

Histopathological Spectrum of Central Nervous System Lesions in a Tertiary Care Hospital in Eastern India

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ABSTRACT

BACKGROUND

Tumours of central nervous system (CNS) are reported to be less than 2 % of all malignancies. In India, CNS tumours constitute about 1.9 % of all tumours. The CNS space occupying lesions cause grave life-threatening outcomes irrespective of their nature as they grow in a confined space and are present close to vital structures. Hence, it is of great importance to establish the accurate diagnosis for proper and timely neurosurgical intervention.

METHODS

This was a retrospective study carried out in a tertiary care teaching hospital which caters as a referral unit for neurosurgical cases in Eastern India, for a duration of one and half year (January 2018 - July 2020) among 185 cases of CNS lesions collected from archives of Department of Pathology. The tumours were reclassified and graded according to the most recent World health organisation (WHO) classification of CNS tumours (2016).

RESULTS

Neoplastic lesions (168 cases, 91.35 %) were commoner than non-neoplastic entities and amongst the neoplastic lesions, meningioma was the commonest entity followed by diffuse astrocytic and oligodendroglial tumours while least incidence was noted for neuronal and mixed neuronal glial tumours. Out of all the tumours for which World Health Organization (WHO) grading was done, highest was WHO grade I (80 cases, 54.8 %) and least was grade III tumours (10 cases, 6.8 %). Male predominance was seen overall except in meningioma. Some rare and interesting cases like solitary fibrous tumour / hemangiopericytoma (anaplastic type), primary CNS diffuse large B cell lymphoma (DLBCL), CNS plasmacytoma which we came across are also highlighted.

CONCLUSIONS

The present study helps to provide information regarding the disease burden in our area. This study attempts to categorise various CNS neoplasms as per recent WHO classification (2016) which has not only diagnostic implication but also has significant prognosis and predictive value.

KEYWORDS

Central Nervous System, Immunohistochemistry, Eastern India, Meningioma, Solitary Fibrous Tumour / Hemangiopericytoma, Diffuse Large B Cell Lymphoma

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BACKGROUND

The human central nervous system (CNS) is a unique and enormously complex organ that acts as a processing centre and an integral link between the body and outer world. The CNS encompasses cerebrum, cerebellum, brain stem, spinal cord, meninges, 12 pairs of cranial nerves and blood vessels supplying these structures. The lesions arising in CNS are heterogenous with a wide spectrum of histological entities such as inflammatory, infectious, metabolic and neoplastic in origin. The neoplastic lesion includes both primary and secondary (metastatic). The tumours of CNS are reported to be less than 2 % of all malignancies.¹ In India, CNS tumours constitute about 1.9 % of all tumours.² However the CNS tumours are associated with high morbidity and mortality which makes them the most dreaded form of cancer.³ The CNS space occupying lesions cause grave life threatening outcome irrespective of their nature. Reason behind this is because lesions grow in a confined space and are present close to vital structures.⁴ Hence it is of great importance to establish the accurate diagnosis for proper and timely neurosurgical intervention.⁵ Tumours of the CNS show a bimodal distribution of age with one peak in children and second peak in 45 - 70 years of age.⁶ These CNS tumours affect more commonly in males than in females except for meningiomas which show female preponderance.^{7,8} In adults most of the tumours arise above tentorium while 70 % of intracranial tumours in children arise in posterior fossa.⁹ Majority of the brain tumours are sporadic lesion and risk factors for neuro carcinogenesis. It is a combination of genetic predisposition with exposure to high doses of ionising radiation.¹⁰ Recently, the international agency for research on cancer also classified overexposure to low frequency non-ionising electromagnetic waves through mobile phones as possibly carcinogenic to human and risk factors for brain tumours such as glioma, meningioma, and acoustic neuroma.

The purpose of this study was to provide frequency of CNS tumours in our tertiary care teaching hospital and to classify according to recent World Health Organization (WHO) classification 2016 along with age groups, gender distribution, topography and to compare the frequency of these CNS tumours with published literature in India and worldwide.

METHODS

This study is a retrospective study carried out over a period of one and half year (January 2018 - July 2019) among 185 cases of CNS lesion. All the cases of CNS lesions were collected from the archive of Department of Pathology in a tertiary care teaching hospital, Bhubaneswar, Odisha which is one of the referral centres for neurosurgical cases in eastern India. In all cases, clinical data including age, sex, site of lesion, and imagological details were obtained wherever possible. The haematoxylin and eosin (H & E) stained slides and immunohistochemistry (IHC) slides were reviewed by 4 pathologists including the first author and histological diagnosis was confirmed and categorised using

WHO classification of tumours of the central nervous system, revised 4th edition, 2016. Since molecular and cytogenetics techniques facility was not available in our institution, those tumours were categorized under not otherwise specified (NOS). Final results were analysed, and data was prepared to study the histological pattern of CNS tumours with age groups, gender distribution, topography of the lesion. One year follow up post therapy was studied, wherever available.

Statistical Analysis

The statistical calculations such as mean age of presentation and percentage calculation was done using Microsoft Excel version 12.0.

RESULTS

It was observed that overall, there was a male preponderance (60.54 %) in CNS lesions, with male to female ratio of 1.53:1 (Figure 3c). The age group was divided into two categories of paediatric and non-paediatrics population comprising of adolescents & above, between which the later were the majority in number (89.73 %) and in only 10.27 % of cases there was a younger age of presentation (Figure 3b). Out of the total 185 histopathology cases of CNS lesions analysed, majority were neoplastic lesions (168 cases, 91.35 %) and rest were non-neoplastic entities (17 cases, 9.18 %). Out of all the neoplastic CNS lesions, majority were meningiomas (54 cases, 29.18 %) followed by diffuse astrocytic and oligodendroglial tumours (46 cases, 24.86 %), schwannoma (23 cases, 12.4 %), ependymal tumours (9 cases, 4.86 %), mesenchymal tumours (6 cases, 3.2 %), medulloblastoma (5 cases, 2.70 %) (Figure 1h), craniopharyngioma (4 cases, 2.16 %), metastasis (3 cases, 1.62 %), choroid plexus papilloma (2 cases, 1.08 %) and only 2 cases (1.08 %) belonged to the category of neuronal and mixed neuronal glial tumours consisting of one case each of DNET and gangliocytoma (Table 1).

There was a case of 44-year male patient, presenting with headache and vomiting for 11 months, histomorphology of which revealed overlapping features both anaplastic ependymoma and medulloblastoma. A series of immunohistochemical (IHC) markers were applied to solve the dilemma since the grade would alter between the two and hence the treatment and prognosis. The tumour cells showed strong and diffuse positivity for GFAP, S100, vimentin and synaptophysin and negativity for EMA with ki67 labelling index of 50 %, hence a final diagnosis of anaplastic medulloblastoma (WHO grade IV) was rendered. Amongst the various types of meningiomas, meningothelial meningioma was the commonest (20 cases, 10.8 %), followed by transitional type (19 cases, 10.2 %) (Figure 1b), atypical meningioma (10 cases, 5.4 %), psammomatous (7 cases, 3.7 %), microcystic type (5 cases, 2.70 %), with only single case each of fibrous and secretory type (0.5 % each).

Diffuse astrocytic and oligodendroglial lesions which was the second most common entity of all neoplastic categories, glioblastoma, NOS topped the chart (28 cases, 15.13 %)

(Figure 1f) with a single case diagnosed as gliosarcoma (Figure 1g) followed by pilocytic astrocytoma (8 cases, 4.32 %) (Figure 1a), diffuse astrocytoma, NOS (5 cases, 2.70 %), Oligodendroglioma, NOS (3 cases, 1.62 %) (Figure 1e) and least was anaplastic astrocytoma, NOS & anaplastic pleomorphic xanthoastrocytoma (1 case each, 0.5 %). Among the ependymal tumours, classic ependymoma was the majority (5 cases, 2.70 %), followed by anaplastic ependymoma (3 cases, 1.62 %) (Figure 1c, 1d), meanwhile only a single case of myxopapillary ependymoma (0.5 %) was encountered. There were 2 cases (1.08 %) of choroid plexus papilloma. Amongst the CNS mesenchymal tumours, almost all were solitary fibrous tumour / hemangiopericytomas of anaplastic variant (5 cases, 2.70 %) (Figure 2a-e) and one case (0.5 %) of hemangioblastoma.

All these SFT / HPC cases were rendered with the diagnosis of anaplastic type, belonged to middle age group and only a single case was there of one and half year male child. Special stain with reticulin was invariably performed in all the five cases which showed positivity around the tumour cells. These findings were supplemented by a battery of IHC with CD34, SMA, Vimentin, STAT 6 (3 +) and EMA. Immunohistochemically the tumour cells were Vimentin, CD34 and STAT6 positive and negative for EMA with ki67 labelling index ranging in between 20 - 25 %. There were 5 cases of malignant lymphoma of CNS out of which 3 cases (1.62 %) of primary CNS lymphoma of diffuse large B cell lymphoma were reported amongst which 2 cases were activated B cell type and a single case of post germinal B cell type of triple expressor type (Figure 2f-j). There were two cases of CNS plasmacytoma seen in a 65-year male and 72-year female in left cerebellopontine angle region and cerebrofrontal region respectively. Histo-morphologically, these cases showed plasmacytoid cells including mature and immature forms along with few binucleated plasma cells and plasmablasts with intervening paler acellular area of eosinophilic material like that of amyloid. IHC was done for CD 138, CD19, CD20, Kappa and lambda light chain which revealed intense diffuse membranous and cytoplasmic positivity for CD 138, intense diffuse cytoplasmic positivity for Kappa and negative expression for CD 19, CD 20 and

Lambda (Figure 2k - 2o). CNS being a common site of distant metastases, was seen to be involved by 2 cases of adenocarcinoma, of which both were having primary malignancy as adenocarcinoma lung, metastasizing to cerebro-frontal region. There was only a single case of 57-year female with squamous cell carcinoma of possibly in cervix metastasising to left cerebro-parietal region which showed strong nuclear positivity for p63. Amongst the non-neoplastic entities (17 cases, 9.18 %) majority were pituitary adenoma (11 cases), followed by meningomyelocele and arachnoid cyst (2 cases each) and least in this category was reactive gliosis and granulomatous inflammation (1 case each). All the neoplastic entities were categorised according to the recent most WHO classification and grading of CNS tumours 2016, grade I being the commonest (80 cases, 54.8 %), grade IV (33 cases, 22.6 %), grade II (23 cases, 15.8 %), grade III (10 cases, 6.8 %) (Figure 3a).

The CNS lesion were categorised based on the topographical distribution of the tumour, in which cerebro-frontal was the commonest site of affection (42 cases, 23 %), followed by cerebro-temporal (38 cases, 25.54 %), sellar / suprasellar (25 cases, 13.5 %), cerebro-parietal (24 cases, 10 %), cerebellopontine region (17 cases, 9 %), brain stem (13 cases, 7 %), ventricles (9 cases, 4.86 %), spinal cord (8 cases, 4.22 %), cerebellum (6 cases, 3.24 %) and least affection was encountered in cerebro-occipital region (3 cases, 1.62 %) (Table 2). Out of 185 cases, more than half of the patients presented clinically with headache (105 cases, 56.7 %) followed by vomiting along with headache (35 cases, 19 %) and seizures (23 cases, 12.4 %) and rest 13 cases (7 %) presented with mixed symptoms.

One year follow up was available for 82 cases while rest lost to follow up. All the patients were doing well post therapy while only 17 patients succumbed, reason being elderly age, late clinical presentation such as in glioblastoma, post therapeutic complication and aggressive tumour pathology. Out of the 5 cases of SFT / HPC cases, 4 cases underwent radiotherapy and are under regular follow up with disease free survival for last one year, whereas unfortunately, only one case of SFT / HPC of a 44-year male succumbed to disease 4 days after discharge.

Type of CNS Lesion	Number of Cases (%)	WHO Grade	Mean Age (in Years)	Type of CNS Lesion	Number of Cases (%)	WHO Grade	Mean Age (in years)
Non-neoplastic				Embryonal tumours			
Meningomyelocele	2 (1.08 %)		1	Medulloblastoma	5 (2.70 %)	IV	84.4
Pituitary adenoma	11 (5.94 %)		42.7	Tumours of cranial and Paraspinal Nerves			
Arachnoid cyst	2 (1.08 %)		24.5	Schwannoma	23 (12.4 %)		53.23
Granulomatous inflammation	1 (0.5 %)		45	Meningioma			
Reactive gliosis	1 (0.5 %)		55	Meningothelial	20 (10.8 %)	I	50.14
Neoplastic				Fibrous	1 (0.5 %)	I	52
Diffuse astrocytic and oligodendroglial tumours				Transitional	19 (10.2 %)	I	54.36
Diffuse astrocytoma, OS	5 (2.70 %)	II	32	Secretory	1 (0.5 %)	I	24
Anaplastic astrocytoma, NOS	1 (0.5 %)	III	26	Atypical	10 (5.4 %)	II	55.55
Glioblastoma (including gliosarcoma & NOS)	28 (15.13 %)	IV	51.07	Psammomatous	7 (3.7 %)	I	49.8
Oligodendroglioma, NOS	3 (1.62 %)	II	37.66	Microcystic	5 (2.70 %)	I	50
Pilocytic astrocytoma	8 (4.32 %)	I	16.75	Mesenchymal			
Anaplastic PXA	1 (0.5 %)	III	5	SFT / HPC (Anaplastic)	5 (2.70 %)	III	35.4
Ependymal tumours				Hemangioblastoma	1 (0.5 %)	I	22
Ependymoma	5 (2.70 %)	II	32.48	Lymphoma			
Myxopapillary ependymoma	1 (0.5 %)	I	25	Plasmacytoma	2 (1.08 %)		67.5
Anaplastic ependymoma	3 (1.62 %)	III	39	Primary CNS DLBCL	3 (1.62 %)		55.2
Choroid plexus papilloma	2 (1.08 %)	I	34	Sellar / Suprasellar tumours			
Neuronal and mixed neuronal glial tumours				Craniopharyngioma	4 (2.16 %)	I	28
DNET	1 (0.5 %)	I	17	Metastasis	3 (1.62 %)		54
Gangliocytoma	1 (0.5 %)	I	32				
Total number of cases					185		

Table 1. Distribution of CNS Lesions Based on Recent (2016) WHO Classification with Mean Age of Presentation (N = 185)

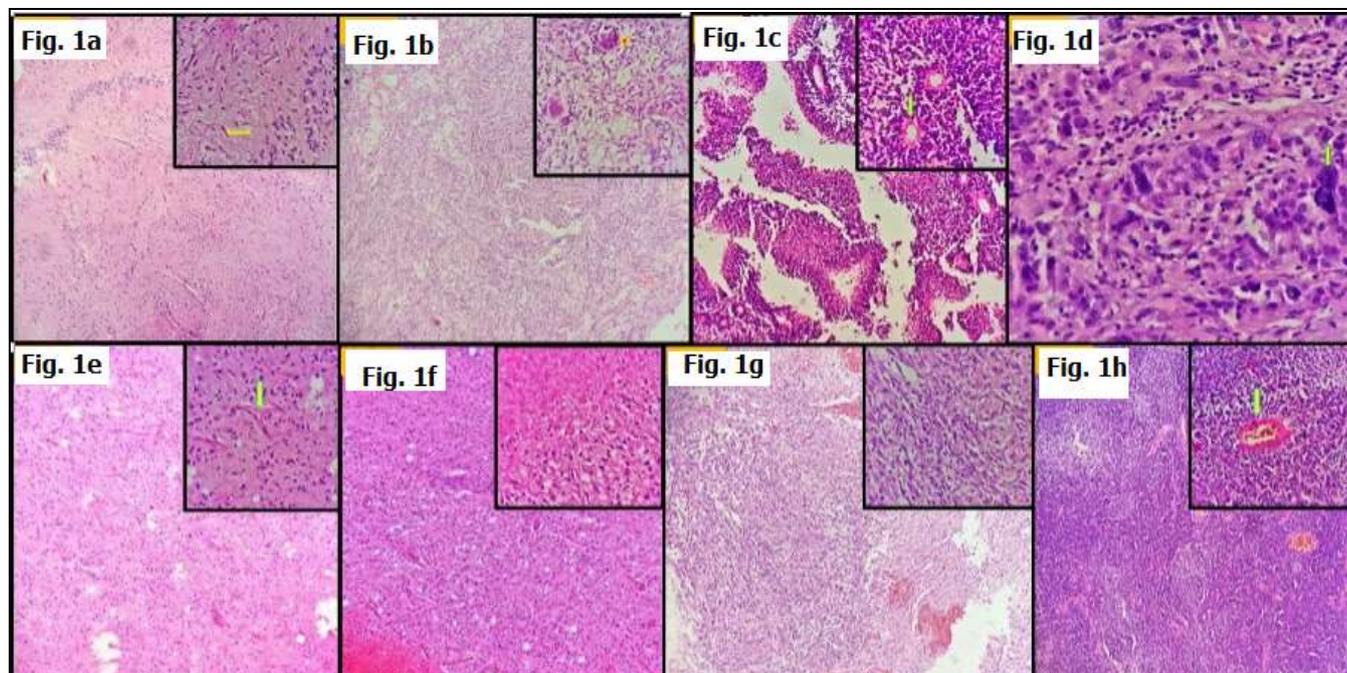


Figure 1. Histomorphological Spectrum of CNS Tumours According to WHO (2016) Grading. 1a (H & E, 100x) - Photomicrograph of Pilocytic Astrocytoma with Numerous Rosenthal Fibres (Arrowed) (Inset), (WHO Grade-I). Fig. 1b (H & E, 100x) - Photomicrograph of Meningioma with Psammoma Bodies (Starred) (Inset), (WHO Grade-I). Fig. 1c (H & E, 100x) - Photomicrograph of Anaplastic Ependymoma with Perivascular Pseudorosettes (Inset), Fig. 1d (H & E, 100x) - Photomicrograph Showing Nuclear Pleomorphism and Bizarre Tumour Giant Cells in Anaplastic Ependymoma (WHO Grade-III). Fig. 1e (H & E, 100x) - Photomicrograph Showing Oligodendroglioma (WHO Grade-II) with Characteristic Chicken Wire Blood Vessel (Arrowed) (Inset). Fig. 1f (H & E, 100x) - Photomicrograph of Glioblastoma, NOS Showing Pleomorphic Tumour Cells and Areas of Necrosis (WHO Grade-IV). Fig. 1g (H & E, 100x) - Photomicrograph of Gliosarcoma, (WHO Grade-IV). Fig. 1h (H & E, 100x) - Photomicrograph of Medulloblastoma (WHO Grade-IV), with Perivascular Pseudorosette (Inset)

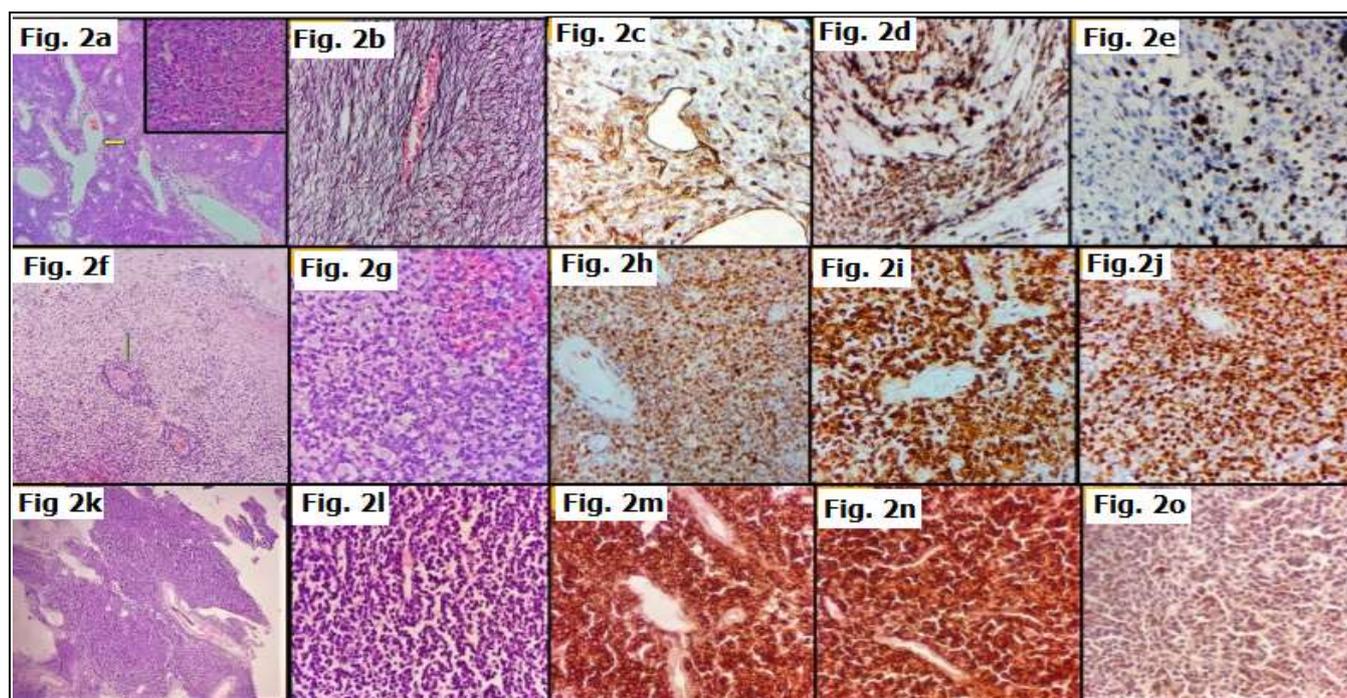
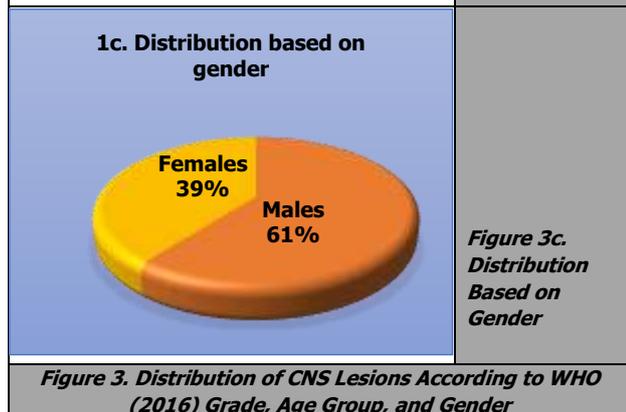
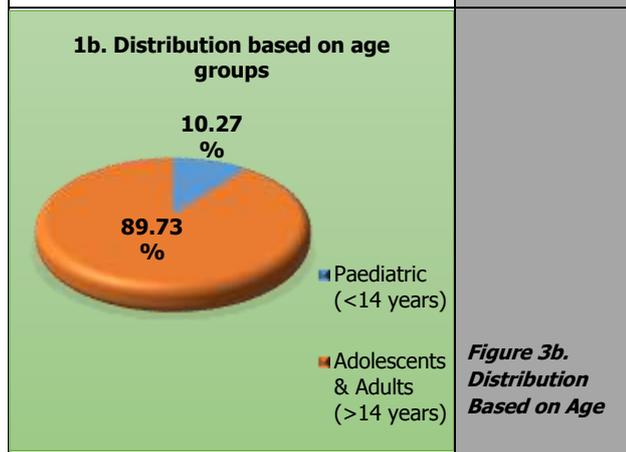
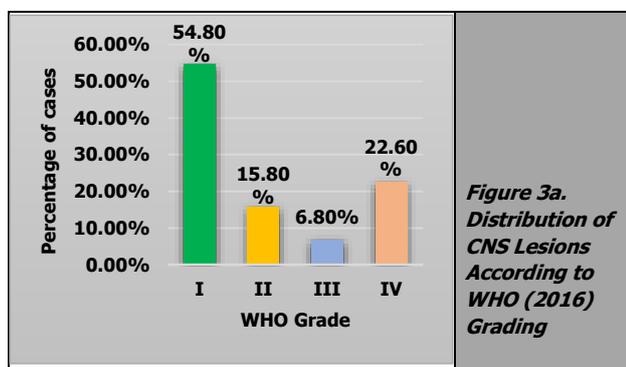


Figure 2. Rarely Encountered CNS Tumours with Immunohistochemistry. Fig 2a. (H & E, 100x) - Photomicrograph Showing Staghorn Pattern of Blood Vessel (Arrowed), in SFT / HPC (Anaplastic Variant), Fig 2b. (H & E, 100x) - Special Stain for Reticulin Shows Positive Staining Around the Tumour Cells, Fig 2c. (IHC, CD34, 100x) - CD34 Positivity for Tumour Cells, Fig 2d. (IHC, STAT6, 100x) - Nuclear Positivity Seen in the Tumour Cells, Fig 2e. (IHC, Ki67, 100x) - 20 % Ki67 Labelling Index. Fig 2f (H & E, 100x) - Photomicrograph of Primary CNS DLBCL with Angiocentricity (Arrowed), 2g (H & E, 400x) - Photomicrograph Showing Small to Medium Sized Cells Arranged Diffusely with Mitotic Figures, Fig 2h. (IHC, BCL6, 100x) - BCL6 Positivity of Tumour Cells, Fig 2i (IHC, BCL2, 100x) - BCL2 Positivity of Tumour Cells, Fig 2j. (IHC, C Myc, 100x) - C Myc Positivity of Tumour Cells. Fig 2k (H & E, 100x) - Photomicrograph of Plasmacytoma, Fig 2l (H & E, 400x) - Photomicrograph Showing Sheets of Plasmacytoid Cells Including Binucleated and Immature Forms, Fig 2m. (IHC, CD138, 100x) - CD138 Positivity of Tumour Cells, 2n (IHC, Kappa, 100x) - Kappa Positivity of Tumour Cells, Fig 2o. (IHC, LAMBDA, 100x) - Lambda Negativity of Tumour Cells

Topography of Tumour	Number of Cases (%)
Cerebro-parietal region	24 (13 %)
Cerebro-frontal region	42 (23 %)
Cerebro-temporal region	38 (20.54 %)
Cerebro-occipital region	3 (1.62 %)
Cerebellum	6 (3.24 %)
Brain stem	13 (7 %)
Cerebellopontine angle	17 (9 %)
Sellar / Suprasellar	25 (13.5 %)
Spinal cord region	8 (4.22 %)
Ventricular	9 (4.86)
Total number of cases	185

Table 2. Distribution of CNS Lesion Based of Topography in CNS (N = 185)



agreement with other studies by Alam et al. Nibhori et al. and Dogan where neoplastic lesions were commoner than non-neoplastic lesions.¹¹

Our study showed CNS lesion to be more common in males as compared to females similar to many studies done in Asian regions.^{11,12,13,14} Contrast to our finding in this context was observed in a study by Kaki RR in which they showed female predominance.¹⁵ The only exception to the overall gender distribution is meningioma which was more common in females. This observation was supported by several studies which may be due to hormonal influence as reported by Kothari et al.^{16,17,18,19}

The most common presenting symptom in this study was headache which was supported by several other studies.^{17,18,20,21} WHO grade I tumours constituted the most common primary neoplastic CNS lesions in this study followed by grade IV tumour which was well correlated with Sunila et al. Changoria et al and Jat Ke et al.^{12,22,23}

According to topography, cerebro-frontal region was the most common site of involvement (23 %) which is in close correlation with the finding in studies conducted by Hamdani SM et al. Torres et al. Jalali & Dutta.^{24,25}

In our study among the neoplastic entities, meningioma topped the chart, which is well correlated with Surawicz et al. in the USA and Lee et al in Korea. Among Meningioma, the most common histological type was meningothelial meningioma (10.8 %) followed by transitional meningioma (10.2 %) which was correlated with G. Basina et al.^{26,27,28}

Amongst the astrocytic tumour, glioblastoma (NOS) is the most common entity with mean age being 51.07 years similar to other studies done by G. Basina et al. Hamdani SM et al and Kothari et al. but discordant with study conducted by Anadure et al. where glioma grade I was most common type.^{24,29}

CONCLUSIONS

This study highlights the spectrum of various neoplastic and non-neoplastic CNS lesions and gives us relative frequency of various CNS malignancies in a tertiary care hospital in Eastern India. It was seen that neoplastic lesions were commoner in CNS than non-neoplastic entities and most of the former occur in 'adolescence and above' age group. Overall male preponderance was documented, only exception to this is meningioma. Amongst the neoplastic entities, meningioma was the commonest meanwhile neuronal and mixed neuronal glial tumours were very less in number, in our study. Some interesting and rare cases like SFT / HPC, desmoplastic nodular medulloblastoma in 4th ventricle, CNS plasmacytoma, and primary CNS DLBCL were encountered in our setup.

DISCUSSION

Classification of CNS tumours has changed over the years from 2008 to 2016 with inclusion of many IHC and molecular markers. Thus, the study attempts to document the spectrum of CNS tumour according to most recent WHO classification (2016) of CNS tumours. Out of the total cases, neoplastic lesions were in majority. This finding was in

Limitations

Although there is availability of advanced imaging techniques at present, still histopathological examination with IHC is the gold standard in the diagnosis. Molecular study, mutational analysis, and disease classification, were

not done due to non-availability of such facility in our scenario which is the limitation in our study.

The study conducted was a retrospective, single centre analysis and hence the data is not representative of the national epidemiology of CNS tumours. Our hospital being a tertiary care teaching hospital mainly catering to the low to mid socioeconomic status population of the society, limited the number of cases included in the study which can be the basis for hospital bias.

In developing countries like India, newly diagnosed cases are not registered routinely with local cancer registries which results in underestimation of such cases and data. Therefore, hospital-based prevalence data is the basis to estimate the disease load.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

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