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Original Article

Pediatric Intracranial Tumors over a 5-Year Period in a Tertiary Care Center of North Kerala, India: A Retrospective Analysis

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Abstract

Background: Pediatric brain tumors are unique in terms of distribution, clinical presentation, pathologic types, management, and prognosis. There are not many studies from India which have looked into the epidemiology of pediatric brain tumors. **Aims:** This study aimed to analyze the epidemiology of pediatric brain tumors in North Kerala and compare it with data from the rest of India and other countries. **Materials and Methods:** This is a retrospective study of 5-year data of pediatric brain tumors which were operated in a tertiary referral center in North Kerala, India, from 2009 to 2013. The data were procured from the departments of neurosurgery and pathology of the institution. The data were tabulated and analyzed using SPSS software. **Results:** A total of 71 children had histologically proven brain tumors during the 5-year period. There were 34 boys and 37 girls. Distribution in different age groups was as follows: infancy –5 (7%), 1–5 years –22 (31%), 6–10 years – 21 (29.6%), and 11–18 years – 23 (32.4%). The most common tumors were primitive neuroectodermal tumors (PNETs). In infancy, the number of high-grade tumors was more, whereas in the 11–18 years' age group, there were a significantly higher number of low-grade tumors ($P = 0.04$). **Discussion:** Pediatric brain tumors were distributed almost equally in both sexes. PNET was the most common. We could not get statistical significance in many of our values due to small sample size. **Conclusion:** This study highlights the need for diligent collection of data and maintenance of a registry for brain tumors to study the disease in the Indian population.

Keywords: *Pediatric, epidemiology, India, intracranial tumors, Kerala*

Introduction

Pediatric brain tumors are unique in terms of distribution, clinical presentation, pathologic types, management, and prognosis. Even within the pediatric age group, there are differences in early and late childhood in various factors.[1-3] There are not many studies from India which have looked into the epidemiology of pediatric brain tumors and compared it with data from the rest of the world.[4-12] Since this is a hospital-based study, it may not reflect the true epidemiology of the tumors, but nevertheless, it is the first attempt of its kind from Kerala. The aim of this study was to analyze the epidemiology of pediatric brain tumors in North Kerala and compare it with data from the rest of India and other countries.

Materials and Methods

This is a retrospective descriptive study of 5-year data of pediatric brain tumors which underwent surgical resection in the department of neurosurgery of a tertiary referral center from January 2009 to December 2013. The center caters to the five northern districts of Kerala state, India. The study was approved by the Institutional Ethics Committee. The data were procured from the operation registers and discharge summaries of the department of neurosurgery and the records of department of pathology of the institution. Consent was obtained from patients to use their data. The WHO 2007 Classification of Tumors of the Central Nervous System (CNS) was used for typing of tumors.[13] The data were tabulated and analyzed using predictive analytics software(PASW) statistics 18.0 (SPSS Inc., Chicago, IL).

Results

A total of 71 children had histologically proven brain tumors during the 5-year period. There were 34 boys (47.9%) and 37 girls (52.1%) [Figure 1a]. Distribution in different

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age groups was as follows: infancy – 5 (7%), 1–5 years – 22 (31%), 6–10 years – 21 (29.6%), and 11–18 years – 23 (32.4%) [Figure 1b]. The youngest child was a 2-month-old girl diagnosed with choroid plexus papilloma. The mean age was 8.3 years. There were 56.3% supratentorial and 43.7% infratentorial tumors [Figure 1c].

The frequency and percentages of tumors are summarized in Table 1. The most common tumors were primitive neuroectodermal tumors (PNETs) including medulloblastoma, atypical teratoid rhabdoid tumor, and embryonal tumor with multilayered rosettes (ETMR). As a single entity, medulloblastoma topped the list (22.5%) followed by ependymoma (15.5%) and pilocytic astrocytoma (14.1%). The grade distribution is shown in Figure 1d. Overall, Grade IV tumors were more common followed by Grade I. We divided the tumors into low- and high-grade groups and cross tabulated with age groups [Table 2]. Infants and children <10 years of age had more of high-grade tumors and low-grade tumors were more common in children above the age of 11 years. $P = 0.04$ was considered statistically significant. We could not identify a single age group in which any of the tumors were most common, maybe due to the small sample size. However, desmoplastic medulloblastomas were found to be more common below 3 years and the mean age was 2.9 years. Most of the children presented with features of raised intracranial pressure. Six tumors were associated with intractable seizures, the most common being dysembryoplastic neuroepithelial tumor ($n = 4$). There was one case of subependymal giant cell astrocytoma in this group which was in a tuberous sclerosis patient. The radiological and histopathological images of some of our interesting cases are depicted in Figure 2.

Table 1: Number and percentage of different tumors in the study population

Tumor	Frequency (%)
Pilocytic astrocytoma	10 (14.1)
Glioblastoma	4 (5.6)
Ependymoma	11 (15.5)
Choroid plexus papilloma	1 (1.4)
Choroid plexus carcinoma	1 (1.4)
Ganglioglioma	1 (1.4)
DNET	5 (6)
Atypical central neurocytoma	1 (1.4)
SEGA	1 (1.4)
Medulloblastoma	16 (22.5)
ATRT	3 (4.2)
ETMR	1 (1.4)
PNET	2 (2.8)
Pinealoblastoma	1 (1.4)
Germinoma	2 (2.8)
Immature teratoma	1 (1.4)
Craniopharyngioma	7 (9.9)
Meningioma	3 (4.2)
Total	71 (100)

DNET – Dysembryoplastic neuroepithelial tumor; SEGA – Subependymal giant cell astrocytoma; ATRT – Atypical teratoid rhabdoid tumor; ETMR – Embryonal tumor with multilayered rosettes, PNET – Primitive neuroectodermal tumor

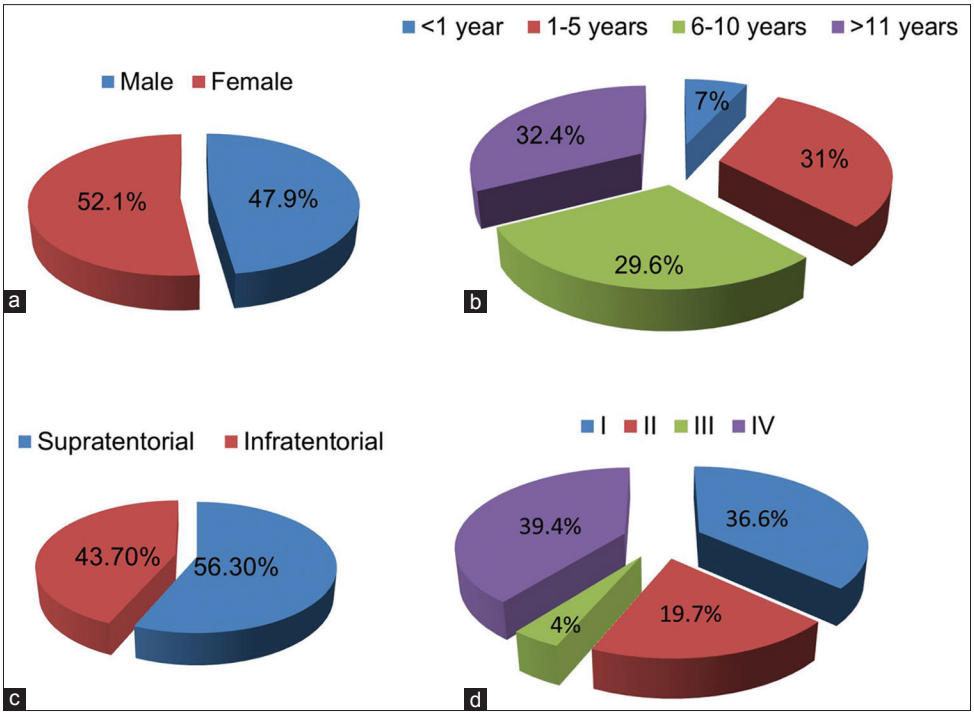

Figure 1: (a) Tumor distribution according to sex. (b) Tumor distribution according to age group. (c) Tumor distribution according to location. (d) Tumor distribution according to grade

Discussion

Brain tumors are the most common form of pediatric solid tumors. The present study was conducted to know the features and peculiarities, if any, of pediatric intracranial tumors in our region since there are geographical differences in the pattern of pediatric brain tumors with respect to frequency, age group, morphologic subtype, and location. Such regional differences are important in planning healthcare delivery and further research on tumors in these areas. Since this is a hospital-based study including only the tumors which were operated, it may not reflect the true incidence of the different entities. It may be that these tumors become symptomatic earlier in our population. Though many of the studies are hospital based, some have taken into account only the clinicoradiological features and do not have histopathological confirmation for all the tumors.

Table 2: Age group × grade-recoded crosstabulation

	Grade recoded		Total
	Low grade	High grade	
Age group (years)			
<1			
Count	1	4	5
Percentage within age group	20.0	80.0	100.0
Percentage within grade recoded	2.6	12.5	7.0
Total percentage	1.4	5.6	7.0
1-5			
Count	11	11	22
Percentage within age group	50.0	50.0	100.0
Percentage within grade recoded	28.2	34.4	31.0
Total percentage	15.5	15.5	31.0
6-10			
Count	9	12	21
Percentage within age group	42.9	57.1	100.0
Percentage within grade recoded	23.1	37.5	29.6
Total percentage	12.7	16.9	29.6
11 and above			
Count	18	5	23
Percentage within age group	78.3	21.7	100.0
Percentage within grade recoded	46.2	15.6	32.4
Total percentage	25.4	7.0	32.4
Total			
Count	39	32	71
Percentage within age group	54.9	45.1	100.0
Percentage within grade recoded	100.0	100.0	100.0
Total percentage	54.9	45.1	100.0

We compared the data from various studies from different regions of Asia [Table 3] and the world [Table 4].[1,2,14-22] Most studies from all over the world including India quote a male predominance in pediatric brain tumors.[1-3,11,23] However, in our series, the incidence was almost equal in both sexes. We had more tumors in the supratentorial location similar to a group from Germany but this is against most studies which report more of infratentorial tumors.[11,14,24] Grade IV tumors were the most common. But, when we divided the tumors into low- and high-grade groups and cross tabulated with age groups, infants had more of high-grade tumors and low-grade tumors were more common in older children.

PNETs were the most common tumors unlike in most other studies in which astrocytomas headed the list.[1,4,11,14] The most common single entity encountered was medulloblastoma, consistent with data from different parts of the world.[11] Only one study each from India and Pakistan showed the highest frequency of embryonal tumors.[2,8] An analysis from Nigeria showed an equal

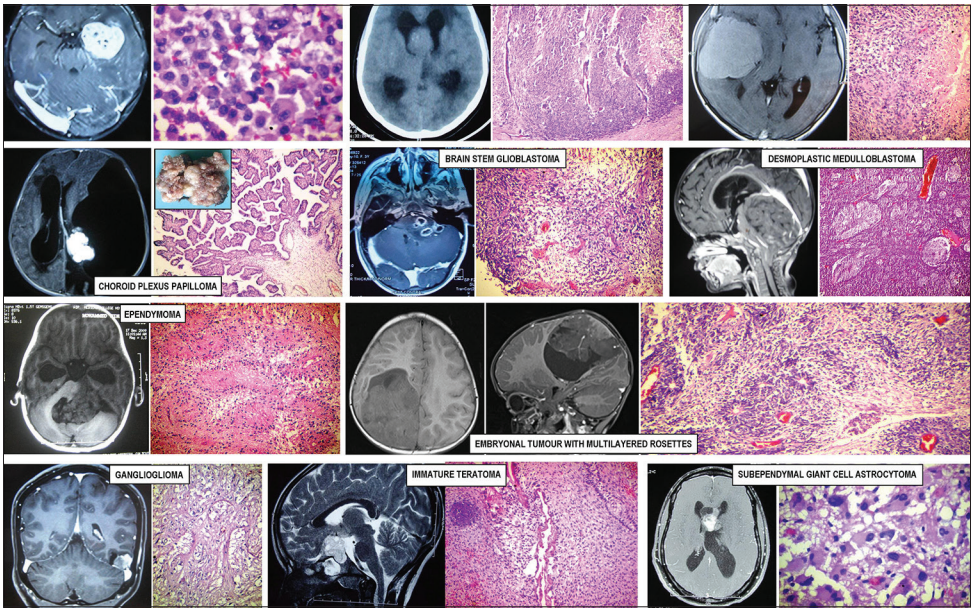

Figure 2: Imaging and photomicrographs of interesting cases

Table 3: Comparison of data of the present study with that of studies from Asia

Tumor type	Pakistan (Naseem Ahmed *et al.*)	Kuwait (Katchy *et al.*)	Japan (Makino *et al.*)	China (Zhou *et al.*)	Nepal (Azad *et al.*)	India (Jain *et al.*)	India (Asirvatham *et al.*)	India (Madhavan *et al.*)	Present study
Astrocytoma	34.6	45	35.7	30.5	15	34.7	47.3	52	19.7
Oligodendroglioma	1.2	NA	NA	6.2	NA	1.1	NA	6	0
Ependymoma	9.9	8	4.8	5.6	17.5	9.4	4.8	10.4	11
Choroid plexus tumors	NA	4	NA	NA	NA	1.8	NA	NA	2.8
Neuronal/glioneuronal tumors	NA	NA	NA	NA	NA	2.4	NA	NA	10.2
Medulloblastoma and other embryonal tumors	49.4	31	10	NA	15	22.4	11.4	21.6	30.9
Craniopharyngioma	NA	6	10.5	NA	NA	10.2	9.7	3.6	9.9
Pineal tumors	NA	NA	NA	NA	NA	1.3	NA	2.4	1.4
Germ cell tumors	NA	NA	14.3	NA	NA	2	NA	1.6	4.2
Meningeal	NA	2	NA	NA	NA	3.2	NA	NA	4.2
Cranial nerves	NA	NA	NA	NA	NA	3.6	4.1	NA	0
Hematopoietic	NA	NA	NA	NA	NA	0.5	NA	NA	0

NA – Not available

Table 4: Comparison of data of the present study with that of countries outside Asia

Tumor type	Egypt (El-Gaidi)	Denmark (Raaschou-Nielsen *et al.*)	Morocco (Karkouri *et al.*)	Brazil (Rosemberg and Fujiwara)	Germany (Kaatsch *et al.*)	Canada (Kaderali *et al.*)	Sweden (Hjalmars)	Present study
Astrocytoma	35	15.6	37.1	32.5	41.7	39.4	51	19.7
Oligodendroglioma	2.2		1.7	0.9	1.1	1.7	0	0
Ependymoma	10.4	3.7	11.3	7.4	10.4	7	8	11
Choroid plexus tumors	2.4	NA	NA	3	NA	2.3	1.9	2.8
Neuronal/glioneuronal tumors	1.3	NA	1.3	7.6	3.2	<2	0	10.2
Medulloblastoma and other embryonal tumors	23.1	7	30.5	13.9	25.7	15.4	17	30.9
Craniopharyngioma	11.3	NA	6.6	11	4.4	6.8	4.6	9.9
Pineal tumors	0.9	NA	0.7	NA	1.3	0.5	2.7	1.4
Germ cell tumors	2.4	NA	0.9	3.6	NA	3.1	1.5	4.2
Meningeal	4.4	NA	2.2	3	1.2	<2	1.6	4.2
Cranial nerves	0.7	NA	NA	NA	NA	3.5	1.5	0
Hematopoietic	0.2	NA	NA	NA	NA	NA	NA	0

NA – Not available

incidence of astrocytomas and medulloblastomas.[25] Desmoplastic variant of medulloblastoma was more common below 3 years of age as in some studies.[2]

The frequency of ependymoma was comparable to most other series although some studies showed a low frequency.[6,15] A study from Nepal shows a high frequency of over 17%.[21] One group from China and one from India reported a high incidence of oligodendroglioma.[5,22] We did not have any oligodendroglial tumors during the study period.

The frequency of craniopharyngioma (9.9%) in the present study was high but comparable to some studies from India and other countries such as Egypt, Japan, and Brazil.[3,4,6,14,17] Most of the studies from around the world show a frequency of <5% for germ cell tumors as in our case, but Japan had the highest incidence in this group (~15%)[3] in a population-based survey.

In the present study, there was a high incidence of tumors belonging to the neuronal/glioneuronal group. The group from Brazil has reported a somewhat comparable but lower percentage.[17] Only one study from India has mentioned the percentage of glioneuronal tumors and that was a low value when compared to the present study.[4] This was similar to the data in many studies.

The frequency of other entities such as choroid plexus tumors, meningiomas, cranial nerve tumors, and pineal tumors was comparable in the different populations.

Pediatric neurosurgery is a specialized branch of neurosurgery which requires a great expertise and may be a tough ground to tread for the novice when compared to surgery in adults. Mortality including sudden death is more in pediatric patients. The important concerns in pediatric neurosurgery may be divided into pre-, intra-,

and postoperative. Preoperative assessment is difficult in pediatric patients and this becomes more with decreasing age because they are unable to communicate effectively. Drug and fluid dosage calculations can be hampered by dehydration caused by vomiting and decreased food intake. In infants, nutrition is mainly dependent on breastfeeding. Obtaining consent prior to surgery may become a big hurdle, especially in infants. During the procedure, the main concerns would be regarding anesthesia including intubation and blood loss. Intraoperative morbidity and risk is increased in children due to their lower circulating blood volume. Even a small amount of blood loss can lead to hypotension and can many a time restrict the amount of tumor tissue resected.[26] There is an increased risk of allogeneic blood transfusion and the risk increases with younger age, prolonged duration of surgery, and a low preoperative hemoglobin value.[27] Postoperative management and recovery from intraoperative injuries is different in pediatric patients. Setting up ventilatory parameters, obtaining blood samples for analysis, and assessment of sensorium are challenges that are usually encountered. Hyponatremia is more common in children in the postoperative period and recovery after correction is delayed and sometimes poor.[28] Postoperatively, great care should be given to temperature regulation, ventilation, wound hygiene, prevention of hypoglycemia, and monitoring of head circumference in infants. Tumor location-specific complications encountered include higher incidence of mutism following posterior fossa surgery and diabetes insipidus after surgeries in the sellar-suprasellar region. In larger lesions, the incidence of transient subcutaneous and subdural effusions is greater. A dedicated pediatric anesthesia unit and Intensive Care Unit are ideal and this is lacking in our center. Overall prognosis is poor for high-grade lesions in young patients due to restrictions in providing adjuvant treatment. Occurrence of more number of high-grade tumors in infants and younger children necessitates complete removal. Radiation therapy can be given only after the age of 2 years due to adverse effects on the developing brain and skeleton in infants. Subtotal resections will not do well in infants as only adjuvant chemotherapy can be given. Chemotherapy predisposes to sepsis and necessitates continuance of intravenous line which adds to the problem. The common problems that we face in our institute are hypotension, sepsis, and subdural collection in the perioperative period. On long-term follow-up, tumor recurrence and effects of therapy are the common complications.

In this study, we have followed the then available WHO Classification of Central Nervous System tumors, 2007, for the diagnosis of different tumors. Molecular techniques including mutational analysis have greatly influenced the classification and prediction of treatment outcome in different tumors. The updated WHO Classification of Central Nervous System tumors, 2016, has many new entities, some of which are pediatric neoplasms. Diffuse midline glioma H3 K27M-mutant, RELA fusion-positive ependymoma, genetically defined variants of medulloblastoma, and ETMR are some of the important names among these. The term CNS PNET no longer exists and the term CNS embryonal tumor, not otherwise specified, can be used if the tumor does not fall into any specific category.[29]

Many of our values did not have statistical significance probably due to the low sample size, though the number of cases is comparable to other studies with respect to time frame. There are definite differences in the distribution of tumors in this region as compared to the rest of India and the world. Longer study periods are necessary to arrive at definite conclusions. Nevertheless, it is one of the few reports of the kind in published literature from South India and it highlights the need for conducting such studies in the Indian population.

Conclusions

1. Pediatric brain tumors were distributed almost equally in both sexes and a male preponderance was not seen as reported by many authors. Supratentorial location was more common
2. PNETs were the most common as in some similar studies from different parts of the world. Desmoplastic medulloblastomas were more common in children <3 years of age which is concordant with some studies
3. High-grade tumors occurred more in children <10 years of age
4. Glioneuronal tumors formed a significant proportion of pediatric tumors as opposed to other studies
5. We could not get statistical significance in many of our values due to the small sample size. However, this study highlights the need for meticulous data collection and maintenance of a registry for brain tumors to study the epidemiology of the disease in the Indian population.

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Conflicts of interest

There are no conflicts of interest.

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