of leprosy[2,3]. Mycobacterium leprae, the causative agent of leprosy, can remain viable in dried nose secretions and in moist soil at room temperature for 46 days. It is more prevalent in the warm and humid climates. Crowding, poor sanitation, malnutrition and unhygeinic environmental conditions seem to favour its transmission[1]. Skin to skin or airborne transmission is most probable route of transmission and humans are the only host in most countries. In Southeast Asia, leprosy is endemic in India (2.6 per 10,000 population) and Nepal (3.1 per 10,000 population) where 70% of the world's leprosy patient live in[2,4].

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In Bangladesh, Hansen's disease becomes a public health problem with an estimate of 0.51 per 10,000 populations and in endemic areas it is 10.0[4-6]. At present (2008) it may be increasing with time. The environmental factors that favour M. *leprae* transmission are extremely prevalent in Bangladesh. In addition, intercountries human trafficking and tourism between India, Nepal and Bangladesh is remarkably high.

In Bangladesh, as due to strong religious impact and backward social tradition, leprosy and leprosy related matters are not discussed freely in the community. There is a social stigmatism; leprosy is a curse of God. People who have the disease are often thought of as unclean, scary, or are believed to have done something bad to deserve this punishment. They perceived it is an affliction for which people hated and feared them. They should be segregated from their family and society. Therefore, people who suspect that they might have the disease keep it secret so that their families, friends, communities, and employers will not ostracize them[4-6]. The result of this stigmatization may develop disturbance in thoughts, feelings and perceptions of the people *who* suspect leprosy or *who* have been suffering from leprosy and follow by the progress of mental disorders such as anxiety, depression, and phobia etc[1]. Psycho-education and psychotherapy, in addition to pharmacotherapy, seems to be key intervention in the enhancement of treatment and improvement of long-term outcome in several medical conditions such as leprosy, cardiac illness, diabetes, cancers etc[7]. In Addition, behavioral therapies, psycho-education, family and social participation jointly can overcome social stigmatism, can learn to control their crisis and be trained to maintain their normal and productive life in family or in work place or in the community.

Update treatment facilities in leprosy endemic areas is very inadequate in Bangladesh. A little information about leprosy may be obtained from government or nongovernment organizations. Even there is not, so far known, a single scientific study on mental health of the patients living with leprosy in Bangladesh. However, it is necessary to initiate scientific study on mental health in leprosy, because once their mental state assessment data has been collected, a plan for effective treatment and prevention modality against leprosy can be established. International studies shows that the beliefs and practices engendered by the intense stigma associated with leprosy in traditional-bound country like India, Bangladesh are likely to affect the mental health of the patients living with leprosy[8]. In addition, most of the psychological therapies report positive results on maintenance when used as an adjuvant treatment, and efficacy in chronic illnesses[7]. Therefore, the aim of this study and in continuation of research in this field was to include psychiatric morbidity in Hansen's disease.

Subjects and Methods

Study population

The research participants were leprosy patients admitted in Leprosy Hospital, Mohakhali, Dhaka from March 2005 to September 2005. A total of 100 leprosy patients, 76 male and 24 female, were included in this study. They were selected consecutively on the basis of defined criteria include confirmed diagnosis of leprosy by clinical and pathological investigations, age in between 16-60 years and did not suffer from other diseases. Research instrument was an interviewer-administered questionnaire and standard mental state examination criteria.

A questionnaire was developed and pre-tested among admitted leprosy patients, who were excluded from the study population. It was designed to include general information, socioeconomic profile and mental state examination criteria. The socioeconomic profile included education, occupation, income class, age, marital status and social background. The mental state examination criteria included period of suffering, mood/affects, motor activity, speech, judgement, sleep, food habit, anxiety, sexual dysfunction, behaviour, perception, thought, attention & concentration, orientation, memory and insight.

Initially a psychiatrist briefed objectives, benefits, risks and burdens of this study to the admitted leprosy patients and their close relatives. Only positive respondents were selected as research participant consistent with the selection criteria. A written consent was taken from each of the selected patients with maintaining full autonomy. Then socioeconomic profile was recorded following the questionnaire. Finally, two psychiatrists including author(s) were assigned psychiatric diagnosis according to DSM-IV and other standard criteria[9-12]. In addition, comorbid psychiatric diagnosis was also considered. Of them, who had been diagnosed as depressive illness. Beck Depressive Inventory (BDI) criteria were applied to quantify the depression[13]. Each of the participants was examined individually in a separate room for maintaining their privacy strictly as well. In addition, close relatives were also interviewed, if necessary, to confirm the symptoms of mental troubles. The study did not involve in any social, mental or physical risk to the patients. Prior to conduct, institutional permission was taken from the director of the hospital. As leprosy patients are vulnerable, the procedures followed for this study were in accordance with the CIOMS guidelines as updated in 2002[14]. No wedge-compensation was given to the participants.

Statistical analysis

A software package of SPSS (version 12.0: SPSS Inc., Chicago, IL, USA) was used for analysis of the data. Descriptive statistics was used for all variables. Values were expressed as percentage.

Results

Socioeconomic profile of the leprosy patients is summarized in the Table-I. Of the 100 leprosy patients, 58.0% (n-58) were literate and 42.0% (n-42) were illiterate. Among literate leprosy patients, 30.0% (n=30) were educated upto secondary level, 12.0% (n-12) were upto primary level, 6.0% (n-6) were upto higher secondary level and rest (10.0%, n=10) were graduate or postgraduate. Comparatively, prevalence of illiteracy is higher in female leprosy patients than male (Table-I). Among current profession, most of the female leprosy patients had no occupation except household works. Among the male leprosy patients, majority of them have had particular occupation in which 15.8% (n-12) were service-holders, 18.4%(n-14) were students, 18.4%(n-14) were cultivators, 15.8%(n-12) were businessmen, 13.2%(n-10) were day-labourer and rest (18.4%,,n=14) were unemployed. Fifty percent (n-50) of the leprosy patients were the members of low economic class (monthly income <Tk. 10,000) of population, 48.0% (n-48) were of middle economic class (monthly income Tk. 10,000-20,000) and only 2.0% (n-2) were high economic (monthly income >Tk. 20,000) class of population. Majority of the leprosy patients 58.0% (n-58) were adolescents and young adults having age from 16-35 years, 18.0%

(n-18) were adults of 36-45 years of age and rest 24.0% (n-24) have age above 45 years.

In marital status, 72.0% (n-72) of them were married and 28.0% (n-28) were found to be unmarried. Fifty-four percent (n-54) of them living in rural areas and 46.0% (n-46) in urban areas (Table-I).

Table-I

Socioeconomic profile of the leprosy patients

Parameters	Male (n=-76) % (n)	Female(n=24) % (n)	Total (n=100) % (n)
Education			
Illiterate	38.2(29)	54.2(13)	42.0(42)
Primary (1-5 class)	10.5(8)	16.7(4)	12.0(12)
Secondary (6-10 class)	35.5(27)	12.5(3)	30.0(30)
HSC (11-12 class)	5.3(4)	8.3(2)	6.0(6)
Above 12 class	10.5(8)	8.3(2)	10.0(10)
Occupation			
Households	0	83.3(20)	20.0(20)
Service	15.8(12)	16.7(4)	16.0(16)
Students	18.4(14)	0	14.0(14)
Cultivators	18.4(14)	0	14.0(14)
Business	15.8(12)	0	12.0(12)
Day labourers	13.2(10)	0	10.0(10)
No works	18.4(14)	0	14.0(14)
Economic class			
Low	46.1(35)	62.5(15)	50.0(50)
Middle	51.3(39)	37.5(9)	48.0(48)
High	2.6(2)	0	2.0(2)
Age in year			
16-25	34.2(26)	33.4(8)	34.0(34)
26-35	25.0(19)	20.8(5)	24.0(24)
36-45	15.8(12)	25.0(6)	18.0(18)
>45	25.0(19)	20.8(5)	24.0(24)
Marital status			
Married	68.4(52)	83.3(20)	72.0(72)
Unmarried	31.6(24)	16.7(4)	28.0(28)
Social background			
Rural	46.1(35)	79.2(19)	54.0(54)
Urban	53.9(41)	20.8(5)	46.0(46)

1. Income group
Lower income: Monthly income < Tk. 10,000.
Middle income: Monthly income Tk. 10,000 - 20,000.
Higher income: Monthly income >Tk. 20,000

Table II

Psychiatric morbidity among leprosy patients

Psychiatric morbidity	Male (n=76) no. (%)	Female(n=24)) no. (%)	Total (n=100) no. (%)
Period of suffering in years			
1-5	69.7(53)	45.8(11)	64.0(64)
6-10	21.1(16)	25.0(6)	22.0(22)
11-15	7.9(6)	16.7(4)	10.0(10)
15-18	1.3(1)	12.5(3)	4.0(4)
Psychiatric disorders			
Major depressive	75.0(57)	91.7(22)	79.0(79)
Generalized anxiety	13.2(10)	8.3(2)	12.0(12)
Dysthima	7.9(6)	0	6.0(6)
No psychiatric disorder	3.9(3)	0	3.0(3)

In the assessment of psychiatric disorders including comorbidity of the leprosy patients, results showed that they are living with leprosy for 2-18 years. Most of them (79.0%; n-79) suffering from major depressive disorders (MDD). Twelve percent (n-12) were suffering from generalized anxiety disorders and 6.0%(n-6) from dysthima. Only 3.0%(n-3) have had no psychiatric problems. Among the female leprosy patients, more than 90% were found to be suffering from depressive illnesses. None of them were free from anxiety and worries. Symptoms of other mental disorders did not found in studied leprosy patients. Results of the co-morbid mental problems among the leprosy patients are described in the Table-II.

Discussion:

Social stigmatism, warm and humid climates, poor sanitation, malnutrition, unhygeinic environment and crowding are the major influencing factors for spreading of leprosy, which are highly prevalent in Bangladesh. People living with leprosy or any other chronic diseases are the victim of social infernos of stigmatisms that results suffering of mental disturbances. The Hansen's disease as well as social stigmatisms in Bangladesh critically affects physical, mental and social health of the patients. Government of Bangladesh in joint collaboration with World Health Organization (WHO) has undertaken multiple preventive measures against this human catastrophe[4]. It is one of the major causes of human's disability in leprosy endemic countries including Bangladesh. In light of the incidence of disability and fatality associated with leprosy, the present study was undertaken to investigate the mental disturbances of the patients living with this disease.

The Leprosy Hospital, Mohakhali, Dhaka, the only specialized public hospital for leprosy patients in Bangladesh, presents

a special opportunity to study a variety of mental problems of the leprosy patients in a semi-controlled environment. There is a shortcoming; compliance with mental treatment regimens are not available in the hospital. It is well established that scientific evaluation and enlightened motivated attitudes towards chronic diseases including Hansen's disease might have abolish the forcible incarceration of the patients from pejorative languages and social stigmatisms. It may be aware of the patients to the concomitant loss of many of their civil rights[15]. In addition, it helps in the development of faithful adherence of the patients to the treatment schedules.

In this study, it has been found that most of the leprosy patients have been suffering from major depressive illnesses, anxiety disorder and dysthimic problems. There are many factors that may be attributed for major depressive disorder and other mental illnesses. The most important factor was the diagnosis of Hansen's disease which altering the emotional effect of the patients and/or family members. Initially, they harboured a considerable degree of negative attitude towards their illness. They perceived it was an affliction for which people hated and feared them. However, after diagnosis, the patients go through a sequence of reactions: denial, anger, bargaining, and acceptance. In addition, general population begins to outcast, shunt and fears them and too frequent hurt them with pejorative languages. All of these factors critically influences the self-efficacy and attitudes of the patients and increasingly fail to perform effective coping with these negative manners of the disease. They begin to belief that their disease will not cure, ultimate consequence will be disability and it is the curse of God. These unpleasant negative emotional state and social stigmatisms may be the important contributing factors in the development of anxiety and worries followed by depression and major depressive disorders, and other mental illnesses. Similar mental characteristics of the leprosy patients are consistent with reported data[8-15].

Only 10.0% of the leprosy patients were found to be graduates or post graduate level of education and most of them still in service. Forty-eight percent of them had basic education (primary to higher secondary) and professionally they have no capacity to get a satisfactory occupation. Few of them were small businessmen or cultivators or other inequitable profession. It, possibly, may be due to economical predicament of the nation or social infernos. Most of the female leprosy patients were illiterate and household works were their principal occupation, and most of them had no income. Patriarchal society, religious belief, social stigmatisms as well as conventional socio-cultural impact may be the important contributing factors for such type of socioeconomic characteristics of the women in Bangladesh. Majority of the leprosy patients were married and their social background as well as other socioeconomic profile are consistent with the reported national statistical data[16].

In conclusion, this study revealed that most of the patients living with leprosy have been suffering from depressive illnesses and anxiety. In combination with medication and motivational enhancement therapies such as counseling, behavioural therapies and family counseling can be the only applicable way to perform better management of the

leprosy patients in Bangladesh[17]. It needs to ensure easy availability of the mental healthcare services in every leprosy hospitals.

One of the shortcomings of this study is to include only 100 patients from one hospital. The reason of it is that there is no other public hospital for leprosy patients in Bangladesh. A few Christian Missionary Hospitals are in the hilly remote areas where leprosy treatment facilities are available. Fund constrian and lack of transport facilities limited us to study in this public hospital only. However, it is the first attempt to address mental health of the leprosy patients in Bangladesh.

Acknowledgement

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The Surgical Management of Trigeminal Schwannomas

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Introduction:

SCHWANNOMAS are tumours of the nerve sheath that usually exhibit benign behavior[1,2].

Benign trigeminal schwannoma of the trigeminal nerve comprises only 0.2% to 0.4% of all intracranial tumours and primarily arises in the gasserian ganglion[2,3]. Trigeminal schwannomas are benign tumours of Schwann cell origin, are relatively rare and much less common than acoustic neuromas[3].

Most trigeminal schwannoma (neurinomas) irrespective of the site of spread have an association with this region of the nerve[2,3]. The tumour grows larger and spreads in the available spaces[3].

The Meckel's cave can accommodate a large amount of the tumour, which bloats up the cave[4]. The tumour being soft is unable to open up the dural sheath beyond the ganglion into the roots. This may be the reason that in most of the cases tumour does not extend beyond the dilated cave[4,5]. The tumour presses the adjacent normal fifth nerve, most of which is clinically involved by direct pressure of the tumour[7]. In the posterior fossa the trigeminal neurinomas are located intradurally[7]. The part in proximity to the brain stem is in most cases like any other extra-axial tumour with a well-defined plane of cleavage[5]. In general these tumours involve the adjoining cranial nerves, blood vessels and brain only by displacement and not by invasion[4,5].

We retrospectively analyzed the clinical profiles of 6 patients who were surgically treated for trigeminal schwannomas. The aim of this study was to analyze the presenting clinical and radiological features of these tumours, to establish factors that might affect surgical decision-making, to critically evaluate the appropriate surgical route, depending on tumour location, and to assess the long-term outcomes after radical tumour resection.

Surgical Anatomy

Recent advances in understanding the microsurgical anatomy of skull base structures are hallmarks of modern neurosurgery[6]. The trigeminal nerve has an extensive anatomic course[5,6]. Comprehensive knowledge of trigeminal nerve anatomy facilitates understanding of the relationship between the brainstem, skull base, and facial area[6]. The trigeminal nerve trifurcates into ophthalmic, maxillary, and mandibular (division) nerves distal to the trigeminal ganglion[6]. The ophthalmic nerve passes forward in the lateral wall of

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the cavernous sinus. It gains access into the orbit via the superior orbital fissure. The ophthalmic nerve then divides to supply ipsilateral sensation to the eyeball, lacrimal glands, conjunctiva, part of the nasal mucosa, skin of the nose, eyelids, and forehead[4,6].

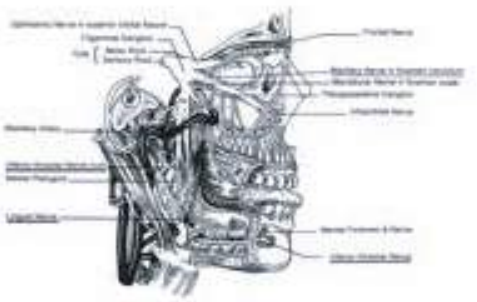

Fig. 1: *Shows the anatomical distribution of trigeminal nerve.*

Classification of Tumour Extension

Trigeminal schwannomas may originate from the root, the ganglion, or the peripheral branches of the trigeminal nerve[8]. Jefferson initially divided these tumours into 4 groups depending on their anatomical location: Posterior fossa (Root type), Combined posterior fossa–middle fossa (Dumb bell type), Middle fossa (Ganglion type), and Peripheral (Division type)[8].

Samii et al[13]. classified the tumour extension into 4 categories based on radiological findings: Type A, intracranial tumour predominantly in the middle fossa; Type B, intracranial tumour predominantly in the posterior fossa; Type C, intracranial dumb bell-shaped tumour in the middle and posterior fossa; and Type D, extracranial tumour with intracranial extensions[13].

Methods:

This series includes 6 patients who were surgically treated between 2005 and 2008 at our institution. No patients received a diagnosis of Neurofibromatosis type-2 (NF2).

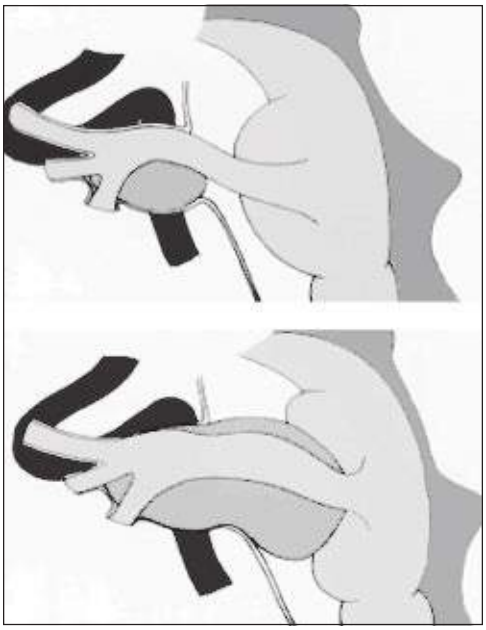

Fig. 2, 3 : *Shows the direction of growth of trigeminal schwannoma.*

Results:

Total tumour excision was possible in 4 patients, whereas total removal were not achieved in 2 patients. The extent of resection was graded according to the surgeons' impressions, confirmed by postoperative imaging in all patients. "Total" resection was defined as complete resection of the tumour and its capsule. "Radical subtotal" was assigned to the resection when tumour capsule fragments remained on vital structures. When the tumour capsule remained in the cavernous sinus or on the brain stem, the resection was graded as "subtotal"[2,3]. Out of the six patients one undergone subtotal resection, two patient required a staged procedure with a large dumb bell type lesion. There were no operation related death or mortality.

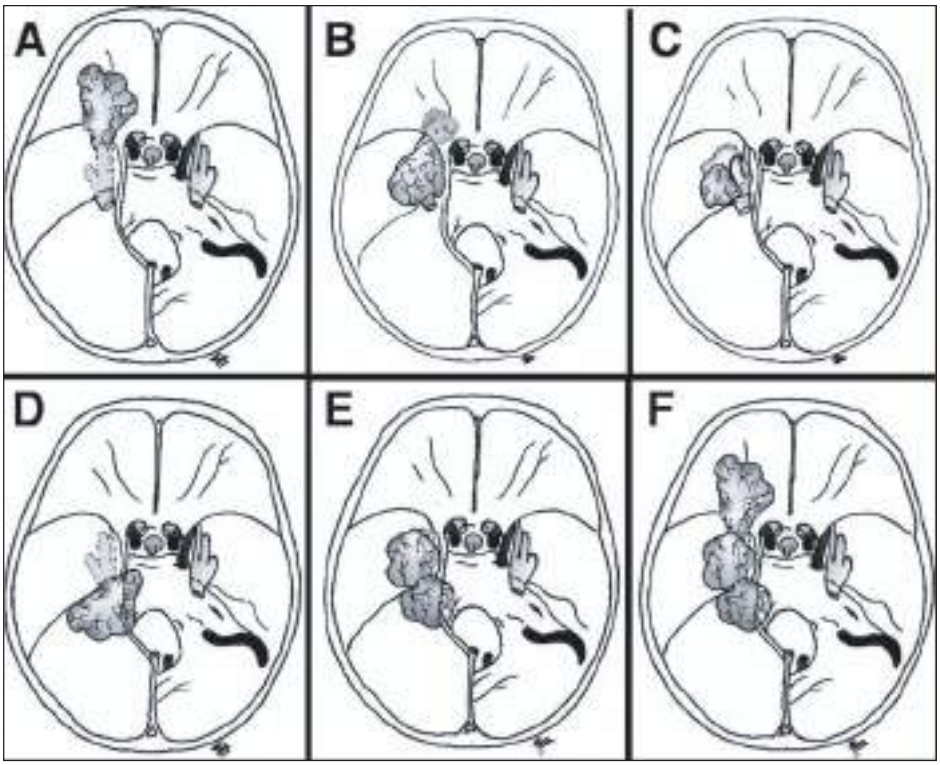

Fig.-3: *Drawings showing the 6 types of Trigeminal schwannomas (TS). A: Large extracranial TS with a small middle fossa extension (Type A). B: A TS with its main portion in the middle fossa and a small extracranial extension (Type B). C: A middle fossa TS (Type C). D: A posterior fossa TS (Type D). E: A TS with middle and posterior fossa extensions (Type E). F: A TS with extracranial, middle,and posterior fossa extension (Type-F).*

Table-I

Results of surgical procedures and outcomes after surgery of patients with TSs.

Operative approaches	Number of Patients (%)
Retrosigmoid approach	3 (50%)
Subtemporal transtentorial approach	3 (50%)
Subtemporal interdural approach	2 (33.3%)
Fronto-temporopolar extradural approach	1 (16.6%)
Operative Outcomes	
Total resection	4 (66.6%)
Radical subtotal resection	1(16.6%)
Subtotal resection	1 (16.6%)
Recurrence	Nil
Operation related death	Nil

"Functional outcome was assigned a grade of 'excellent' if the patient returned to his or her preoperative employment and was living independently[2]. It would be preferable to compare the real functional outcome (i.e., according to the functions of the fifth nerve and/or other neural structures of the neighbouring areas)[2]. Hence, an excellent result is achieved when there are no new neurological deficits[2].

Discussion:

Trigeminal neurinomas are relatively rare tumours and represent 0.2% of all intracranial tumours[1,2,9,11]. They usually arise from the Schwann cells of the sensory root and can originate in any section of the fifth cranial nerve and correspondingly a variety of symptoms and signs may develop[2,5,7,9].

Table-II

Shows the distribution of cases

Case no	Age/ sex	Presentations	Location	Name of operation	Complications	Follow up
1.	28/F	Headache , facial hypoaesthesia	Middle fossa	Fronto-temporopolar extradural approach	No	Lost from follow up
2.	55/M	Deafness, facial hypoaesthesia, ataxia	Posterior fossa	2 stages 1. retrosigmoid approach 2. subtemporal transtentorial	No	3 years no recurrence
3.	35/M	Headache, visual blurring,	Combined	Extended subtemporal transtentorial approach	3rd nerve palsy, tinnitus	2 years, no recurrence
4.	25/M	Facial hypoaesthesia, facial asymmetry due to atrophy of muscles.	Middle fossa	Subtemporal interdural approach	No	1 year, no recurrence
5.	12/F	Ataxia, deafness, respiratory distress, dysphagia.	Combined	2 stages 1. Retrosigmoid approach 2. subtemporal and retrosigmoid approach	Facial palsy, exposure keratitis, dysphagia	3 months
6.	35/M	Dysphasia, facial asymmetry,	Combined	Extended subtemporal approach	No	3 months
7	30/M	Temporalis muscle atrophy, ataxia, dysphagia,	Combined	Right extended subtemporal approach	Nil	3 months

Clinical Presentations:

There was significant sex variation in our series, with the male/female ratio being 2:1. The age of presentation ranges from 12 years to 55 years.

The clinical presentation was usually in the form of paresthesia or numbness, often in more than one division of the nerve. Severe or neuralgic pain was uncommon and was not observed in any of the cases. Wasting of the temporalis and pterygoid muscles were common and occurred in 66.6 % of cases. The corneal reflexes were depressed or absent in all patients. The symptoms of involvement of adjacent cranial nerves in the cavernous sinus and in the cerebellopontine angle have been frequently reported in 2 cases. These symptoms probably because of the large sizes of the tumours encountered in this series. The large tumour size was also responsible for the relatively infrequently encountered symptoms of increased intracranial pressure and ophthalmoscopically demonstrated papilloedema, which were observed in 4 cases (66.6%). One patient demonstrated contralateral hemiparesis and pyramidal signs related to severe compression of the brainstem. The unusual symptom of pathological laughter was observed in one case of large, dumb bell-shaped tumour. The clinical features of slowly progressive symptoms and the predominant presence of trigeminal nerve-related symptoms of numbness and muscle wasting are usually diagnostic[5,7].

Table-III

Preoperative clinical symptoms in 7 patients with TSs

Symptom	Number of Patients (%)
Trigeminal hypoesthesia	6 (100%)
Facial pain	4 (66.6%)
Headache	3 (50%)
Hearing symptoms	3 (50%)
Hemiparesis & increased ICP with papilloedema	2 (33.3%)
Diplopia	2 (33.3%)
Ataxia	2 (33.3%)
Pathological laughter	1 (16.6%)
Seizure	Nil

Radiological Features

Erosion of the petrous apex, as noted on plain x-rays or computed tomographic scans, was uniformly observed for larger tumours, and this finding was of diagnostic significance[5,7]. (Fig-4).

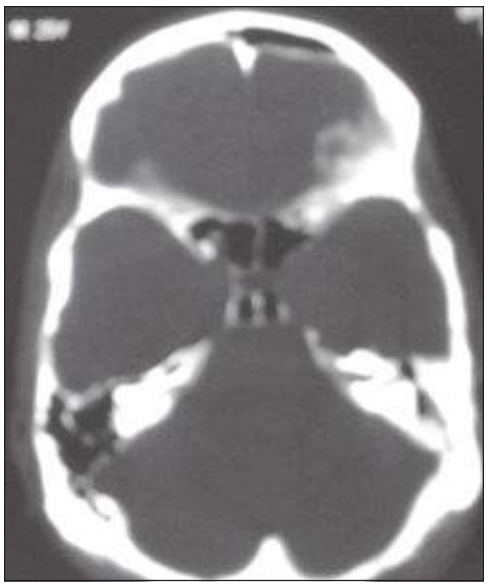

Fig.-4: *Shows erosion of petrosal apex on left side.*

Lesions are usually isodense on unenhanced CT but may reveal variable attenuation. There is usually homogenous enhancement with contrast[9,11]. Because of its multiplanar capability, exquisite anatomic detail, and characteristic tissue signal intensity, MRI is helpful in the differential diagnosis of primary tumours of the trigeminal nerve and Meckel's cave, and in the evaluation of tumour involvement for preoperative planning[7,9]. MRI with contrast enhancement is preferable to CT scanning because of multiplanar capability and absence of Hounsfield artefact from the skull base[11,14]. In addition MRI is sensitive for detection of additional neuromas, which is a consideration in neurofibromatosis (NF2) patients[5,6].

Trigeminal schwannomas show homogeneity on *T*1-weighted images and variable heterogeneity on *T*2-weighted images with prolongation of *T*1 and *T*2 relaxation times[5,7]. There is usually intense heterogeneous enhancement with gadolinium. MRI signal characteristics are similar to those of acoustic schwannoma; the key to this diagnosis is the neuroanatomic localization along the fifth nerve pathway[5,7,11,13].

The postcontrast *T*1-weighted image (Fig.-5) reveals a mass lesion in the left cerebellopontine angle extending anteriorly. The lesion is predominantly hyperintense on *T*2-weighted image (Fig.-6), and enhances homogenously with CT of the skull base shows the grossly enlarged left foramen ovale[5,9].

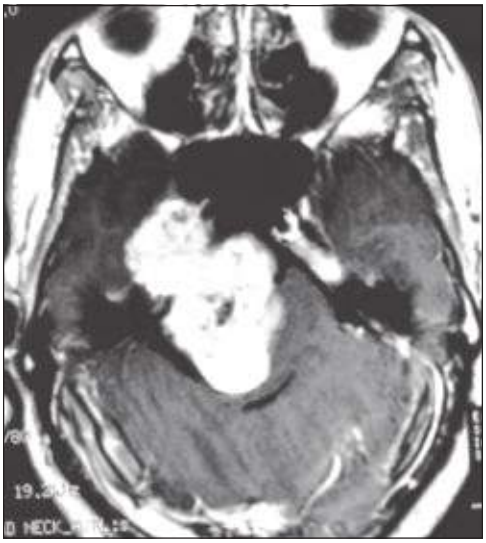

Fig.-5: *Shows bright homogenous contrast enhancement.*

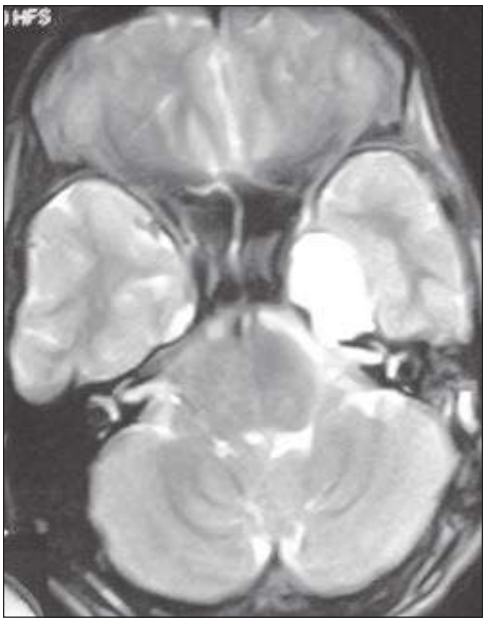

Fig.-6: *Shows hyperintensity in T2WI.*

The characteristic anatomical location, extent, and signal characteristics make the diagnosis of trigeminal nerve schwannoma almost certain[3,5,8].

Although there have been reports of malignant trigeminal neuromas , none of the patients in our series had a malignant neuroma.

Several contemporary series have demonstrated no deaths or major surgical complications with radical removal of TSs[7-10]. In a classic series of 44 patients reported by Dolenc, total resection was achieved in 100% of the patients, including 5 who had undergone incomplete resection elsewhere and underwent another surgery to excise the remainder of the tumour[3]. The authours recommend an epidural approach to schwannomas originating in the fifth cranial nerve peripherally to the Gasserian ganglion and either an epidural-transdural or an epidural transdural- transpetrous approach to lesions originating in the Gasserian ganglion or in the root of the fifth nerve[3,14].

Surgical Strategy:

Recent reports demonstrate a higher percentage of tumour resection, a low surgical morbidity rate, and a lower rate of recurrence. Various reports have stressed the need for radical surgery, because total resection leads to tumour cure and the recurrence rate for cases with partial resection is relatively higher for trigeminal neuromas, compared with acoustic neuromas.

Konovalov et al[2]. on the basis of a comparatively large experience, the authours demonstrate some important points for trigeminal neuroma surgery, as follows. 1) These tumours are usually well separated from the cavernous sinus and the carotid artery, which facilitates their radical removal. 2) Usually the tumour does not completely destroy the trigeminal nerve, and some of its fibers can be preserved (preservation of the first trigeminal nerve division, if possible, is especially important). 3) The basal extradural approach (which the authors call “interdural”) is an effective way to reach and remove small and medium-size trigeminal tumours. There is a behavioural difference between neuromas and neurofibromas, which may infiltrate the nerve. Tumours may spread along the nerve division, far from the Meckel cavity, and other approaches may be necessary for their removal. In every case, selection of an appropriate approach should be strictly individualized[2].

The major impediment to complete removal is inadequate exposure[2,3,5,7]. Because of the location within the layers of the dura in the middle fossa, there was no specific need to achieve proximal control of the carotid artery, as would probably be necessary for some other lesions in this location[5,7]. Under Surgical Technique, the authors state, “A temporal craniectomy (if needed) is performed to obtain a flat viewing angle across the floor of the middle fossa.” Naturally, it is always needed, because this provides better access to the parasellar region and does not necessitate any retraction of the brain. Another statement, “If necessary, the middle meningeal artery is ligated to increase exposure of the lateral middle fossa floor[3,5].

Retrosigmoid Approach. This approach is performed by placing the patient in the dorsal (mastoid) position with the head turned to the opposite side and the

ipsilateral shoulder elevated. A linear incision is placed 4 cm behind the external auditory canal. The asterion is exposed to determine the junction of the tranverse and sigmoid sinuses. A craniotomy 4 cm in diameter is performed, with the superior and anterior margins bordering the transverse and sigmoid sinuses, respectively. The dura mater is opened parallel to the sigmoid sinus; CSF is drained from the cerebellomedullary cistern; and cranial nerves (CNs) VII-XI are identified. The tumour is thereby exposed near the tentorium margin. After intracapsular tumour debulking, microsurgical radical removal is accomplished[3].

Lateral basal subtemporal approach:

The skin incision extends from in front of the ear and travels superiorly and posteriorly. The branches of the facial nerve are saved by working deep to the fascial layers. The exposure is centered on the external ear canal. The temporalis muscle is elevated and displaced anteriorly. The basal extension of the exposure was achieved by resection of the roots of the zygomatic arch, roof of the external ear canal and superior third of the mastoid bone (Figure-7). The temporalis muscle was rotated anteriorly and was thus away from the field. The exposure was centered over the external ear canal in line with the petrous apex. The direction of the approach to the tumour was the shortest and perpendicular from the surface and avoided any neural or vascular manipulation. Inclusion of mastoidectomy in the exposure added the advantages of petrosal approach[5,7].

Fig.-7: *Shows extent of craniotomy in lateral basal subtemporal approach*

Subtemporal transtentorial approach:

We do not advocate approaching these lesions via the subtemporal-transtentorial route, which has been reported previously[2,3]. This approach provides a limited view of the underside of the tumour and its relationship to the vessels and cranial nerves below. A better view of the tumour's relationship to cranial nerves VI, VII, and VIII, the vertebrobasilar system, and the anteroinferior cerebellar artery is provided via the suboccipital portion of the combined petrosal approach[2,3,5,7,14].

Combined (retrosigmoid with subtemporal transtentorial approach):

This is the combination of subtemporal and lateral suboccipital approach for dumb bell-shaped schwannoma. This approach do not need drilling of petrosal bone and exposure of sigmoid sinus, hence less time consuming. Disadvantage is cerebellar retraction[2,3].

Frontotemporal extradural temporopolar approach:

Lesions of the orbital-cavernous and ganglion types were approached via an extradural approach to the cavernous sinus. With the head in three-pin fixation, supine,

rotated approximately 30 degrees, a pterional skin incision is made. The scalp and temporalis muscles are then reflected anteriorly in one layer. In selected cases, a two-layer scalp flap is fashioned to retract the temporalis muscle inferiorly and posteriorly. This maneuver provides a widened corridor to the anterior middle fossa, necessary in approaching larger tumours. A pterional craniotomy is performed, which typically measures 3 × 5 cm. A temporal craniectomy (if needed) is performed to obtain a flat viewing angle across the floor of the middle fossa. The dura is then elevated from the sphenoid ridge and medial frontal fossa. Elevation of the dura of the middle fossa proceeds laterally, to the foramen spinosum. If necessary, the middle meningeal artery is ligated to increase exposure of the lateral middle fossa floor[2,3,5,7].

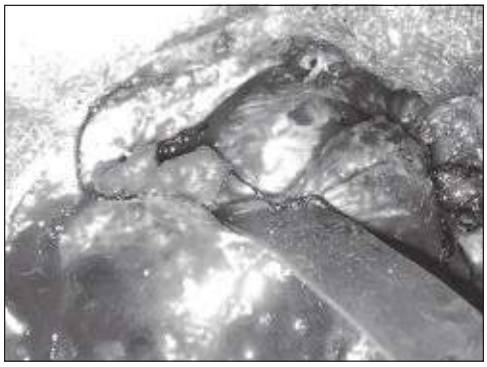

Fig. 8: *Shows operative picture of trigeminal schwonnoma in Frontotemporopolar approach.*

Combined petrosal approach:

Patients with lesions that involve both the cavernous sinus and posterior fossa, the so-called "dumb-bell" type, underwent surgical resection via the combined petrosal approach. The patient is placed in the three-quarter lateral position. An "L" shaped craniotomy is made around the ear to expose temporal and retromastoid dura. A mastoidectomy is then performed, preserving the structures of the bony labyrinth. Extradurally, the petrous apex medial to the internal auditory canal is fenestrated to create a window via the middle fossa trajectory to the posterior fossa[3,7,14] .

Conclusion:

On the basis of our limited experience , we believe that the best treatment for TSs is complete microsurgical removal of the lesion, and that this treatment should be considered the gold standard therapeutic modality for the majority of cases. Hypoesthesia, to some degree, is common after surgery, at least in the early postoperative period.

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Outcome Following Transcranial and Endonasal Transsphenoidal Resection of Craniopharyngiomas: A Case Series

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Introduction

Craniopharyngioma is a histologically benign, extra-axial, slow-growing tumour that predominantly involves the sella and suprasellar space[1,2]. Despite its histologic appearance, craniopharyngiomas occasionally behave like malignant tumours[1-3]. Craniopharyngiomas are dysodontogenic epithelial tumours derived from the Rathke cleft, which is the embryonal precursor to the adeno-hypophysis[2,3]. The craniopharyngeal duct is the embryonal structure along which the eventual adenohypophysis and infundibulum migrate[2,3]. Tumours can occur anywhere along the course of this duct from the pharynx to the sella turcica and third ventricle, which partially explains the location of the tumour[3,4]. The trigger for tumour growth is not clear. Three distinct subtypes of craniopharyngiomas have been distinguished on the basis of histologic appearance These are- adamantinomatous, papillary, and mixed[2-4].

Regarding adamantinomatous tumour (pediatric type), the classic and most common appearance is that of a cystic tumour, usually with a solid component[2-5]. These tumours occur in a wide range of sizes. The cyst contains fluid that can vary in colour, but it usually has a tan appearance similar to that of motor oil. The colour is the result of suspended blood products, protein contents, and cholesterol crystals within the cyst fluid; the colour may be the result of repeated hemorrhage within the cystic cavity[2-5]. Histologically, the cyst has a multistratified squamous epithelium with nuclear palisade. The solid component demonstrates clumps of wet keratin, dystrophic calcifications, trabeculae, nests, and squamous or columnar epithelium[2-5].

Craniopharyngiomas produce symptoms by compression of the surrounding anatomy. Tumour compression at the pituitary gland or stalk produces endocrine disorders. Compression at the visual nervous system causes visual disorders, and compression at the hypothalamus can cause obesity, loss of body mass, or complex disorder of vital functions[4-6]. The blockage of fluid passage at the third ventricle by tumour compression can produce hydrocephalus[6].

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Craniopharyngioma represents approximately 3-5% of intracranial tumours and 6-10% of pediatric brain tumours[1,5,6]. In pediatric patients, craniopharyngiomas represent the most common intracranial tumour of nonglial origin; they account for approximately 54% of all sellar and suprasellar tumours[5,6].

A bimodal age distribution is seen, with the first peak occurring in childhood and early adolescence, predominately at age 5-10 years. The second peak (for papillary types) occurs at age 40-60 years[3-6].

The most common presenting symptoms are headache, nausea, vomiting, and visual disturbances. The most common visual disturbances are bitemporal hemianopia, homonymous hemianopia, and amblyopia[5,6]. Visual disturbances usually improve after treatment[5,6].

Growth failure and headache are part of the most common presentations of paediatric patients with craniopharyngioma; for children, the median age at presentation is 5 years.

Other presenting symptoms are those of pituitary and adrenal hypofunction, diabetes insipidus, obesity, weakness, ataxia, coma, chemical meningitis (from rupture of cyst contents into subarachnoid space), and seizures[5,6]. In particular, children can present with growth failure, obesity (one third to one half), and hypothyroidism (two thirds). Precocious puberty has been reported, as has diabetes insipidus (which affects up to one fifth of patients). Poor school performance is also common, as are psychological problems. In patients with tumours larger than 5 cm, postoperative recurrence and morbidity rates are higher than in patients with smaller tumours[2,3,5-7].

Retrochiasmatic craniopharyngiomas are difficult to expose and have been associated with high surgical mortality, failure of total removal, increased surgical complications, particularly hypothalamic complications, and higher recurrence rates[1,2,6-8]. Several approaches have been used for total removal of retrochiasmatic craniopharyngiomas[2,6-8]. Because these lesions are hidden behind the chiasm and extend upward into the third ventricle and downward in front of the brain stem, their exposure with conventional approaches is unsatisfactory compared with the more accessible prechiasmatic craniopharyngiomas[1,2,6-8]. By mobilizing the sigmoid sinus medially, the petrosal approach allows an upward projection that facilitates dissection of the tumour under direct vision and with a wide exposure. Through this avenue, the tumour renders itself to removal from below and behind, maintaining the integrity of the hypothalamus and the optic pathways. Hakuba et al.[6] have admirably initiated and advocated the use of the petrosal approach for retrochaismatic craniopharyngiomas.

Methods

This is a retrospective review study of patients treated between July 2005 to January 2009. Patients characteristics (age, sex, follow-up), tumour factors (size, position, extension, previous surgery), and outcomes (visual, endocrine, and surgical morbidity) were defined and sought in patients who had resection of craniopharyngiomas.

Table-I

Surgical findings of 17 patients treated for craniopharyngioma using transcranial and transsphenoidal approaches.

Pt no	Age/ Sex	Sella size	Tumour location	Relationship of lesion with chaism	Tumour characteristics	Surgical procedure
1	41/M	Enlarged	Suprasellar	Retrochaismatic	Solid calcifed	Trans-sphenoidal
2	40/M	Normal	suprasellar	Pre & retrochaismatic	Cystic	Transcranial, bilateral, subfrontal
3	18/F	Enlarged	Sella & suprasellar, Extra ventricular & HCP	Retrochaismatic	Solid &cystic	Pterional
4	17/M	Enlarged & calcified	Sellar, suprasellar, retrosellar, cereb-ello-pontine angle,	Retrochaismatic & posterior fossa	Calcified and cystic	Pterional
5	18/M	Normal	Suprasellar	retrochaismatic	Cystic	1st-Orbito-frontal, 2nd – bifrontal
6	16/F	Normal	Supra and retrosellar	retrochaismatic	Cystic	Pterional
7	14/M	Normal	Suprasellar	Pre & Retrochaismatic	Calcified, cystic	Pterional
8	45/M	Normal	Suprasellar, intra-ventricular & HCP	retrochaismatic	Solid	Pterional
9	55/M	Normal	Suprasellar & intra-ventricular & HCP	Retrochaismatic	Solid	Bifrontal
10	15/M	Normal	Retrosellar, suprasellar, extraventricular	retrochaismatic	Cystic	Pterional
11	15/M	Normal	Retro and extraventricular	Retrochaismatic	Cystic	Bifrontal
12	48/M	Normal	Retro and extra-ventricular with unilateral HCP	Retrochaismatic	Cystic calcified	Bifrontal
13	18/M	Normal	Retro and extra-ventricular with HCP	Retrochaismatic	Cystic	Bifrontal
14	20/M	Enlarged	Sellar and suprasella	sellar	Cystic	Endoscopic transsphenoidal
15	35/M	normal	Suprasellar, intraventricular	retrochaismatic	solid	Bifrontal
16	35/M	Normal	Sellar & suprasellar	Intrasellar	Calcified	Endoscopic
17	30/M	Enlarged	Sellar, suprasellar	Sellar	cystic	Microscopic-2 times

Operative Technique

Transcranial approach : commonly 2 types of craniotomy done.

1. Bifrontal basal approach :

Fig.-1: *shows the position of bifrontal based approach-25ºelevation of head, head is fixed by local made 4 pin head fixator.*

Fig.-2: *postoperative 3d bone window shows the extent of craniotomy in bifrontal based approach.*

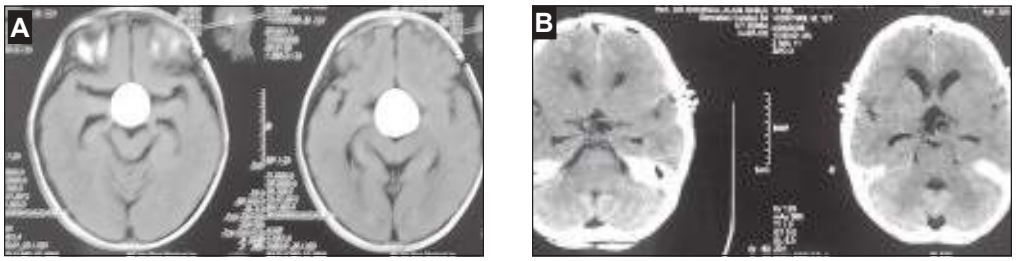

Fig.-3: *Preoperative (A) and Post-operative (B) picture of retrochaismatic craniopharyngioma showing total removal of tumour by translamina terminalis approach.*

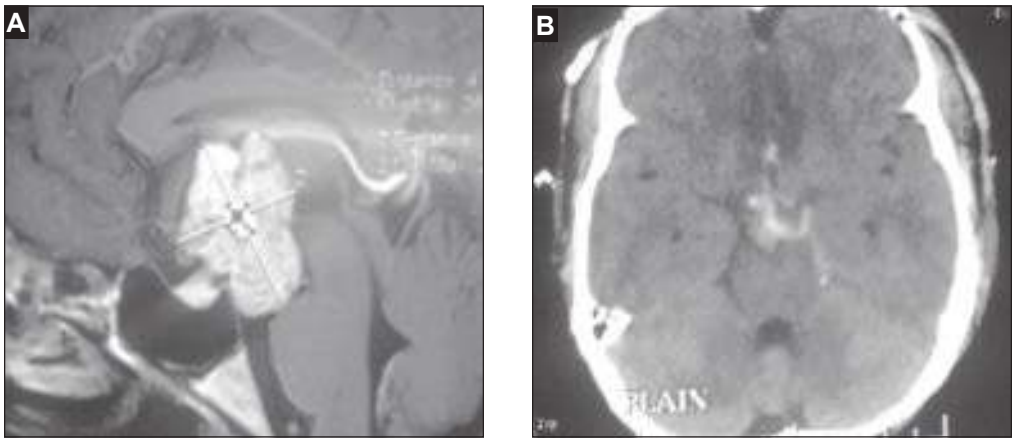

Fig.-4: *Preoperative (A) and Post-operative (B) picture of retrochaismatic craniopharyngioma showing total removal of tumour by translamina terminalis approach.*

2. Pterional approach

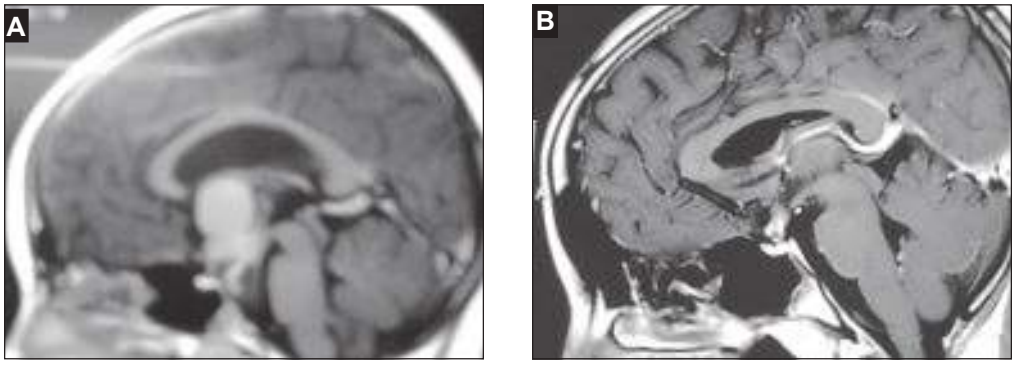

Fig.-5: *Pre-operative (A) and Post-operative (B) picture of retrochaismatic craniopharyngioma showing total removal of tumour by pterional transsylvian apparoach.*

Endonasal transsphenoidal approach either using Microscope or Endoscope.

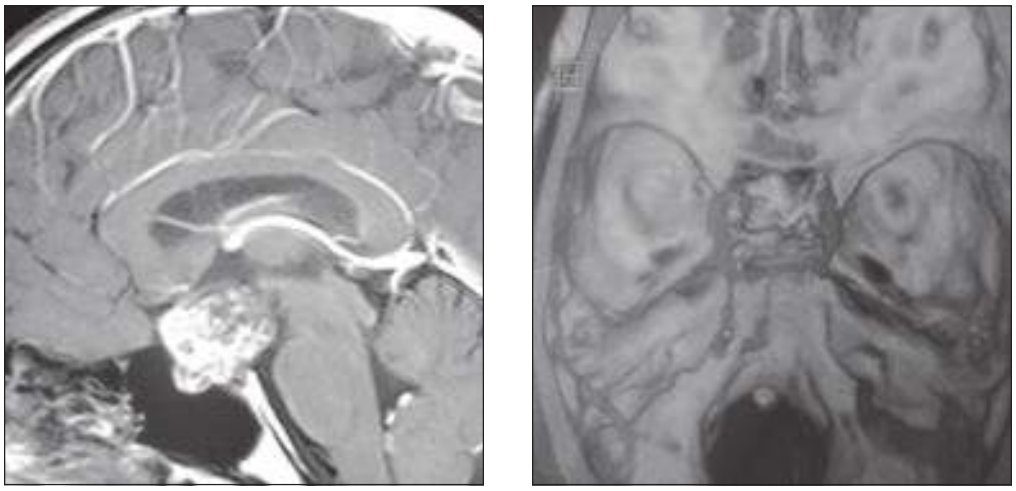

Fig.-6: *Pre-operatove (A) and Post-operative (B) picture of calcified craniopharyngioma showing total removal of tumour by endoscopic endonasal approach.*

Results:

Ophthalmological results

Visual outcome were assessed postoperatively. All patients with visual field and/or visual acuity defect improved except two patients.

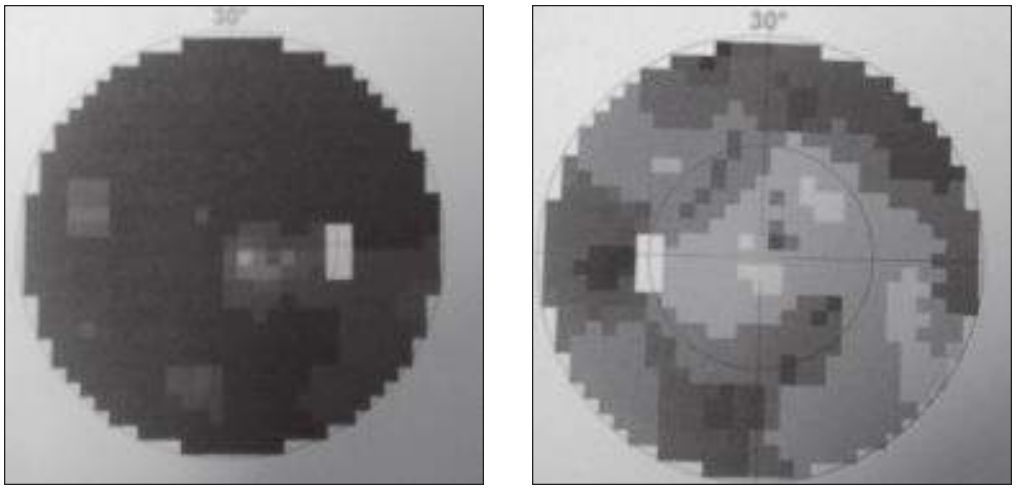

Fig.-7: *Pre-operative (A) and Post-operative (B) picture of visual field of right eye showing significant improvement. Tumour removal was done by endoscopic endonasal approach.*

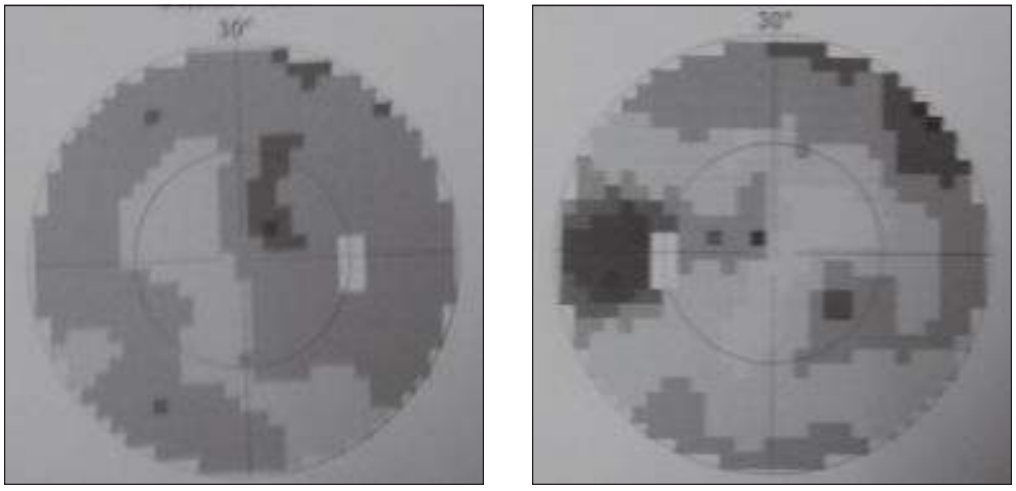

Fig.-8: *Pre-operative (A) and Post-operative (B) picture of visual field of left eye showing significant improvement. Tumour removal was done by endoscopic endonasal approach.*

Endocrine results

Preoperative anterior pituitary dysfunction did not improve in any patient. We observed the new occurrence of transient diabetes insipidus in almost all cases. Among them permanent diabetes insidious developed in 4 cases (23%).

Table-II

Clinical findings and surgical outcomes of 17 patients treated for craniopharyngioma using transcranial and transsphenoidal approaches

Pt no.	Age/ sex	Preoperative endocrinological symptom	Preoperative visual symptoms	Surgical procedure	Extent of removal	Postoperative endocrinological symptoms	Postoperative visual symptoms	Complications
1	49/m	Normal	Rt –blind, Lt-temporal field defect	Microscopic Transsph-enoidal	Partial	Unchanged	Unchanged	Diabetes insipidus (DI)
2	40/M	Panhypopi-tuitarism	Bitemporal field defect	Bilateral subfrontal	Total	Improved	Improved	Transient DI
3	18/F	Panhypopi-tuitarism	Rt –blind, Lt-temporal field defect	Pterional	partial	Not improved	Not improved	Pseudom-eningocele expired
4	17/M	Panhypopit-uitarism & DI	Lt –blind and Rt temporal field defect	Pterional	Partial	Not improved	Not improved	Expired
5	28/M	Panhypopit-uitarism & DI	Bil. Upper quadrantan-opia	1st-Orbito-frontal, 2nd -bifrontal	Partial-total	Not improved	Improved	Expired
6	16/F	Panhypopit-uitarism	Bil. Upper quadrantan-opia	Pterional	Subtotal	Improved	Improved	Transient DI
7	14/M	Panhypopit-uitarism	Bitemporal field defect	Pterional	Subtotal	Not improved	Improved	Transient DI
8	45/m	Panhypopit-uitarism	Right-blind, Lt.-temporal field defect	1st v-p shunt 2nd pterional	Partial	Not improved	Not improved	DI Expired
9	55/M	Panhypopit-uitarism	Right-blind, Lt. temporal field defect	Bifrontal	Total	Not improved	Not improved	DI Expired
10	15/M	Panhypopit-uitarism	Normal	Pterional	Ruptured and biopsy	Not improved	Normal	Nil
11	15/m	Panhypopit-uitarism	Bitemporal homonymous hemiamopia	Bifrontal	Total	Not improved	Improved	Transient DI
12	45/m	Panhypopit-uitarism	Right-blind Lt-temporal field defect	Bifrontal	Total	Not improved	Improved	Transient DI
13	18/m	Panhypopit-uitarism	Right-blind, Lt-temporal field defect	1st -transco-rtical, 2nd -bifrontal	Total	Not improved	Not improved	Transient D.I. Wound infection
14	20/M	Hypothyro-idism	Bitemporal field defect	Endoscopic transsphe-noidal		Total	Improved	Improved Transient D.I.
15	35/m	Hypothyroi-dism	Lt sided blindness, Rt temporal field defect	Bifrontal	Total	Improved	Improved	Transient DI
16	35/m	Hypothyroi-dism	Bitemporal field defect	Endoscopic transsphen-oidal	Total	Not improved	Improved	Transient DI, Wound infection
17	30/m	Hypothyroi-dism	Bitemporal	1st -Micros transs, 2nd– micros transs	Total	Not improved	improved	Nil

Extent of Resection and Recurrence

Among them 13 cases underwent transcranial approach, 2 cases by microscopic transsphenoidal and rest 2 cases by pure endoscopic transsphenoidal approach. Among transcranial approaches bifrontal basal approach were more preferred for retrochaismatic craniopharyngioma (Fig.-3,4).

Total tumour removal was done in 9 cases – subtotal removal in 2 cases and partial in 4 cases. Cyst wall pucture and biopsy was taken in 2 cases.

Recurrence were observed in 2 cases which required reexploration - one by transcranial and another by transsphenoidal approach.

Postoperative complications:

Among transcranial cases 2 patients had wound infection which were managed by antibiotics and dressing. In late follow up we found 3 patients deteriorated and expired who were operated transcranially.

Patients who were undergone transsphenoidal approaches no one developed CSF leak or extensive epistaxis.

Discussion:

A transcranial microscopic approach has traditionally been preferred for removal of tumours located entirely within the suprasellar extra or intraventricular in location[8-10].

The transsphenoidal approach, either microscopic or endoscopic, has been restricted to intrasellar subdiaphragmatic tumours that extend upward from an enlarged sella turcica, and only partially involve the anteroinferior part of the third ventricle[7-10].

This dogmatic statement can be considered questionable after the introduction of the extended transsphenoidal approach for treatment of suprasellar supra-diaphragmatic craniopharyngioma, as it provides additional bone removal –the tuberculum and some part of planum sphenoidale[6-10] (Fig-6) .The site of origin, extent and direction of growth, location of the tumour, site of invasion of the third ventricle and neurosurgeons choice and expertise play important roles in the choice of the proper approach[3.6,10].

Transcranial versus Transsphenoidal Approach

Our personal series involve patient populations that are too small to allow conclusions to be made regarding clinical results and outcomes.

Several transcranial approaches have been advocated for the resection of craniopharyngiomas, and each has both advantages and limits. Although each surgeon uses his or her most familiar technique, the pterional approach seems to have several advantages over other craniotomies[10] (fig-5). Nevertheless, a single route for craniotomy has proven insufficient in many cases, as highlighted by Fahlbusch et al[1]. Furthermore, once the intradural space has been reached, various surgical corridors are presently used to access the areas where the tumour is localized. As a matter of fact, Yasargil[8] and Almefty et al [10] described seven different intradural corridors to manage all the different extensions of the craniopharyngiomas in his series. The tumour can be removed by extra-axial dissection in the parachiasmatic area, such as the prechiasmatic space, the opticocarotid triangle, and the superior carotid bifurcation triangle and carotido-

oculomotor triangle[8,10]. In a complex situations, combined approaches have been proposed to perform gross total lesion removal, such as retrochaismatic translamina terminalis for suprasellar craniopharyngiomas that occupy the anterior portion of the third ventricle; and transcallosal-translamina terminalis for craniopharyngiomas that extend within the third ventricle[10] (Fig-3,4). Hakuba et al[6] prefers transpetrosal approach for removal of retrochaismatic craniopharyngioma. The petrosal approach is excellent for removing retrochiasmatic craniopharyngiomas. It provides a direct and unobstructed view of the tumour and minimizes manipulation of the chiasm, optic nerve, major vessels, and perforators. Vascularization and the function of the hypothalamus are thus preserved[6,10].

Conclusions

Using the endoscopic endonasal approach for suprasellar craniopharyngiomas allows the surgeon to avoid brain retraction, permits early exposure of the lesion, provides good visualization of the pituitary gland, stalk, and main vascular structures, and minimizes optic apparatus manipulation.

By using bifrontal basal approach for midline suprasellar craniopharyngiomas it provides well visualization of optic apparatus,great vessels, easy entry to 3rd ventricle by lamina-terminalis incision and entry to lateral ventricle by incising corpus callosum.

By pterional approach for off midline tumour removal through prechaismatic, optico-carotid and carotido-oculomotor triangle are safe.

Regardless of the surgical option selected for a single case, whether transsphenoidal or transcranial, it is crucial to relate the goal of surgery to the single patient's needs and clinical conditions.

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Role of Cytological Smear in the Intra-operative Diagnosis of Central Nervous System

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Abstract :

Intra-operative cytologic diagnosis of lesions of central nervous system (CNS) possible with high accuracy. It can be performed from tiny piece of tissue preserving the same tissue for paraffin section. It permits examination of multiple sites of a lesion including margin of a tumour. Over a period of 18 months, a total of 110 cases with CNS lesions were included. Among these meningioma was the commonest (26%, n-29) tumour, of which 27 (93%) were correctly classified by intra-operative cytologic smear. Astrocytoma represented 19 cases (17%) and astrocytic nature of the tumour were identified in 17 cases (90%) by smear preparation. By intra-operative smear 16 out of 18 cases of schwannoma (89%), 8 out of 9 cases of craniopharyngioma (89%), all 4 cases of (100%) medullblastoma, 5 out of 7 cases of inflammatory (71.43%) lesions and 2 out of 4 ependymomas (50%) were classified correctly. Of the 110 cases, only 2 (1.82%) cytologic smear revealed inadequate material. The predictive value for positive and negative diagnosis were 86.36% and 95.38% respectively. The diagnostic accuracy of intra-operative cytologic smear was 91.7%.

Introduction:

An intra-operative diagnosis is of great importance for the management of patients suffering from CNS diseases. Neurosurgery is facilitated by the use of intra-operative diagnostic neuropathological service. There are two main techniques for the intra-operative diagnosis they are frozen section and smear preparation. Lesions of the CNS are usually soft and particularly suitable for cytological preparations. Cytologic preparations of lesions of CNS have many advantages over conventional frozen sections[1]. One of the primary advantages is diagnostic accuracy despite the small sample. The smears are superior in displaying abnormal cellularity, nuclear and cytoplasmic details and occasionally even tissue architecture. They are also enable for preservation of the sample for paraffin sections. In contrast to easily obtainable good quality cytologic preparations, quality frozen sections are difficult to obtain on brain tissue. The soft consistency and gelatinous matrix of cerebral tumours is often accompanied by edema, which makes cryostat sections from such tissue prone to ice-crystal artifact even when prepared under most carefully controlled circumstances[2]. In addition, freezing

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distorts the nuclei of astrocytes and introduces artifacts in permanent sections[3].

Several studies have demonstrated that the diagnostic accuracy of frozen sections and smears in neurosurgical specimens are essentially equivalent. Compared with permanent sections, the diagnostic accuracy of smears ranges from 83-94% while that of frozen sections is 90%[3]. The smear technique can provide rapid intra-operative diagnosis to the neurosurgeon and facilitate to take instant and rapid decision about the mode of' surgery and thus further management of the patient. Smear diagnosis is relatively new in the diagnosis of CNS lesions in our country. In the light of above facts the present study is undertaken with the aim to see the role of cytologic smear in the intra-operative diagnosis of CNS lesions.

Materials and methods:

This study was carried out at the department of pathology, BSMMU during the period from December 1998 to May 2000. Clinically and radiologically suspected 120 patients of different age and sex groups were selected from BSMMU, Dhaka Medical College Hospital and Metropoliton Hospital, Mahakhali, Dhaka.

Before proceeding to intra-operative diagnosis, relevant clinical information including x-ray, CT and MRI scans were collected. All the necessary and relevant data were recorded methodically and meticulously.

Smear preparation was performed in all 120 cases intra-operatively immediately after taking the biopsy. We followed the techniques of smear preparation according to Ironside 1994[2], and Sidawy and Jannotta 1997[4].

Cytologic smears were stained by Hematoxylin and Eosin stain. Usually at least two slides of cytologic smear were prepared for each case where the biopsy sample were tiny. The smears where material was too scanty to evaluate or cellular morphology not well preserved were termed as unsatisfactory.

The sample for histopathological study were collected in container containing 10% formalin as fixative. Then these samples were subjected to gross examination and subsequent tissue processing and staining of histopathology slides.

Observations and results:

This study was undertaken with the aim to evaluate the effectiveness of cytologic smear in the intra-operative diagnosis of CNS lesions. Out of 120 biopsies examined, the final diagnosis in 10 cases remained in doubt even after examination of paraffin sections. These 10 cases had therefore been excluded from the analysis. Thus, this study was based on the data obtained from 110 patients.

Of the total 110 cases, 73 were male (66.36%) and 37 (33.64%) were female. The male to female ratio was 1.9:1. The age ranged from 2 months to 70 years with an average of 32 years.

Cytopathological diagnosis of 110 CNS lesions:

0f the 110 cases, satisfactory smear was obtained in 108 (98.18%) cases. The most frequent benign lesions were meningioma (26.4%, n-29), followed by schwannomas - (14.55%, n-16) and craniopharyngiomas (7.3%, n-8). Glial tumours were the commonest primary malignant tumour (27.3%, n-30). Cytologically 4 cases (3.6%) revealed inflammatory lesions and 2(1.8%) revealed normal brain tissue. Table I shows cytological diagnosis of 110 CNS lesions.

Table-I

Cytological diagnoses of 110 CNS lesions

Cytological diagnoses	Frequency	Percentages
Meningioma	29	26.4
Astrocytoma	22	20.0
Schwannoma	17	15.5
Craniopharyngioma	8	7.3
Anaplastic astrocytoma	4	3.7
Medulloblastoma	4	3.6
Ependymoma	2	1.8
Glioblastoma multiforme	2	1.8
Oligodendroglioma	1	0.9
Chordoma	2	1.8
Hemangiopericytoma	1	0.9
Benign Fibrous Histocytoma (BFH)	1	0.9
Pitutary adenoma	1	0.9
Malignant Peripheral Nerve Sheath Tumour (MPNST)	1	0.9
Metastatic poorly differentiated carcinoma	1	0.9
Lymphoma	1	0.9
Small round cell tumour	1	0.9
Tuberculoma	1	0.9
Gliosis	4	3.7
Glial tumour	3	2.7
Normal brain tissue	2	1.8
Inadequate	2	1.8
Total	110	100

Histopathological correlation of cytopathology findings:

Biopsy specimens were available for histopathology in all the cases. Table II shows the histopathological correlation of 110 CNS lesions with cytopathological diagnosis. Out of 110 cases, 92 were correctly diagnosed and classified by cytopathology. Among the remaining cases, the glial type of tumour was identified in 08 cases, but proper classification was not possible. In this study 02 lesions revealed inadequate smear for proper evaluation, one of which was diagnosed histologically as astrocytoma and the other was diagnosed as haemangiopericytoma.

Table-II

Histopathological correlation with cytopathology findings

Diagnosis	Histopathological diagnosis	Cytopathological diagnosis				Inadequate
		No	Correctly classified		Other diagnosis	
			No	%		
Benign 59	Meningioma	29	27	93.1	Astrocytoma (2)	0
	Schwannoma	18	16	88.9	Meningioma (1), A (1)	
	Craniopharyngioma	9	8	88.9	Astrocytoma (1)	
	Neurofibroma	1	1	100		
	Pituitary adenoma	1	1	100		
	BFH	1		100		
Malignant 42	Astrocytoma	19	15	79	AA(2), M(1)	
	Anaplastic astrocytorna	3	1	33.4	Astrocytoma (2)	
	Glioblastoma	3	2	67	A S (1)	
	Medulloblastoma	4	4	100		
	Ependymoma	4	2	50	Glial tumour (2)	2 cases
	Oligodendroglioma	1	0	0	Glial tumour (1)	
	Metastatic	1	1	100		
	Ewing's sarcorna	1	1	100		
	Lymphoma	1	1	100		
	Hemangiopericytoma	2	1	50		
	Chordoma	2	2	100		
	MPNST	1	1	100		
Inflammatory - 7	Tuberculoma	1	1	100		
	Gliosis	6	4	66.7	A (LG) 10 (1)	
	Normal tissue	2	2	100		

AA = Anaplastic astrocytoma
A (LG) = Astrocytoma, low grade
A = Astrocytoma
M = Meningioma
0 = Oligodendroglioma
BFH = Benign fibrous histiocytoma
MPNST = Malignant Peripheral Nerve Sheath Tumour

Evaluation of cytological diagnosis in 110 cases of CNS lesions:

In the present study, there were 38 true positive and 62 true negative diagnosis. False negative cases were 03 and false positive cases were 06. Table III shows statistical data.

Table-III

Statistical evaluation of cytological diagnosis in CNS lesions

Sensitivity %	Specificity %	PPH %	NPV %	Accuracy %
92.68	91.18	86.36	95.38	91.7

PPV= Predictive value for positive diagnosis

NPV = Predictive value for negative diagnosis

Discussion:

The smear technique as a method of intra-operative diagnoses of neurosurgical biopsies has had numerous advocates since its introduction in the early 1930s[5]. The principal advantages of this technique are its technical simplicity, adequacy in spite of tiny neurosurgical biopsy, high diagnostic accuracy and rapid evaluation[5]. The process from smear preparation up to mounting requires 2-4 minutes. Another 6-8 minutes is required for microscopic examination. It is also cost effective. Although there is inevitable considerable loss of intrinsic tissue architecture[5], it was not a major problem for diagnosis.

Due to such advantages of smear technique in neurosurgical diagnosis, this study was performed with a view to determine the feasibility of this technique as diagnostic tool for rapid diagnosis of neurosurgical biopsies in our country.

In the present study, 110 cases with CNS lesions were included. Of the 110 cases, satisfactory smear was obtained in 108 (98%) cases. Only 02(1.8%) cases showed inadequate smear. Most of the authors stated some cases of inadequate smear in their studies[6]. They mentioned that probably the neurosurgeons could not obtain abnormal tissue in their biopsy.

Of the total 110 cases, 73 were male and 37 were female. The male to female ratio was 1.9:1. The age ranged from 2 months to 70 years with an average of 32.26 years. These findings were close to that of Torres and Collanco, 1993[7] who found male to female ratio of 1.2:1 and age ranged from 15 days to 83 years (average 34.18 years).

Of the 110 CNS lesions, in 90(81.8%) cases brain and in 20 (18.2%) cases the spinal cord were affected. The cerebrum was the commonest site of brain lesion, which was affected in 50 (55.56%) cases. Of the 90 brain lesions, meningioma were 26 (29%) which was a little bit higher than that described by Cotran et al, 1989[8] who stated that 20% of intracranial tumours are meninigiomas. Out of 29 histologically diagnosed meninigiomas, 27 (93%) were diagnosed correctly by cytology and 2 (2.2%) were misdiagnosed as astrocytoma. In these two cases, smear revealed naked eye nuclei and focal areas of fibrillary like structures. It was the wispy processes of the cytoplasm of meningothelial cells, which resembled fibrillary processes of astrocytomas. Sidawy et al, 1997[4] also observed this pitfall of cytologic diagnosis of meningiomas.

Out of 18 histologically diagnosed schwannomas, 16 (80%) were diagnosed

accurately by cytology. Among the two wrong diagnoses, one was meningioma and another was astrocytoma. It was observed that in smear preparation schwannoma shaded cells from dense hypercellular area of Antoni A and spongy hypocellular area of Antoni B. Tissue fragments from Antoni A region showed parallel rows of spindle cells with wavy nuclei, which favoured diagnosis. But the cells of the spongy hypocellular are of Antoni B were smaller, round and the nuclei were darker resembling that of meningioma. This observation was also noted by Burger, 1985[9]. In one case, in addition to these features some cells also showed short cytoplasmic processes, which lead to the diagnosis of astrocytoma.

Craniopharyngiomas represented 10% (n-9) of intracranial lesions. In the study of Willems and Willems, 1984[6] the frequency of craniopharyngiomas were 6% which was slightly lower than the present study. Cytological diagnosis correlated with histology in 8 (89%) cases. Of the 9 craniopharyngiomas, one was diagnosed cytogically astrocytoma. In that case, craniopharyngioma was a differential diagnosis. The tissue was tiny and no squamous cell was in smear. The scanty fibrous stroma of the lesion gave impression of fibrillary process, which mislead to the diagnosis of astrocytoma.

Pituitary adenoma was 1% (1 case) and was diagnosed correctly by cytology. Marshall et al, 1973[10] found 6 (3%) pituitary adenomas, one of which was correctly diagnosed by cytology as oligodendroglioma. They mentioned that neurosurgeon gave wrong information about the actual site of the lesion, which mislead them to diagnose oligodendroglioma as two tumours are very similar in cytologic appearance.

In this study, the other two benign tumours of CNS were neurofibroma in the spinal region and benign fibrous histiocytoma in the sacrococcygeal region, both of' which were correctly diagnosed cytologically prior to histological diagnosis.

Table-IV

Benign tumours correctly diagnosed by smear technique

Tumour	Total number	Correctly diagnosed	%
Meningioma	29	27	93.1
Schwannoma	18	16	88.9
Craniopharyngioma	9	8	88.9
Neurofibroma	1	1	100
Pituitary adenoma	I	I	100
BFH	1	1	100
Total	59	54	91.5

BFH = Benign fibrous histiocytoma

Table-V

Errors in the diagnoses of benign lesions

Cytological diagnoses	Number	Histological diagnosis
Astrocytoma	4	Meningioma (2), Schwannoma (1), Craniopharyngioma (1)
Meningioma	1	Schwannoma

In this study, 30 (33.3) cases were glial neoplasms. Astrocytoma was the commonest glial tumour. Of the 19 histologically diagnosed astrocytoma, 15(78%) were classified correctly by smear technique. But astrocytic composition of' the tumour was identified in 17 (90%) cases, 2 among them were diagnosed as anaplastic astrocytoma. Between these two, one showed markedly hypercellular smear with pleomorphic nuclei. In this regard it is important to note proliferated blood vessels and mitosis for the diagnosis of anaplastic astrocytoma[7]. Of the astrocytomas, one case was misinterpreted as meningioma. The smear of this revealed round cells with well defined eosinophilic cytoplasm resembling meningothelial cells. But after review, glial nature of' the tumour was identified. The other case revealed inadequate smear and was histologically diagnosed as astrocytoma.

Anaplastic astrocytoma were 3(33%) in number in the present study. Only one was properly classified by cytopathology. Other two were diagnosed as astrocytoma. This may be due to heterogenous nature of the tumours of astrocytes[2]. Probably smear was prepared from less aggressive area of the tumour. Same idea is applicable to one case of glioblastoma multiforme, which was diagnosed by cytology as anaplastic astrocytoma. Other two glioblastomas were correctly diagnosed by cytological smear. In this study, glioblastamas were 3.3% (n-3) of CNS lesions.

Medulloblastoma represented 4.4% (n-4) of CNS lesions. All the medullobalstomas were correctly classified by smear preparation. This correlate with other studies[7,10]. So, smears of medulloblastoma showed high diagnostic accuracy.

Ependymoma represented 4.4% (n-4) of CNS lesions. Among the 4 cases, 2 were diagnosed correctly. Other two were diagnosed as glial tumours because no rosette or typical features of ependymoma was present but glial nature of the tumour was well identified. It should be mentioned here that in one case typical ependymal rosette was seen in the smear, which confirmed the diagnosis, where as histology was unable to classify the tumour.

Hemangiopericytoma were 2.2% (n-2), of which one was diagnosed correctly by cytology. The other smear was inadequate for evaluation. Cytologically this case was suggested as vascular tumour but could not be classified further.

Ewing's sarcoma (1 case) was diagnosed correctly from smear. A spinal lesion was diagnosed by smear as meningeal lymphoma, which was confirmed by histology.

In this study, Inflammatory lesions represented 7 (6.4%) cases of which 6 cases were diagnosed as reactive gliosis, 4 were correctly interpreted by smear. Another two were diagnosed as oligodendroglioma and low grade astrocytoma. Oligodendroglioma was diagnosed due to uniform round cells in a moderately cellular smear with fibrillary background. Failure to distinguish between a well differentiated astrocytoma and reactive gliosis is a well established difficulty[10].

Frequency of metastatic carcinoma in the present study is 1%, which is less than the observation of other authors who stated metastatic carcinoma ranging from 5-15% except Willems and Willems[16] who reported 1.7% metastatic carcinoma. In our country, most of the patients are poor and they can hardly bear the expense of treatment of primary malignant tumour. After metastasis the patients or their family lose interest or can not afford further treatment for the metastatic lesion because by that time they are already informed the fate of malignant tumour. This may be the cause for which metastatic carcinoma in intracranial location are so seldom operated in our country.

In his study, the sensitivity is 92.68% and specificity is 91.18%. Mouriquand C. et al, 1987[11] stated 88.8% sensitivity and 81.9% specificity. The accuracy in the present study is 91.7% which closely agrees with the accuracy stated in other literatures. The diagnostic accuracy of' intra-operative cytologic smear stated by other authours ranges from 87-95%.

Table-VI

Accuracy rates comparing smear preparations with histology in different studies

Author	Year	Number of cases	% accuracy
Berkerley et al[5]	1978	216	93
Willems et al[6]	1984	112	87
Chahil et al [12]	1985	32	90
Mouriquand et al[11]	1987	312	87.5
Torres et al[7]	1993	307	92.2
Present study	2000	110	91.7

This table (Table-VI) shows that the accuracy of the present study is similar to other studies done by different authors. Thus, this study emphasizes the high diagnostic accuracy of cytologic smear in the diagnosis of CNS lesions. Intra-operative cytologic preparations provide accurate diagnosis and enable the pathologist to preserve a sample for permanent sections. So, it may be recommended as a primary means of evaluating neurosurgical biopsies.

Summary and Conclusion:

Intra-operative morphological diagnosis of CNS lesions is of great importance as it helps the neurosurgeons to take proper decision about surgery. In developed countries of Europe, intra-operative diagnosis of CNS lesions is performed routinely to help the surgeons and the patients. But in our country, it is not yet practiced. As frozen section produces artifact, smear technique is preferred as a intra-operative diagnostic method by many authors. It is more rapid also. The whole procedure requires only 6-12 minutes. Although neurosurgical facilities are

expanding in Bangladesh but frozen section facilities are only available in few centres of Dhaka city. In this regard, this study was carried out to assess the diagnostic accuracy of smears.

A total of 110 cases of CNS lesions were included in this study from December 1998 to May, 2000. Cerebrum was the commonest (55.56%, n-50) site of brain to be affected and intradural extramedullary location was the commonest (55%, n -11) site among the spinal cord lesions. Meningioma is the commonest (26%. n-29) tumour, of which 27(93%) were correctly classified by intra-operative cytologic smear. Astrocytoma represented 19 cases (17%) and astrocytic nature of the tumours were identified in 17 cases (90%) by smear preparation. By intra-operative smear 16 out of 18 cases of shwannomas (89%), 8 out of 9 cases of craniopharyngiomas cases (89%), all four (100%) cases of medulloblastomas, 5 out of 7 cases of inflammatory (71%) lesions and 2 out of 4 ependymomas were classified correctly. The main errors in intra-operative smear were 2 meningiomas, which were diagnosed by smears as astrocytoma, two shwannomas that were incorrectly diagnosed as meningioma and astrocytoma. In this study, 2 gliosis were incorrectly diagnosed as low grade astrocytoma and oligodendroglioma. This is a well recognized problem even in routine sections and most of the authours have some cases of this type of error. Of the 110 cases, only 2 cytologic smears revealed inadequate material. The predictive value of positive and negative diagnosis were 86.36% and 95.38% respectively. The diagnostic accuracy of intra-operative cytologic smear was 91.7% which supports the diagnostic accuracy of studies done by other authors, which ranged from 83-94%.

In conclusion, the intra-operative diagnosis of lesions of CNS is possible with high accuracy. It can be performed from tiny piece of tissue preserving the same tissue for paraffin section. It permits examination of multiple sites of a lesion including margin of a tumour. It is rapid, reliable and cost effective. So, cytologic diagnosis may be used as a diagnostic method for intra-operative diagnosis of CNS lesions.

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CASE REPORTS

A Case Report on Gilles de la Torette Syndrome

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Master Tashik, 4 years 6 months of age from Azimpur, Dhaka came to Dhaka Medical College Hospital (DMCH) neurology out patient department (OPD) with the complaints of abnormal & straining facial expressions. Gradually those expressions became more sustained & after 7 days along with these problems he developed recurrent involuntary phonation like "ya ya ya". He also adopts abnormal sustained posture of the body & limbs like hands stretched with inner rotation & wrists flexed with fingers extension during the recurrent bouts of phonations & facial expressions. Except when he slept at night, all the time repeatedly he used to do the above activities. He had started going to school 10 days before his illness. He was very willing to go to school & attentive during the days before illness. But after his illness, he became notoriously hyperactive & restless & could not concentrate at all so that his parents had to postpone his school going. He couldn't even write due to his abnormal posture of the fingers. He used to utter obscene words often & curse his parents & elder brother even unnecessarily. He used to repeat what other peoples said. He doesn't have parental consanguinity & his birth history was uneventful & milestones of development were normal. He had his full-blown illness for 20 days, after the gradual start with abnormal facial expressions 7 days before. He received clonazepam initially 0.5 mg tab twice daily. When symptoms were not improving after 7 days the dose was increased up to 0.5 mg 1 tablet twice daily. Some improvement occurred but depending on the electroencephalograph (EEG) findings carbamazepine was started & gradually within 20 days symptoms markedly subsided but still some involuntary facial movements persist like involuntary deviation of the angle of the mouth & nose picking. But still he could not concentrate like before & hyperactivity declined to almost acceptable limit. Now he is on carbamazepine (200 mg) ½ tablet twice daily & clonazepam 0.5 mg 1 tablet twice daily.

All investigations were normal accept EEG which revealed sharp & slow waves in the temporal region (temporal encephalopathy). MRI of brain was normal.

Discussion:

Though previously considered rare Tourette syndrome (TS) is not actually so[1,2]. Recently, the literature on TS has mushroomed with substantial cohorts of TS patients & it is characterized by multiple motor tics plus one or more vocal (phonic) tics, which characteristically wax & wane. It is also recognized to be associated with a wide variety of associated behavioural abnormalities & psychopathologies, like attention deficit hyperactivity disorder

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(ADHD), obsessive-compulsive disorder (OCD), self-injurious behaviours (SIB), anxiety, depression & some personality disorder. Though onset of TS ranges from 2 to 21 years, it is more common in children with a mean of 7 years.

TS is characterised by both multiple motor & one or more phonic tics, which occur many times a day in bouts. The number, frequency & complexities of the tics change over time & they are present for at least 1 year[3,4]. The term phonic tic is preferred to vocal tic, as not all abnormal sounds & noises in TS are produced by the vocal cord[5].The tics usually persist during sleep[5]. Initiation is usually with the motor tics & the onset of phonic tics is later which is also true for our patient. Tics may be abrupt in onset, fast & brief (clonic tics) or may be slow & sustained (dystonic or tonic)[5] like our patient. A recent study[6] showed 22% patients develop so severe tics during the worst ever period that school functioning was significantly impaired like our patient. By 18 years nearly half of the patients became virtually tic free[6]. Patients often display repetitive & annoying motor behavior like sniffing, snorting & jumping. Squatting or turning in a circle, touching of other persons, repeating ones own words (Palilalia), abnormalities of gait & forced touching[2,7]. Coprolalia (inappropriate involuntary uttering of obscenities) occurs in less than one third of TS patients & usually occurs by 15 years of age but our patient had it in a milder form[2]. Echopraxia (imitation of actions of others), Ecolalia (imitation of sounds of others) occur in substantial proportion of patients of TS & our patient also had it. Patients also display explosive & involuntary cursing which was strongly positive in our patient.

It has been suggested[8] that it may be useful to clinically subdivide TS into.

i) Pure TS: Consisting primarily & almost solely of motor & phonic tics.

ii) Full blown TS that includes coprophenomena, echophenomena & paliphenomena.

iii) TS-plus [9] in which an individual also has ADHD, significant OCB & SIB. Our patient probably belongs to this class as he also had ADHD.

Behavioural associations with TS

ADHD:

It begins in early childhood with clumsiness, excessive activity, low frustration tolerance & accident proneness [10]. ADHD & TS are so intimately related that it is valuable to familiarize oneself with this ADHD literature. ADHD occurs in a substantial proposition of TS patients ranging from 21% to 90% of clinic populations[11]. It was shown that children with TS plus ADHD had lower psychological functioning than children with ADHD alone [12]. Our patient had this abnormal behavior pattern along with motor tics & phonetic tics.

OCD:

It is characterized by persistent obsessions, recurrent intrusive senseless thoughts, which are egodystonic (internally uncomfortable) or compulsive (repetitive & seemingly purposeful behaviours which are performed according to certain rules or in a stereotyped fashion).

It is becoming increasingly evident that there is a clear & strong association between TS & OCD, both in TS patients &

in their family members[13]. Obsessions seen in TS have to do with sexual, violent, religious, aggressive & symmetrical themes; the compulsions are to do with checking, ordering, counting, repeating, and forced touching for getting things just right & self-damage or SIB. They are significantly different to the obsessions & compulsions scan is pure OCD.

SIB:

In 1885 Georges Gilles de la Tourette described 2 patients out of them one patient injured himself[14], Thereafter a dozen case reports of SIB published in TS patients[1]. It is reported that it occurred in 33%[1], 34%[15], 43%[16], 48%[17], 53%[18] of TS patients. They include head banging (47%, most common), body punching/slapping, head or face punching /slapping, banging or poking sharp objects into the body, scratching parts of body & curiously inflicting severe eye injuries. Fortunately our patient didn't have these associations.

Anxiety:

It is also common in TS & it is documented that in 52% tics anxiety is the initial complaint. It is also documented as the most frequent symptom[19-21].The exact relationship between TS & anxiety is yet unclear. It may well be secondary to having moderate to severe TS.

Depression:

The aetiology of depression is multi-factorial that includes genetic factors as well as psychosocial variables such as recent adverse life events, adverse childhood circumstances (parental loss, stress or abuses), adverse current social circumstances & physical illness[22]. Several studies have found both children[23] & adult TS patients to be depressed & this may be more so in older individuals with longer duration of illness. Our patient during the course of illness was not depressed.

NOSI:

Non- obscene complex socially inappropriate behaviours[24] & disinhibition behaviours[6] have also been described in TS. NOSI include insulting others e.g. aspersions on weight, height, intelligence, general appearance, breath or body odour, parts of the anatomy, racial or ethnic slurs.

Other behavioral abnormalities like aggression[15,18,25,26,] antisocial behaviours[17], learning disabilities, severe temper outburst[20], schizoid symptoms[27], inappropriate sexual behaviours[18,17] & rage[28] are also seen in TS clinics.

Aetiological aspects:

Genetics:

It is now generally agreed that TS is genetically determined & the genetic inheritance is autosomal dominant[29,30]. There may also be genetic heterogeneity, i.e. different genes may be responsible for TS in different families. Our patient doesn't have a positive family history of TS.

Perinatal factors:

Clinical expression of TS is a product of the interaction of an inherited vulnerability with environmental factors. These may include CNS stimulants or intermittent, uncontrollable stress during a critical period of brain development[6]. Prenatal events or exposure such as maternal life stress during pregnancy, severe nausea & vomiting during pregnancy and antiemetic medications may lead to change in dopaminergic activities of basal ganglia specially in caudate nucleus producing overactivitiy of dopaminergic circuit.

Neuroimmunology & infections:
Some recent studies showed a possible clinical spectrum between TS & Sydenham's chorea, a variant of rheumatic fever with neurological involvement[31], this theory is by the findings of both OCD symptoms [32,33] & vocal tics [34] in Sydenham's chorea (SC).

Antineuronal antibodies were found to be increased in the sera of children with movement disorders including SC& TS[35-37].

Budman & colleagues reported an 11 year old girl who had no family history of TS but who at the age of 5 years began to have symptoms of TS along with ADHD & OCD. Gestation, birth & early development were normal. At 3 years she developed herpes simplex type 1 oral lesions. She continued to have these periodically. Response to traditional treatment with Anti TS medication was variable. Acyclovir was given twice for tic exacerbation & she improved markedly on both occasions[28]. Another patient, a boy who began to blink excessively at the age of 4 years resolved with in a year without treatment, at the age of 9 years he developed multiple tics along with vocal tics & poor impulse control. Results of investigation suggested an infection with Borrelia burgdorferi (Lime disease). He was treated with an intravenous antibiotic (Ceftriaxone 2 gm) daily for 14 days, which resulted in both a decrease of symptoms & decrease in Borrelia specific antibody titres. The authors suggested that such an infection should be considered in all cases of TS in endemic areas[10].

Course & prognosis:
TS has a life long course. Characteristically the course of TS is punctuated by the appearance of new tics & the disappearance of the older ones. During adolescence the symptoms tend to be more unpredictable from day to day, but it is estimated that in 30 to 40% of cases the tic syndromes will remit completely by late adolescence[2] .The period of greatest tic severity occurred at 10 years. Stress has been shown to increase the severity of tics. Case report has documented an increase of tics in TS following the death of a parent, personal illness, birth of a sibling, beginning of school [38,39], parental separation[40], illness of a parent, premenstrual tension[41], thermal stress[42], traumatic war experiences[43]. Three long term single case studies have investigated stress & TS and shown that increased stress increased tics, whereas reduced stress reduce tics[39,44, 45].

Management of TS:
Management should be multidisciplinary. At the onset it must be pointed out that education is mandatory & psycho-behavioural methods & reassurance may well be sufficient for many patients, especially those with mild symptomatology. Psychological techniques include assertiveness training [46], self monitoring[47], & cognitive therapy.

Pharmacological management:
Chemotherapy is at present the mainstay of treatment of the motor & vocal symptoms of TS, as well as some of the associated behaviours. The most commonly prescribed medications for motor & vocal tics have historically been dopamine antagonists. The most successful agents in this group are haloperidol, Pimozide, sulpiride & tiaprite. Haloperidol a butyrophenon derivative is primarily a dopamine D2 receptor blocker. This drug has been the

most tried & tested medication, with many case reports of its successful use, but haloperidol produces unacceptable side effects in 84% of patients. Therefore only minority of patients (20 to 30% of TS patients) can continue treatment for extended period. Pimozide, a dopamine D1 receptor blocker was found to be significantly superior to haloperidol in improving cognitive functioning & haloperidol produced a 3 fold higher frequency of side effects & significantly more extrapyramidal symtoms than pimozide. Sulpiride, the most widely documented benzamide used in the treatment of TS. Positive effects were decreased motor & vocal tics, decreased OCD, decreased aggression, decreased echo phenomena & tension & finally an improved mood. Atypical neuroleptics like resperidone, clozapine & olanzapine are controvertial. Tetrabenazine, which depletes presynaptic storage of monoamines & blocks postsynaptic dopamine receptors, has recently been used successfully in a substantial series of TS patients[5]. There have been some suggestions that tetrabenazine plus a dopamine antagonist could be used together as they may have more lasting effect & fewer side effects because both drugs can be given in lower doses[48]. Clonidine an alpha-2 adrenoceptor agonist is of special use when the TS patient also has ADHD[11]. Antidepressants have been used to treat the depression, the ADHD & particularly the OCD aspects of TS. These include imipramine & nortryptiline which have been successfully used is children with TS & ADHD. Clomipramine is very useful & widely used drug for TS with OCD. SSRI such as fluoxetine, sertraline, paroxetine & citalopram appear to be effective as antidepressants, are less sedative than tricyclic antidepressment (TCA) & have fewer antimuscarinic effects & low cardiotoxicity. They are particularly useful in treating the depression & OCD TS & are used regularly but the dose is high (60 mg fluoxetine per day) Benzodiazepines like Clonazepam was successfully used in some trials [49,50] & it was significantly superior to clonidine & produced fewer side effects[51]. Unfortunately our patient didn't respond to clonazepam 1 mg daily. Calcium channel blockers like verapamil, nifedipine & flunarizine are also used in some patients with success but they are controversial. Botulinum toxin is seen to be effective in coprolalia in TS patients[52]. On the other hand cases have been reported where carbamazepine has reduced the TS symptoms [53]. Carbamazepine was the drug of choice for our patient as his EEG revealed unilateral temporal slowing. With carbamazepine 200 mg daily his symptoms reduced markedly over 20 days.

Nicotine:

A recent study evaluated the effect of nicotine smoking in 47 TS patients. Of the 28 patients only 2 reported a tic reduction when smoking cigarettes[54].

Marijuana:

A recent study evaluated the effect of marijuana smoking in 47 TS patients. Of the 13 patients taking marijuana 11 reported a marked tic reduction[54].

Uncommon Treatments of TS:

Immunomodulatory, antibiotic & antiviral therapy: Several authors have suggested that certain groups of Ab-haemolytic streptococcal infections & some viral infections may precipitate or exacerbate

symptoms in some cases of TS & treatment of infection reduces TS symptoms which was mentioned earlier. Hormonal therapy, based on evidence implicating abnormal gonadotrophic function was given in TS. The anti-estrogenic agent clomiphene citrate was successful in treating TS symptoms. Nonsteroidal androgen blocking agent flutamide also showed improvement.

Acupuncture:

Wu & colleagues treated 156 TS patients with acupuncture is China. The success rate was 92.3%. The cure rate in children aged 11-15 years was markedly higher than in children aged 6-10 yrs. Among the 84 cases with an abnormal EEG the pathological waves disappeared or improved in 54 cases after acupuncture[55].

Conclusion:

TS is probably a heterogeneous condition from an aetiological, genetic, clinical, phenomenological & psychopathological point of view. Our patient do have a few points that might be considered as precipitating factors like he had a history of common cold before his illness which indicates a viral etiology & he was going to school for 10 days before his illness which indicate stress. Another area of significance is that his EEG was also abnormal as he had temporal slowing & interestingly use of carbamazpine dramatically reduced the symptoms. So, there might be some rationality to use carbamazepine in cases of TS patients with abnormal EEG.

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Typical Meningioma Turned into Atypical Meningioma within Six months

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Abstract

A male patient of 50 years of age, was admitted in Neurosurgery department of BSMMU on 7th May, 2008 with progressive swelling over his frontal region for about 3 months, which was rapidly progressive in nature, eroding the frontal bone of the skull, came out of the frontal region and also extended subcutaneously. Plain X-ray skull showed a soft tissue mass over the right frontal region, eroding the frontal bone.

C.T. Scan of brain shows an intensely contrast enhancing hyperdense mass with extensive perilesional oedema.

Through a linear incision over the frontal swelling the tumor was operated on 01/06/ 2008 and was totally removed. Histopathology report came as Atypical Meningioma, WHO Grade-II.

This patient has a history of right frontal convexity space occupying lesion with the symptoms of headache, nausea and vomiting with rapidly increasing generalized convulsion for about 15 months before December, 2007. Right frontal craniotomy and near total removal of the tumor was done on 3rd December, 2007.

Peroperatively on 3rd December 2007 a greyish fleshy tumour was found under the dura, arising from convexity, occupying the whole right frontal lobe and extending to the part of right parietal lobe, frontal crossing across the coronal suture posteriorly and attatched to the falx medially. Histopathology report was WHO Grade -I Meningioma.

As these two histopathological findings are rare and interesting of turning benign meningioma to malignant meningioma within 6th months. For this reason, it has been decided to publish this case in this journal.

Introduction

Intracranial Meningiomas are the most common benign tumours of the brain and constitute about 13-18 percent of brain tumours[1]. Gulati[2], in a comparative study of various indian series reported their incidence to vary from 9-15 percent. Meningiomas constitute about one-fifth of the all primary intracranial tumours[3]. They are slow growing and arise from arachnoid granulations and lie in greatest concentration around the venous sinuses and also occur in relation to surface tributary vein[3]. Occasionally they are multiple and present primarily in the 40-60 age group of patients and have a slight female preponderance[3]. They are principally benign tumours, although 1-2% show malignant changes[3]. The tumour

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surface, often lobulated, is well demarcated from the surrounding brain and attached only by small bridging vessels[3]. Marked oedema often develops in the surrounding brain with a reactive hyperostosis which developed in adjacent bone, forming a swelling on the inner table, occasionally affecting the outer table, that may produce a palpable lump[3]. Tumour texture and vascularity varies considerably from patient to patient- some are firm and fibrous, others soft. Calcified deposits (psammoma bodies) are often found[3]. It is important to identify the anaplastic (malignant) form, as this indicates the likelyhood of rapid growth and a high rate of recurrence following removal[3]. Potentially curable the treatment of meningiomas is a gratifying surgical exercise, when they are avascular and occur on the convexity but when highly vascular and arising deep at the base of the skull, they form one of the most formidable challenges to surgery. Meningiomas has the tendency to cause thickening of overlying bone and left their mark in the form of hyperostosis[3].

Case History

A 50 year old male presented with rapidly progressive swelling over his frontal region for about 3 months who has history of right frontal convexity space occupying lesion with the history of headache, nausea and vomiting with rapidly increasing generalized convulsion for about 15 months which was removed by right frontal craniotomy on 03/12/2007. Part of the frontal bone was found eroded by the underlying tumour. Peroperatively, a greyish fleshy tumour was found under the dura, arising from convexity, occupying the whole right frontal lobe and extending to the part of right parietal lobe, crossing the coronal suture posteriorly and attached to the falx medially. Histopathology report was WHO Grade -I Meningioma.

Patient was admitted in neurosurgery department of BSMMU on 07/05/2008 with the history of progressive swelling over his frontal region for about 3 months. Swelling was rapidly progressive in nature. Local examination reveals that the tumour was mobile, non-tender, nonfluctuating, free from the overlying skin. Local temperature was found raised. Transillumination test was found negative.

Neurologically, the patient was fully conscious, alert, oriented and responded to all vocal commands. All cranial nerves were found intact. Fundoscopy shows bilateral papilloedema. There was no sensory or autonomic impairment.

X-ray skull A/P and lateral view done on 08/05/2008 shows soft tissue mass over the right frontal region with erosion of the underlying cranial bone with the evidence of previous craniotomy.

CT scan of head done on 08/05/08 shows an intensely contrast enhanced hyperdense mass with extensive perifocal edema in the right frontal lobe with ipsilateral compression of lateral ventricle with destruction of overlying frontal bone and extracranial extension of the tumour to the scalp suggestive of a post-operative (reccurence) case of high grade tumor.

Operative procedure: Through a linear incision over the frontal region, debulking of the tumour, which came out from the eroded bony gap was done. Unhealthy bony tissue was nibbled out. Dural gap was repaired by fascia lata (taken from right

thigh) . Bony gap was replaced by bone cement. Redundant skin was excised. Wound closed in layers.

Histopathology: (done on 05/06/08) showed Atypical Meningioma Grade II. Then the patient was treated with Adjuvant Radiotherapy (Gamma ray) with the strength of 5600 Rads in 28 fractions, each day in a single region of the skull in Dhaka Medical College Hospital from 12/06/2008 to 29/9/2008 in the following order:-

1. Location-Right cranium - Measurement- 11 x 14 } 12.3 cm^2, site- on the back, depth-70.42%.
2. Left cranium- Measurement- 11 x 14} 12.14 cm^2, site- on the back, depth-70.42%. a. Right frontal, Measurement- 9x9} 9cm^2 , depth- 83.07%.

   b. Right temporal- Measurement- 9x9} 9cm^2, depth - 88.07%.

But unfortunately patient was again admitted in neurosurgery department of BSMMU on 7th May 2008 with the rapid recurrence of the tumour. Tumour came out aggressively in the same site of the frontal region, which was extended to right upper eyelid, closing the right eye.

On 1st June 2008 through a T shaped incision over the tumour in the right frontal region debulking of the tumour was done as much as possible. Tumour was invaded into the ethmoidal sinus and externally to the right side of the face over the right eyelid. Near total removal of the tumour was done. Dural graft given by taking a fascia lata from right thigh. Haemostasis secured. Wound closed in layers, keeping a drain inside.

Discussion

In most patients a preoperative diagnosis of malignant meningioma is not made[5]. Therefore, the initial management is the same as outlined for each location of tumour[5]. The most important surgical consideration is to make as wide as possible of the dura and / or falx around the tumour. Some patients have required multiple operations. Radiation therefore is important at some point in the management of most of these patients[5]. When to give the therapy has not been defined[5]. When it is thought that there is a gross total removal, then the radiation therapy has been usually postponed and the patient is carefully observed. When there is recurrence and the findings on the scan suggested that another total removal could be done, surgery is performed[5].

The prognostic significance of the Simpson grade of surgical resection and tumour location was also considered. Survival at 5 and 10 years was recorded in 95% and 79% respectively of patients with atypical meningioma and in 64.3% and 34.5% of patients with malignant meningioma ($p=0.001$). Recurrence-free survival and median time to recurrence were also significantly longer in patients with atypical than in those with malignant meningioma : 11.9 versus 2 years (p-0.0001) and 5 versus 2 years ($p<0.0041$) respectively[6].

Meningiomas are rarely malignant in their behaviour. But when malignant, meningioma grow rapidly and are destructive; they are quite difficult to treat, and recur often in less than a year after surgical removal[7]. They are also difficult for the pathologist to diagnose under the microscope. Probably the only findings that correlates well with diagnosis is that numerous cells are seen in division ("mitosis"). Ultimately, the diagnosis is

determined by the activity of the particular tumour over time[7].

But in this case, the transformation of benign meningioma to atypical variety is unusually rapid, within six months. Unfortunately, radiotherapy failed to respond and the recurrence did not stop after repeated exploration and removal of the tumour.

Conclusion:

In conclusion, the current study shows that for most patients with atypical meningioma the prognosis was less severe than those with malignant meningioma, but the risk of a downhill course resulting from malignancy after incomplete resection and recurrence was not negligble (26%). In addition, the WHO classification was found to be inadequate for a minority of the atypical meningioma cases, which currently have the same unfavourable course as cases of malignant meningioma. The results also indicate that objective Simpson Grade I extirpation of convexity meningiomas can be successful despite histopathological findings of malignancy.

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