Review Article

Histopathological analysis of central nervous system tumors; an observational study

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ABSTRACT

Background: Though the central nervous system tumor comprises ~2% of all the tumors, an overall increase has been observed especially in less developed countries. This increase in the incidence may be due to exposure of population to various risk factors or improved diagnosis with advancement in the ancillary studies. This study aims to provide a single centre histopathological spectrum of this type of tumor.

Materials and Methods: A retrospective cross sectional study on a series of cases was performed in the Department of Pathology, Annapurna Neurological Institute & Allied Science , Maitighar, Kathmandu, Nepal from April 2013 to Jan 2016. Data were analyzed using SPSS version 21.0.

Results: A total of 221 brain and CNS tumors (125 females and 96 males) were studied. The mean age at diagnosis was 77 years. The most common tumor was meningioma(67 cases, 30.3%), followed by astrocytic tumor (57 cases, 25.7%) and pituitary adenoma(30 cases,13.6%). The frequency of WHO grade I, II,III and IV tumor were 94 cases (55%), 34 cases (19.9%),10 cases (5.8%), and 33 cases (19.3%) respectively. The astrocytic tumor was most frequent tumor in children (7/20 cases, 37 %).

Conclusion: This study showed the most common CNS tumor to be meningioma followed by astrocytic tumors and pituitary adenoma. The spectrum of CNS tumor in children showed divergent histologic pattern according to the age. In age group 0-10 years embryonal tumors were common whereas 12-20 years age group showed propensity towards astrocytoma as in adults.

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INTRODUCTION

The burden of cancer is increasing worldwide despite advances for diagnosis and treatment.[1] Population based cancer registration provides an essential base for cancer control, providing information not only on incidence and survival but also facilitating confirmation of effectiveness of interventions. Hospital-based registries and even pathology-based registries also can make important contributions.[2]

Though the tumors of the central nervous system (CNS) constitute approximately 2% of all malignancies, the associated morbidity and mortality and the significant proportion of affected young and middle-aged individuals has a major impact in life years compared to other

Table 1: Sex-wise distribution of CNS tumor

Diagnosis	Female		Male		Total	
	n	%	n	%	n	%
Adamantinomatous (fig.1)	4	3.2	6	6.2	10	4.5
Astrocytic tumor	23	40.3	34	59.6	57	25.7
Oligodendroglioma	5	4.0	3	3.1	8.0	3.6
Meningioma	53	42.4	14	14.6	67	30.3
Central Neurocytoma	2	1.6	1	1.0	3.0	1.4
Choroid plexus papilloma	0	0 .0	1	1.0	1.0	0.5
Ependymoma	2	1.6	3	3.1	5.0	2.3
Ganglioglioma	0	0.0	1	1.0	1.0	0.5
Hemangioblastoma	1	0.8	5	5.2	6.0	2.7
Embryonal tumor	1	0.8	2	2.1	3.0	1.4
Metastatic carcinoma	7	5.6	6	6.2	13	5.9
Oligoastrocytoma	8	6.4	2	2.1	10	4.5
Pituitary adenoma	15	12	15	15.6	30	13.6
Lymphoma	4	3.2	3	3.1	7	3.2
Total	125	56.7	96	43.3	221	100

malignancies.[3] Moreover, these tumors are in increasing trend. An overall increase has been observed throughout the world, especially in less developed countries.[4] The importance of descriptive data on the full spectrum of primary brain and CNS tumors has been previously recognized.[5] The current study aims to evaluate and provide overview of descriptive epidemiology of CNS tumors in a single centre over a 3 year study period.Pathological classification of brain tumors is the corner stone upon which the management plan and treatment strategy depends.[6]

MATERIALS AND METHODS

This is a retrospective cross-sectional study performed in the Department of Pathology at Annapurna Neurological Institute & Allied Science, Maitighar, Kathmandu, Nepal. This study was conducted in the histopathology samples received from April 2013 to Jan 2016. Ethical clearance was obtained from institutional review committee.The variables entered in the database were histopathology number, name, age, histopathological diagnoses, site of the tumor and tumor grade. All the histopathologically proven tumor specimens of CNS tumor received in the given time frame were included in the study.The specimens received were processed by fixing, dehydration, and clearing followed by impregnation with wax. The wax blocks were cut in 5-6 μ sections & stained by hematoxylin and eosin stain. The diagnoses were made on histological examination of the processed tissue. In our study the various lesions were studied and classified according to World Health Organisation (WHO) classification (2007). The 2007 WHO classification presented as the standard for the definition of brain tumors to the clinical oncology and cancer research communities worldwide.[7]

The World Health Organization classifies CNS tumors based on cellular origin and histologic appearance.[8] Neuroglial tumors account for more than 80 % of primary brain tumors and derive from astrocytes, oligodendrocytes, or ependymal cells. Gliomas are divided into four grades; grades I and II tumors are low grade, whereas grades III and IV tumors are high grade.[9] Data were analysed using SPSS version 21.0.

RESULTS

A total of 221 brain and CNS tumors (125 females and 96 males) were retrieved retrospectively from the registry during the time duration specified. According to the cell of origin, 88 cases were of neuroepithelial origin and 133 cases were non-neuroepithelial origin.

The age ranged from 6 months to 83 years with a mean age of 43.77 years. The age group ranging from 21-40years most commonly suffered from these tumors (n = 81; 36.7%), followed by 41-60 years (n=79; 35.8%), >60 years age (n=41; 18.6%) and the least common was age <20 years (n=20; 9.0%)

CNS tumors in this study were most frequently encountered in the cerebrum comprising of 98 cases (44.3%) out of which 49 of them were situated in the frontal lobe, followed by the sellar region comprising of 44 cases (19.9%).

The most common tumor in this study was meningioma comprising of 67cases (30.3%). Astrocytic tumor comprised 57cases (25.7%) and third most common pituitary adenoma comprised of 30 cases (13.6%). The number of individual tumor in detail is tabulated. Table 1 and 2.

Table 2: Age-wise distribution of CNS tumors

Diagnosis	Age Group (Years)					
	0-20	21-40	41-60	>60	Total	%
Adamantinomatous craniopharyngioma	2	4	1	3	10	4.5
Astrocytic tumor	7	22	18	10	57	25.7
Oligodendroglioma	0	3	3	2	8	3.6
Meningioma	2	25	30	10	67	30.3
Central Neurocytoma	0	3	0	0	3	1.4
Choroid plexus papilloma	1	0	0	0	1	0.5
Ependymoma	3	2	0	0	5	2.3
Ganglioglioma	0	0	1	0	1	0.5
Hemangioblastoma	0	4	0	2	6	2.7
Embryonal tumor	3	0	0	0	3	1.4
Metastatic carcinoma	0	1	5	7	13	5.9
Oligoastrocytoma	0	5	4	1	10	4.5
Pituitary adenoma	2	11	14	3	30	13.6
Lymphoma	0	1	3	3	7	3.2
Total	**20**	**81**	**79**	**41**	**221**	**100**

In the cases of meningioma, there was female preponderance with M: F= 1:3.7) (14 males and 53 females) andshowed increased frequency in age group 3 (41-60years). As depicted in table 3, the meningothelial and transitional meningioma comprised of 26 cases each (38.8 %) and psammomatous meningioma comprised of 6 cases (9%).

Astrocytic tumor showed male preponderance with male to female ratio of 1.4:1. It was encountered most frequently in the age group of 21-40years. Among astrocytic tumor 27 cases (47.4%) were of glioblastoma multiforme (GBM) seconded by diffuse fibrillary astrocytoma 11(19.3%) cases. (Table 4) Pituitary adenoma was third in proportion with total case of 30 (13.6%), showed equal sex predilection and age propensity to clinically manifest among the age group of 41-60 years.

Among the studied total 221 CNS tumors, in 171 cases, it was possible to grade the tumors according to the WHO classification. The frequency of WHO grade I tumor was considerably higher comprising 94 cases (55%),WHO grade II tumor was 34 cases (19.9%), WHO grade III tumor was 10 cases (5.8%) and WHO grade IV tumor, 33 (19.3%) cases. In this study, WHO grade III tumor was the least , which is shown in bar diagram. (fig.4)

WHO grade IV tumor was higher in age group of 41-60 years (42.42%) whereas WHO grade I, II and III tumor showed preponderance in age group 21-40 years (38.9%, 61.7% and 60% respectively)as depicted in figure 4.

As the CNS tumors of pediatric age group are considered to have its own spectrum, children of age group range 0-20 years were analyzed in our study as well. There was male preponderance with 14 males and six females, M:F=2.3:1 which was contrary to the ratio of overall tumor. The
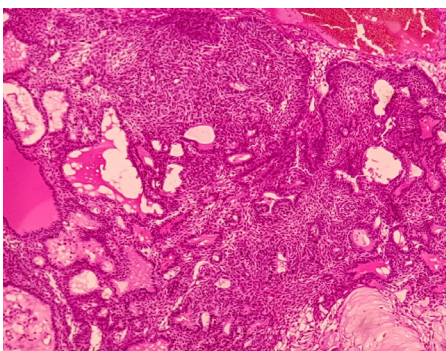

Figure 1: *Adamantinomatous craniopharyngioma: Peripheral palisading of squamous epithelium, ""stellate reticulum" and ""wet keratin" (HE stain; X100).*
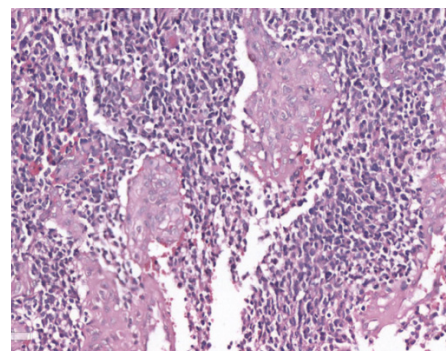

Figure 2: *Glioblastoma multiforme with tumor cells with areas of microvascular proliferations (glomeruloid bodies; HE stain; X200).*

Table 3: Relative frequency of meningioma according to age

Diagnosis	Age Group (Years)									
	<20		21-40		41-60		>60		Total	
	n	%	n	%	n	%	n	%	n	%
Meningothelial meningioma	0	-	10	40	13	43.3	3	30	26	38.8
Transitional meningioma	1	50	12	48	9	30	4	40	26	38.8
Fibrous meningioma	1	50	1	4	1	3.3	0	-	3	4.5
Microcystic meningioma	0	-	1	4	1	3.3	0	-	2	3
Psammomatous meningioma	0	-	0	-	4	13.3	2	20	6	9
Secretory meningioma	0	-	0	-	1	3.3	0	-	1	1.5
Angiomatous meningioma	0	-	0	-	1	3.3	1	10	2	3
Atypical meningioma	0	-	1	4	0	-	0	-	1	1.5
Total	2	100	25	100	30	100	10	100	67	100

Table 4: Relative frequency of astrocytic tumors according to age

Diagnosis	Age Group (Years)									
	<20		21-40		41-60		>60		Total	
	n	%	n	%	n	%	n	%	n	%
Pilocytic astrocytoma	4	57.1	3	13.6	1	6.2	0		8	14
Diffuse gemistocytic astrocytoma	0		0		1	6.2	0		1	1.8
Diffuse fibrillary astrocytoma	1	14.3	9	40.9	1	6.2	0		11	19.3
Pleomorphic xanthoastrocytoma	1	14.3	1	4.5	0		0		2	3.5
Anaplastic astrocytoma	0		4	18.2	1	6.2	0		5	8.8
Glioblastoma (Fig.2)	1	14.3	5	22.7	12	75	9	100	27	47.4
Gliosarcoma	0		0		2		1		3	5.2
Total	7	100	22	100	18	100	9	100	57	100

frequency of individual tumor is tabulated in table 5.

In our study there were 13 cases of metastatic carcinoma among which three were squamous cell carcinoma, Adenocarcinoma, ductal carcinoma, adenoid cystic carcinoma comprised one each however; eight were categorized as metastatic carcinoma and was sent for the identification of primary site with the help of immunohistochemistry. Other tumors like oligodendroglioma, craniopharyngioma, embryonal tumors and ependymomas were seen in different proportions.
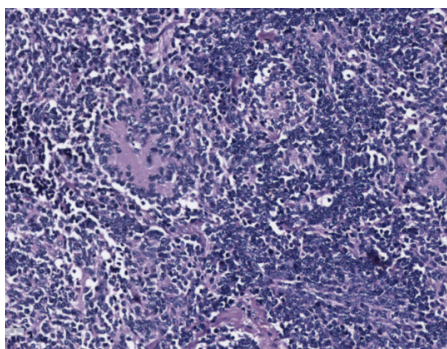

Figure 3: *Photomicrograph showing microscopic view of medulloblastoma with small round tumor cells with a Homer-Wright rosette (HE stain; X200).*

DISCUSSION

The present study comprised of 221 CNS tumors irrespective of age, from a single centre and was categorized according to the recent WHO classification.[8]

Distribution of CNS tumors by sex and age group

In our study male to female ratio was M:F= 1:1.3 showing female preponderance (56.5 %) which is similar to study in Singapore conducted by Das A et al[10] with female occupying 52.6% however, findings of Nibhoria S et al[11] was conflicting with the ratio of M:F= 1.2:1.

The age group of patients with CNS tumors also corroborated with studies like that of Krishnatreya M et al in which the highest number of patients was seen in the age-group of 20-39 years and 21-40 years in our study.[12]

Pattern of common CNS tumor

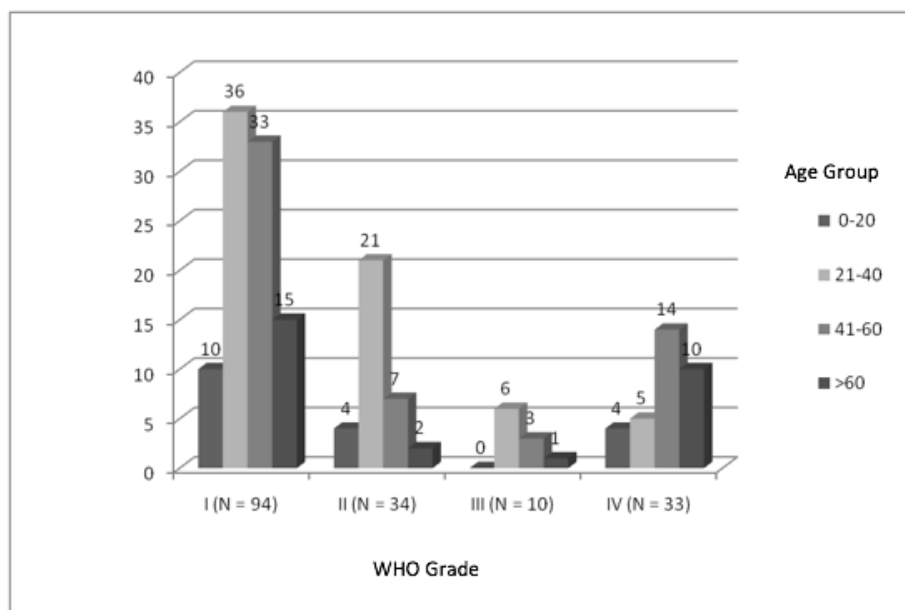Meningioma was the commonest tumor 30.3% which was

Figure 4: Bar diagram showing relative frequency of various WHO grade according to age group

Table 5: Distribution of CNS tumors with histologic subtypes and sex among age 0-20 years

Age (years)	Diagnoses	Sex	N	%
<1	Choroid plexus papilloma	M	1	5
3	PNET, NOS	M	1	5
4	Medulloblastoma (Fig.3)	F	1	5
6	Ependymoma	M	1	5
10	Medulloblastoma	M	1	5
12	Craniopharyngioma	M	2	10
	Pilocytic astrocytoma	M	1	5
	Ependymoma	F	2	10
15	Meningioma	M	1	5
	Pituitary adenoma	F	1	5
17	Pilocytic astrocytoma	M	1	5
	Ependymoma	M	1	5
18	Pilocytic astrocytoma	M	3	15
	Diffuse astrocytoma	F	1	5
19	GBM	F	1	5
20	Pituitary adenoma	F	1	5
	Total		**20**	

comparable with other worldwide studies. Ghanghoria S et al had similar findings in their study comprising of 41.54% of meningioma.[13] Lee et al[14] in Korea and Jazayeri SB et al[15] in Iran also observed that most common tumor was meningioma (31.2% and 27.8% respectively). However, our finding is contrasting with the first study conducted in Nepal. Aryal G et al noticed that the most frequent type of CNS tumor was astrocytoma (38.6%) followed by meningioma (14%).[16] Similarly, a meningioma study

conducted by Wiemels J et al showed the prevalence of pathologically confirmed meningioma to be low, reasoning that a proportion of meningioma are not surgically managed, these estimates may be low.[17]

Meningioma showed female predominance in studies of Nibhoria S et al[11] and Thambi R[18] similar to our findings. As mentioned earlier the most common histological subtype was transitional meningioma and meningothelial type which corroborated with the data of Thambi R et al in which transitional meningioma was followed by meningothelial type in frequency. There were 87.5% of grade I meningioma followed by other grades in her study whereas we encountered 98.5% of grade one meningioma and a single case was of grade II meningioma.[11,18]

The second most common astrocytic tumors (25.7%) was also a relatable finding to Thambi R et al (25%).[18] The peak age group of this tumors was 21 to 40 years according to study conducted by Ayral G et al which is below our peak range of 41-60 years.[16] The reason behind this contrasting finding in the same geographical area may be due to the changing time trends of the tumor and should be evaluated and calculated in depth by epidemiological surveys in other institutions of our country. GBM comprised the highest number of astrocytic tumor with frequency of 31.4%, 50.5% in other studies comparable to our finding of 47.4 percent.[10,16]

This WHO grade IV tumor was seen to be most frequent in the age group 41 to 60 years with a male preponderance. Similar results were obtained in various studies.[4,15,19]

The overall WHO grade IV tumor here was found to be highest in age group of 41-60 years (42.42%). A study conducted by Chen L et al in china also revealed the data of WHO grade III and IV being most frequent in the age group 40-49 and 50-59 years. In both of the studies the oldest age group did not show propensity towards the highest grade of tumor.[4]

Pattern of distribution of CNS Tumors in children

The CNS tumors in children and teenagers showed considerable histologic diversity. The disease pattern was found to be different between the age range of 0-10 years and 12-20 years.The earlier age group showed prevalence of embryonal tumors whereas the older ages suffered more from astrocytic tumors. This similar variance in the distribution of tumors in children was also noticed by Lee CH et al but the differentiating age was from 0-14 and 15-20 years.The most common tumor was astrocytic tumor comprising of 37 % (7/20cases); a slightly higher than the findings of Lee CH et al[14] and NibhoriaS et al[11] (25% and 29.2% resp.) but it was in concordance with Jain et al[20] with proportion of 34.7 percent.

Pediatric GBM is not very common as adult. In our study a case of GBM was seen in a 19 years female. Ansari M et al had studied GBM in paedriatic age group 0-20 years, their mean age was 15.2 years and the median age 16 years.[21]

CONCLUSION

This study showed the most common CNS tumor to be meningioma followed by astrocytic tumors and pituitary adenoma. The spectrum of CNS tumor in children showed divergent histologic pattern according to the age. In age group 0-10 years embryonal tumors were common whereas ages group of 12-20 years showed propensity towards astrocytoma as in adults.

Undeterred by great innovations in ancillary studies, the simple H&E stained slides continue to exist as an invaluable means to diagnose and classify CNS tumors. This study may contribute to revise the changing patterns of incidence, mortality, survival and prevalence of CNS tumors in our part of the world.

Conflict of interest: None

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