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Original Research Article

A histomorphological study of central nervous system tumors in pediatric age group at tertiary care teaching hospital

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ABSTRACT

Background: Central nervous system (CNS) tumors are the second most common malignancies in children after acute lymphoblastic leukemia and constitute a significant cause of morbidity and mortality. Their histopathological classification is essential for diagnosis, treatment planning and prognostication. The present study was undertaken to evaluate the histomorphological spectrum of pediatric CNS tumors in a tertiary care teaching hospital.
Methods: A retrospective observational study was conducted in the Department of Pathology, B. J. Medical College and tertiary care teaching hospital, Ahmedabad, from March 2022 to July 2024. A total of 100 CNS biopsy specimens from pediatric patients aged 0-12 years were included. Clinical, demographic, radiological and histopathological data were collected and analyzed. Tumors were classified and graded according to histomorphological features.
Results: Among the 100 cases studied, males constituted 59% and females 41%, with a male-to-female ratio of 1.4:1. The highest number of cases (34%) occurred in the 0-4 years age group. Supratentorial tumors accounted for 54% of cases, followed by infratentorial tumors (40%) and spinal tumors (6%). Gliomas were the most common tumor category (36%), followed by embryonal tumors (24%) and ependymal tumors (10%). Among gliomas, low-grade astrocytoma (44.4%) and pilocytic astrocytoma (27.8%) were predominant subtypes. Medulloblastoma represented 66.6% of embryonal tumors. Most tumors belonged to lower WHO grades, while all embryonal tumors classified as grade 4.
Conclusions: Gliomas were the most frequently encountered pediatric CNS tumors, with a predominance of supratentorial location and male preponderance. Histopathological evaluation remains indispensable for accurate classification and grading, thereby facilitating optimal management and prognostic assessment of pediatric CNS tumors.

Keywords: Pediatric central nervous system, Histomorphological classification, Gliomas, Tumor grading

INTRODUCTION

The central nervous system (CNS) comprises the cerebrum, cerebellum, brain stem, spinal cord, meninges, twelve paired cranial nerves and the associated vascular networks. Primary CNS tumors account for a significant proportion of childhood malignancies, with an annual incidence of approximately 10-17 cases per 100,000 population, of which nearly 20% occur in the pediatric age group. After acute lymphoblastic leukemia (ALL), CNS tumors represent the second most common childhood malignancy. Epidemiological studies have reported an increasing incidence of pediatric CNS tumors, largely attributed to improvements in neuroimaging and greater diagnostic techniques.[1] Brain growth occurs rapidly during fetal life and reaches its peak around four months after birth and continues until 3-4 years of age before gradually slow down according to Baldwin and Preston-Martin.[2] Due to this prolonged developmental period, the developing brain is particularly susceptible to genotoxic injury and neoplastic transformation. Rapidly proliferating neural cells may be vulnerable to environmental toxins and DNA damage during both prenatal and postnatal life.[2] Furthermore, the fetal brain has limited capacity to repair

DNA alkylation induced by mutagenic agents, while the immature blood-brain barrier may facilitate the passage of carcinogenic substances into neural tissues.[3]

In low- and middle-income countries including India, the actual burden of CNS tumors is likely underestimated because of incomplete registration of newly diagnosed cases in cancer registries, limited access to specialized diagnostic facilities and under reporting of newly diagnosed cases. Consequently, accurate pathological classification remains fundamental for establishing appropriate treatment strategies and management protocols.

The etiology of pediatric CNS tumors is largely unknown, except for established risk factors such as exposure to ionizing radiation and inherited genetic syndromes including Neurofibromatosis, tuberous sclerosis, li-fraumeni syndrome, Gorlin syndrome, familial adenomatous polyposis and constitutional mismatch repair deficiency. Environmental influences, including dietary factors, have also been investigated.[4] Pediatric CNS tumors differ considerably from adult brain tumors with terms of anatomical location, clinical presentation, histological features, metastatic potential and prognosis.[5] Clinical manifestation related CNS neoplasms in pediatrics age group are well known, but at the illness onset, the neurologic and clinical presentation can change according to tumor location, age of child and tumor histology.

We welcome the fifth edition of the WHO classification of tumors of the CNS, published in 2021, is the sixth version of the international standard for the classification of brain and spinal cord tumors. Building on the 2016 updated fourth edition and the work of the consortium to inform molecular and practical approaches to CNS tumor taxonomy, the 2021 fifth edition introduces major changes that advance the role of molecular diagnostics in CNS tumor classification. With the advances in molecular characterization of tumors, considerable advances have occurred in the field of pediatric neuro-oncology.[6] Additionally, this has also altered medical management, with more research and clinical trials targeting these molecular changes. In this review, we will highlight the classifications of common pediatric CNS tumors and review emerging treatment considerations.[7] CNS tumors diagnosed in children provoke emotions but are fortunately cured with a high rate of success. Long diagnosis delay is associate with a high risk of developing life-threatening complications, irreversible neurological damage and cognitive deficiency in later life.

METHODS

This retrospective study included 100 CNS biopsy specimens received in the Histopathology Section, Department of Pathology, B. J. Medical College and tertiary care teaching hospital, Ahmedabad, between March 2022 and July 2024. The study population comprised pediatric patients aged 0-12 years who underwent neurosurgical biopsy procedures.

Inclusion criteria

All CNS biopsy specimens from pediatric patients (0-12 years) received during the study period were included in the study.

Exclusion criteria

Inadequate or poorly preserved biopsy specimens, reactive lesions, CNS infections and non-neoplastic cystic lesions were excluded.

Clinical and demographic details, including patient age, sex, registration number, clinical history, radiological findings, provisional diagnosis and specimen information were obtained from requisition forms and verified with specimen labels.

After accessioning and generation of laboratory identification numbers in the laboratory information system (LIS), specimens were fixed overnight in 10% neutral buffered formalin. Tissue processing was performed using an automated Leica tissue processor with formalin, acetone, xylene and paraffin. Paraffin-embedded blocks were prepared and sections of 4-5 µm thickness were cut and mounted on pretreated slides coated with egg albumin.

Routine hematoxylin and eosin (H and E) staining was performed after dewaxing. Microscopic examination of all stained sections was carried out and tumors were classified based on histopathological features.

Data were compiled and analyzed using Microsoft Excel and descriptive as well as analytical statistical methods were applied.

RESULTS

Among the 100 pediatric CNS tumor cases analyzed, males constituted 59% and females 41%, resulting in a male-to-female ratio of 1.4:1. Age-wise distribution showed that 34% of cases occurred in children aged 0-4 years, while 33% each were observed in the 5-8 years and 9-12 years age groups. A male predominance was noted across all age categories. Regarding anatomical location, 54% of tumors were situated in the supratentorial compartment, 40% in the infratentorial region, and 6% involved the spinal cord. Within supratentorial compartment, the sellar-suprasellar region represented the most common site (22.2%), followed by temporal lobe (16.6%), third ventricle (11.1%), and frontal lobe (11.1%). Following sites for tumors are presented in Table 1.

Site-wise analysis with histomorphological analysis demonstrated that gliomas predominantly involved the supratentorial region (75%), whereas embryonal tumors

were more frequently observed in the infratentorial compartment (75%).

Table 2 reflect morphologically, gliomas were the most prevalent tumor category, accounting for 36% of cases, followed by embryonal tumors (24%) and ependymal tumors (10%). Pineal and choroid plexus tumors were the least common, each comprising 1% of the study population. Among gliomas, low-grade astrocytoma was the most frequently encountered subtype (44.4%), followed by pilocytic astrocytoma (27.8%).

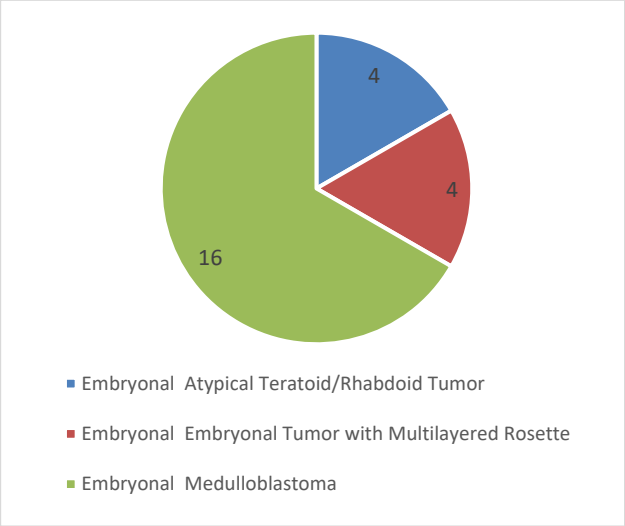

Figure 1: Entities of embryonal tumors.

Figure 1 show among embryonal tumors, medulloblastoma represented majority (66.6%), whereas atypical teratoid/rhabdoid tumor and embryonal tumor with multilayered rosettes each accounted for 16.7%.

Along with morphology grading were also done (Table 3). Tumor grading revealed that most pediatric CNS tumors belonged to lower-grade categories, with 36 cases classified as grade 1 and 20 as grade 2. Of 36 gliomas, 58.3% were grade 1, 36.1% were grade 2 and only 5.6% were grade 4 (Figure 2).

All 24 cases of embryonal tumors were classified as grade 4 category.

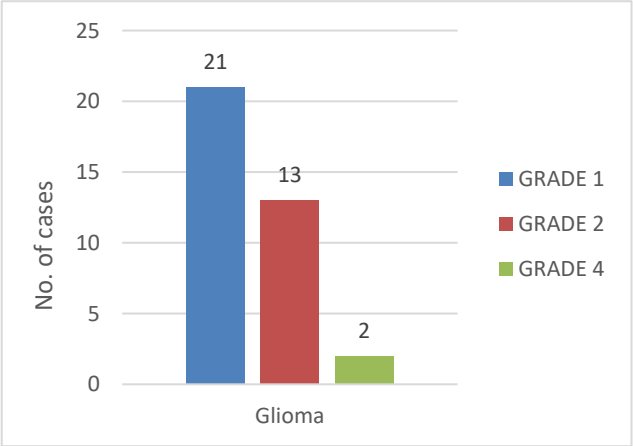

Figure 2: Glioma and its grade.

Table 1: Distribution of tumors in supratentorial.

Site of tumors	N	Percentage
Sellar-suprasellar regio	12	22.2%
Temporal lobe	9	16.6%
3rd ventricle	6	11.1%
Frontal lobe	6	11.1%
Optic region	6	11.1%
Temporo-parietal region	3	5.6%
Thalamic region	3	5.6%
Pineal region	3	5.6%
Lateral ventricle	2	3.7%
Occipital lobe	2	3.7%
Parital lobe	2	3.7%
Total	54	100%

Table 2: Morphological distribution of CNS tumors in pediatric age group.

Morphological type of tumors	N	Percentage
Gliomas	36	36%
Embryonal tumors	24	24%
Ependymal tumors	10	10%
Tumors of Sellar region (Craniopharyngiomas and pituitary tumor)	8	8%
Mesenchymal tumor	6	6%
Nerve sheath tumor	4	4%
Glioneuronal	3	3%

Continued.

Morphological type of tumors	N	Percentage
Meningioma	3	3%
Germ cell tumor	2	2%
Hematolymphoid tumors	2	2%
Choroid plexus tumors	1	1%
Pineal tumors	1	1%
Total	100	100%

Table 3: CNS tumors with grade.

Tumors	Grade 1	Grade 2	Grade 3	Grade 4	Total	Percentage
Astrocytoma	9	7	-	-	16	18.00%
Medulloblastoma	-	-	-	16	16	18.00%
Ependymoma	-	7	3	-	10	11.30%
Pilocytic Astrocytoma	10	-	-	-	10	11.30%
Craniopharyngioma	8	-	-	-	8	9.00%
Atypical teratoid/ rhabdoid tumor	-	-	-	4	4	4.60%
Embryonal tumor with multilayered rosette	-	-	-	4	4	4.60%
Oligodendroglioma	-	3	-	-	3	3.40%
Meningioma	3	-	-	-	3	3.30%
Pleomorphic xanthoastrocytoma	-	2	-	-	2	2.20%
Glioblastoma	-	-	-	2	2	2.20%
Hemangioblastoma	2	-	-	-	2	2.20%
Ganglioglioma	2	-	-	-	2	2.20%
Gliosarcoma	-	-	-	1	1	1.10%
Central neurocytoma	-	1	-	-	1	1.10%
Ganglioglioma	1	-	-	-	1	1.10%
Choroid plexus papilloma	1	-	-	-	1	1.10%
Mature teratoma	1	-	-	-	1	1.10%
Pineoblastoma	-	-	-	1	1	1.10%
Solitary fibrous tumor	1	-	-	-	1	1.10%
Total	36	20	3	29	88	100%

DISCUSSION

Several studies have documented that the epidemiological pattern of pediatric CNS tumors differs base on age, sex, ethnicity, and geographic region. Comparable finding was noted observed in the present study, which demonstrated differences in tumor distribution based on demographic and anatomical factors.

The study presents a detailed examination of the epidemiological characteristics of pediatric CNS tumors, revealing several findings when compared to existing literature. The study observed a higher prevalence of males (59%) compared to females (41%) among children diagnosed with CNS tumors. This finding contrasts with studies by Santos et al, Alexiou et al and Lannering et al where a more balanced gender distributions were reported.[7-9]

This divergence from other studies may reflect regional epidemiological variations or differences in the demographic composition of our patient cohort.

Regarding the anatomical distribution of tumors reveals a predominance of supratentorial lesions (54%), whereas infratentorial tumors constituted 40% of cases. This finding somewhat similar to study from Alexiou et al (50.8%) who also reported higher percentages of supratentorial tumors.[8]

The incidence of astrocytoma in the present study (33%) was lower than the Alexiou et al (41.5%), Lannering et al (44.6%), Santos et al (40%), Rickert et al (47.3%) and Kaatsch et al (44.4%).[7-11] This difference could potentially be attributed to variations in diagnostic criteria, geographical or demographic factors influencing disease prevalence, or differences in tumor subtyping methodologies. Further investigation into these factors could provide insights into the observed discrepancy.

The frequency of medulloblastoma (16%) was comparable with previous research Alexiou et al (18%), Lannering et al (18.8%), Rickert et al (16.3%) and Kaatsch et al (18.1%) indicating consistency in diagnostic criteria and patient selection criteria.[8-11]

Similarly, incidence of ependymoma (10%) is consistent with other studies like Lannering et al (10.5%), Rickert et al (10.1%) and Kaatsch et al (10.4%) suggesting reliability in data collection methods or patient inclusion criteria.[9-11]

Our study identified an increased incidence of craniopharyngioma (8%) compared to some previous reports, Alexiou et al (6%), Lannering et al (5.6%) and Rickert et al (5.6%).[8-10] Our finding highlights the importance of regional variations or institutional practices in detecting and diagnosing less common tumor types like craniopharyngioma. Additionally, our study reported a lower incidence of glioneuronal tumors (2%) compared to the higher rates noted in Santos et al (12%).[7] However, the study finding consistent with other studies (Lannering et al 2.6%, Rickert et al 2.5).[9,10] The study reported a lower incidence of choroid plexus tumors (1%) compared to rates reported by Alexiou et al (22%), Lannering et al (2%) and Santos et al (2.7%).[7-9] However, finding consistent with finding of Rickert et al showed 0.9 % incidence.[10] The incidence of pineal tumors in our study (1%) aligns closely with findings reported by Santos et al (1.3%).[7] Study identified a higher incidence of atypical teratoid/rhabdoid tumors (4%) compared to rates reported by other studies (Alexiou et al 2.20%, Lannering et al 0.30%, Santos et al 1% and Rickert et al 1.30%).[7-10] Study reported a similar incidence of meningiomas (3%) compared to findings by other studies (Alexiou et al 2.30%, Santos et al 2.80%, Kaatsch et al 3%).[7,8,11] Furthermore, our findings for germ cell tumors (2%) were consistent with some previous studies but lower than reported rates by Santos et al (4.1%).[7] Overall, the study contributes valuable insights into the epidemiology and distribution of pediatric CNS tumors.

Limitations

This was a single center, retrospective study with a relatively limited sample size. Immunohistochemistry (IHC) was not performed routinely in all cases; therefore, diagnosis was based primarily on histomorphological features. Molecular diagnostic techniques (such as IDH mutation analysis, BRAF alteration, H3K27M, DNA methylation profiling, etc.), which are recommended in the WHO 2021 classification for several pediatric CNS tumors, were not available which limiting molecular classification and clinical follow-up, treatment response, survival, and prognostic outcomes were not evaluated in this study.

CONCLUSION

This study demonstrates that gliomas were the most common pediatric CNS tumors, followed by embryonal tumors with a predominance of supratentorial location and male preponderance. Histomorphological examination remains the cornerstone for the diagnosis and grading of pediatric CNS tumors, particularly in resource-limited settings. However, incorporation of IHC and molecular diagnostic techniques, as recommended by the WHO 2021 CNS tumor classification, would further improve diagnostic accuracy, tumor classification, prognostic stratification, and patient management. Larger multicenter studies with integrated histopathological and molecular evaluation are warranted to better characterize the spectrum of pediatric CNS tumors.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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