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Relationship between Histopathological Subtypes of Intracranial Astrocytoma Patients

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Abstract:

Background : *The study was carried out in the department of neurosurgery, BSMMU, Dhaka during the period of July 2003 to June 2005.* ***Objective:*** *This study was done to elucidate the relationship between age groups and histopathologicas subtypes in case of intracranial astrocytoma patients. For this purpose, a total number of 44 cases were studied.* ***Results:*** *The mean age of all the patients was 33.1 years (range:1-65 years). The highest incidence was found in the age group of 20 years or below group. Male were more commonly effected than female. WHO grade I astrocytoma was the commonest type. Mean age of low grade astrocytoma (WHO grade II) and glioblastoma were nearly similar to other studies, but the mean age of presentation of grade I astrocytomas patients was little late and for anaplastic actrocytoma a little early in comparison to other study.* ***Conclusion:*** *This showed subtype of astrocytoma has definitive relation to age.*

Key words: *Histopathological subtype, astrocytoma, glioblastoma, oligodendroglyma, ependymoima.*

Introduction:

Glial cells are five to ten times more frequent than the trillion brain neurons and compose half the central nervous system (CNS) by volume[1].

Corresponding to the three histologic groups of glial cells are the following three major types of gliomas: i) astrocytoma, ii) oligodendroglima iii) ependymoma[2].

Astrocytomas do not fall within discrete, easily definable categories but instead represent a biologic continuum that ranges from hitologically well-differentiated tumor to poorly or undifferentiated neoplasms with nuclear and cellular pleomorphism, vascular endothelial proliferation and necrosis[3].

The first widely influential system was devised in 1926 by Bailey and Cushing, who divided these neoplasm into three entities according to their histological similarity to normal embryonic glia[4].

In 1949, Kernohan et al, proposed a four tiered system based on the degree of anaplasia[5].

For many years the Kernohan system was the mainstay of pathologic classification of glial tumor and it remains influential today because of its widespread use in the training of pathologists and neuro-pathologists[6,7].

In 1950, Ringertz proposed a three tiered system that was later popularized by Burger et al and used in many cooperative brain tumor clinical trials[8].

The most recently introduced grading system is that of the revised World Health Organization[9].

Pilocytic astrocytomas presumably arise from a class of astrocytes that is inconspicuous in normal brain but may become prominent in reactive gliosis and neoplasia[10].

Incidence all gliomas 5% to 10% of but account for nearly one third of pediatric neoplasm[11].

Pilocytic astrocytomas typically are tumors of children and young adults, most tumors in the cerebellum become symptomatic during the first two decades of life[12].

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Pilocytic astrocytomas are characteristically located around the third and fourth ventricles. Less common locations include the brainstem and basal ganglia[13]. The frontal lobe are the most common location of hemispheric pilocytic astrocytoma[14].

Zulch[11] showed that average age of intracranial astrocytoma was 36.15 years when it was 31.51 years in Dastur's[15] series. According to the study of Mc Kernan and Thoma[16] mean age for low grade astrocytoma was 37.4 years.

Cerebral hemispheres specially frontal (40%), temporal (25%), and parietal (25%) lobes[16]. Others (10%) include thalamus, midbrain and pons.

Anaplastic Astrocytomas are in Kernohan's grade three and in WHO grade III.

Age incidence of glioblastoma multiforme is usually in patients over 50 years and are rare in patients under 30. Glioblastoma can occasionally be found at any age.[2] According to Burger P. C.[17] median age 50 to 60 years.

Incidence of gliomas are 45% to 50%.[18] Any region of CNS possible; cerebral hemispheres predominate (40% frontal, 25% temporal, 25% parietal)[19].

Symptoms of raised intracranial pressure more common than with lower grade tumors.[20] Mental status changes and motor deficit also common. Seizure at presentation is approximately 32%[21].

Methodology:

This is a cross sectional study which was carried out at the Department of Neurosurgery, Bangabandhu Sheikh Mujib Medical University (BSMMU). The study was carried out from July 2003 to June 2005. 44 cases were studied. Inclusion criteria are patients with intracranial astrocytomas admitted in dept. of neurosurgery, BSMMU. Exclusion Criteria are patients of intracranial astrocytomas who denied to be included in the study.

A questionnaire was prepared considering the variables such as age and sex of the patient, clinical features, site of tumor, image findings, per operative findings and histopathological reports. Histopathological report of the tumor was collected and then recorded.

Data were processed through computer software SPSS version 11. Statistical calculations were performed by SPSS software. Chi-square test was applied to test for significance and conclusion was drawn at 1% level of significance.

Results:

The study was done on 44 patients of intracranial astrocytomas, all patients underwent craniotomy or burr hole biopsy to prove the histopathological diagnosis.

Table-I

Distribution of the cases according to age (N=44):

Frequency of age (years)	No. of cases	Percentage
≤20	12	27.3
21-30	9	20.4
31-40	11	25
41-50	7	15.9
> 50	5	11.4
Sex		
Male	36	81
Female	8	19

Table I shows the distribution of cases according to age frequency. 12 cases (27.3%) were of 20 or below 20 years, 9 cases (20.4%) were of 21 to 30 years age group, while 31 to 40 years age group comprises of 11 cases (25%).

Table-II

Distribution of the cases by presenting symptoms (N=44)*

Presenting symptoms	No. of cases	Percentage
Headache	36	81.8%
Vomiting	29	65.9%
H/O Convulsion	26	59%
H/O altered consciousness	19	43.2%
Blurring of visual	21	47.7%
Limb weakness	20	45.5%

* Total was not correspond to 100%, because of multiple symptoms in same patient

Table II shows the presenting symptoms of the study patients. More than 80% patients presented with

headache, 65.9% of cases admitted with vomiting, nearly 60% had history of convulsion at least once during the period of illness.

Table-III

Distribution of the patients by status of consciousness (N=44):

GCS score	No. of cases	Percentage
15	38	86.3
13-14	5	11.4
7-12	01	2.3
Total cases	44	100

Table III shows the consciousness level of the patients. 38 patients (86.3%) were found conscious oriented. 5 cases (11.4%) were confused (GCS, 13-14) and 1 patient had GCS 7-12.

Table-IV

Distribution of the cases by speech pattern and gait (N=44):

Speech pattern	No. of cases	Percentage
Normal	35	79.6
Dysphasia	6	13.6
Dysarthria	3	6.8
Gait pattern		
Normal	24	54.5
Hemiplegic	19	43.2
Ataxic	01	02.3

Table IV shows the speech pattern of the patients. Put of 44 patients 35 cases (79.6%) did not have any speech defect. Out of 44 patients 24 (54.5%) had normal gait.

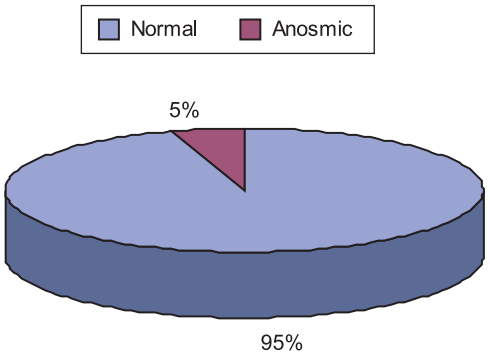

Fig.-2: *Distribution of the cases by olfactory nerve function (N=44):*

Fig.-2. shows most of the cases (95.5%) had normal Olfactory nerve function while only 2 cases (4.5%) had anosmia.

Table-V

Optic nerve function occulomotor, trochlear abducement nerve

Optic nerve function	No. of cases	Percentage
Normal	16	36.4
Defective acuity of vision	08	18.2
Defective field of vision	05	11.4
Papilloedema	17	38.6
Optic atrophy	06	13.6
Oculomotor, trochlear and abducent nerves function		
Normal	40	90.9
Abnormal size of pupil	4	9.1
Extraocular palsy	01	2.3

* Total was not correspond to 100%, because of multiple symptoms in same patient

Table V shows the distribution of patients by the status of optic nerve, 36.4% of the patients had normal optic nerve function while 38.6% had papilloedema and 13.6% had optic atrophy. The functional status of Oculomotor, trochlear and abducent nerves. 90.9% of the patients had normal function, 4 cases (9.1%) had abnormal size of pupil and 1 patient (2.3%) had extraocular muscle palsy.

Regarding the function of Trigeminal, Glossopharyngeal, Vagus, Accessory and Hypoglossal nerves all the patients were found to be normal.

Table-VI

Function of facial nerves (N-44)

Nerves function	No. of cases	Percentage
Facial nerves function		
Normal	34	77.3
Upper motor type deficit	10	22.7
Lower motor type deficit	0	0
Vestibulocochlear nerves function		
Normal	42	95.5
Hearing impairment	2	4.5
Balance impairment	0	0

Table VI shows the function of facial nerves. 77.3% of the patients were found to have normal function of facial nerves whereas 22.7% of them had upper motor type of facial palsy. The function of vestibulocochlear nerves. 95.5% of the patients were found to have normal function and the rest (4.5%) of them had hearing deficit.

Table-VII

Motor Function, sensory function and cerebellar function (N-44)

Function	No. of cases	Percentage
Motor function		
Normal	27	61.4
Hemiparetic	16	36.4
Monoparetic	1	2.2
Sensory function	44	100
Normal	43	97.7
Impaired pain and temperature	0	0
Impaired cortical sensation	1	2.3
Cerebellar function		
Normal	43	97.7
Impaired	1	2.3

Table VII shows the motor function of the patients. 61.4% of the patients did not have any motor deficit, 16 cases (36.4%) had hemiparesis and I patient presented with monoparesis. The sensory function of the patients. 97.7% of the patients did not have any sensory deficit and only 1 patient (2.3%) showed impairment of cortical sensation. The cerebellar function of the patients. 97.7% of the patients had normal coordination of movements and only 1 patient (2.3%) showed impairment of cerebellar function.

Table-VIII

Distribution of the cases according to CT / MRI findings (N-44)

CT / MRI Findings	No. of cases	Percentage
Change in attenuation, no mass effect,no enhancement	1	2.3
Change in attenuation + mass effect ,no enhancement	19	43.2
Enhancement but no necrosis	16	36.3
Enhancement with necrosis (ring enhancement)	8	18.2
Total cases	44	100

Table VIII Imaging study of 19 patients (43.2%) showed change in attenuation, mass effect without any enhancement of contrast agent. Imaging of 36.3% patients showed contrast enhancement without necrosis 18.2% of them showed enhancement with necrosis and imaging of one patient (2.3%) showed only attenuation change without mass effect and enhancement.

Table-IX

Distribution of the patients according to histopathological subtypes (N-44)

Histopathological subtypes	No. of cases	Percentage
WHO Grade I	15	34.1
WHO Grade II	10	22.7
WHO Grade III	9	20.5
WHO Grade IV	10	22.7
Total cases	44	100

Table IX presents the distribution of the patients according to histopathological subtypes. WHO grade I astrocytomas were found in 15 cases (34.1%). WHO grade II were found in 10 cases (22.7%), 9 cases (20.5%) were in WHO grade III and rest of the cases were in WHO grade IV astrocytoma. They were 10 cases (22.7%).

Table-X

Mean age of the different histopathological subtypes (N-44)

Histopathological subtypes	Mean age (years)	Standard deviation	Mean age of all cases
WHO Grade I	23.7	13.30	
WHO Grade II	30.7	5.30	33.1
WHO Grade III	36.4	19.90	
WHO Grade IV	46.5	12.02	

From table X we get the information that mean age of WHO grade I (pilocytic astrocytoma and sub-ependymal giant cell astrocytoma) patients was 23.7 years, mean age of WHO grade II (low grade astrocytoma) was 30.7 years, mean age of WHO grade III (anaplastic astrocytoma) was 36.4 years and mean age of WHO grade IV (glioblastoma multiforme) was 46.5 years. When we calculated

Relationship between age groups and histopathological subtypes:

Table-XI

Cross tabulation of age group and histopathological subtypes (N-44)

			histopathological subtypes				
			grade I	grade II	grade III	grade IV	Total
age of	<20	Observed count	9	0	3	0	12
Patients		Expected count	4.1	2.7	2.5	2.7	12.0
	21-30	Observed count	2	5	0	2	9
		Expected count	3.1	2.0	1.8	2.0	9.0
	31-40	Observed count	3	4	1	3	11
		Expected count	3.8	2.5	2.3	2.5	11.0
	41-50	Observed count	1	0	3	3	7
		Expected count	2.4	1.6	1.4	1.6	7.0
	>50	Observed count	0	1	2	2	5
		Expected count	1.7	1.1	1.0	1.1	5.0
Total		Observed count	15	10	9	10	44
		Expected count	15.0	10.0	9.0	10.0	44.0

the mean age of all the 44 patients it was 33.1 years (SD ±15.6).

Above table IX shows in 20 or less than 20 years age group highest number of cases found in Grade I subtype. In both 21-30 and 31-40 years age group highest frequency was observed in Grade II subtype, in 41-50 years age group highest frequency was in both Grade III and Grade IV and in more than 50 years age group highest number of observation was in Grade III and IV too.

After preparing the above 20 cells table Chi-square (χ^2) test was applied and value of χ^2 comes to 28.46 where degree of freedom =(4-1) X (5-1) or 12. at 12 degrees of freedom table value of is 21.13 when $p < .05$ and 26.12 when $p < .01$.

Here the calculated value of χ^2 is higher than the table value at 1% level of significance ($p < .01$). Hence the test is significant.

So there is association between age group and histopathological subtype in case of intracranial astrocytoma patients.

Discussion

Age incidence of intracranial astrocytomas is a very important variable which varies from study to study. Age incidence of astrocytoma was 31.51 years in Dastur's (1969) series[22].

According to the study of McKeran and Thomas mean age for low grade astrocytomas was 37.4 years, for anaplastic astrocytomas 45.8 years and for glioblastoma multiforme 52 year[23].

According to Youman's study, pilocytic astrocytomas occurred in childhood, low grade astrocytomas are non contrast enhancing area usually present in fourth decades[4].

According to Osborn[2] pilocytic astrocytomas typically are tumors of children and young adult.

In our study we found that mean age of low grade astrocytomas (WHO grade I) was 30.7 years. This is almost similar to other international studies. Mean age of anaplastic astrocytoma (grade III) was 36.4 years, which is little earlier than the other studies. In case of glioblastoma multiforme mean age was 46.5 years, which is near to the study of McKeran and Thomas[24]. Mean age of pilocytic astrocytomas (grade I) was 23.7 years, which is little older than the international studies where it was during the first two decades of life.

In our study mean age of all intracranial astrocytoma patients was 33.1 yaers which is very close to the result of Dastur's (31.51 years) study.

Sex incidents of intracranial astrocytomas also varies from study to study. In our study, we found a

male predominance at the ration of 4.5:1. So, if we compare our study with other international studies, we will find more male predominance.

In this study highest number of cases were found in less than 20 years group and it was 15 cases. The youngest patient was 1 year old and the oldest patient was 65 years old showing that no age group is exempted for intracranial astrocytomas.

In our study the percentage of glioblastoma multiforme was 22.7% which is surprisingly low than the international studies where it was the common of all gliomas. Probably poor prognosis and rapid deterioration may be one of the important cause of not reaching of such types of patients in hospital in proper time. Headache or seizure is sometimes the early or only symptom for intracranial astrocytoma patients which are ignored by a lot of patients or attendant vary frequently. Investigation of intracranial astrocytoma patients (CT/MRI) are very expensive which were also avoided by the patients or their relatives very frequently which is another important cause of not reaching hospital in time.

Analysis of clinical features revealed that presenting symptoms were headache, vomiting, convulsion, altered consciousness, blurring of vision, limb weakness and cranial nerve dysfunction. Most of the symptoms were related to raised intracranial pressure and mass effect by the tumor.

Jackle et al. reported seizure in 65-70% of low grade glioma and 30-50% in glioblastoma patients[24].

Tandon showed apathy, change in personality, impaired memory attention concentration and inappropriate social behavior are the common feature of fronto temporal astrocytomas[25].

In this study we observed 81.8% patients presented with headache, 59% of the patients had history of seizure, 47.7% of them had visual disturbance and limb weakness was present in 45.5% of the patients. So, the presenting symptoms of this study is almost similar to other studies.

McKeran and Thomas reported 50-70% patients with papilloedema.[16] In our study 38.6% of the patients had papilloedema which is very near to that study.

This study showed 77.3% of the patients with normal facial nerve function and 22.7% with upper motor type deficit.

In this study 79.6% patients were found with normal speech, 13.6% with dysphasia and 6.8% with dysarthria. Early dysphasia is often overlooked or confused with memory impairment[25].

In imaging (CT / MRI) study 36.4% patients had complex enhancement, 18.2% had enhancement with necrosis and rest 45.4% without enhancement. Piepmier[26] had shown in a large series that those patients whose tumors enhance on imaging had a poorer prognosis than those whose lesion did not enhance after administration of I/V contrast.

In this study, mean age of WHO grade I is 23.7 years, WHO grade II is 30.7 years, WHO grade III is 36.4 years and WHO grade IV is 46.5 years. So the histopathological subtypes of astrocytomas are related to age group.

Conclusion:

This study has shown that there is significant relationship between age groups and histopathological subtypes in case of intracranial astrocytoma patients.

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