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Pathology

CLINICOPATHOLOICAL SPECTRUM OF EMBRYONAL BRAIN TUMORS AND THEIR PROGNOSTIC SIGNIFICANCE – A THREE YEARS INSTITUTIONAL STUDY AT A TERTIARY CARE HOSPITAL IN SOUTH INDIA

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ABSTRACT

BACKGROUND: Central nervous system tumors constitute second most common paediatric cancers.Embryonal tumors are neoplasms of immature cells resembling primitive neuroepithelium.All are similarly aggressive and have a tendency to disseminate throughout CNS.Therefore identification of specific subtype helps in prognosis evaluation,to avoid unnecessary treatment related neurotoxicity and further treatment implications.

METHODS: This is a retrospective study conducted at The Department of neuropathology, Institute of neurosurgery MMC/RGGGH from January 2015 to December 2017.A total of 34 cases of Embryonal tumors were reviewed during this period.Among which Medulloblastoma was reclassified histopathologically based upon the World Health Organisation 2016 classification of CNS tumors.Data on clinical presentation and radiological features of all cases were collected from patients records.In all cases gross features were recorded during grossing of the resected tumors.The tissue sections were processed and stained as per standard protocols. IHC markers were done in deserving cases .Age predilection,Sex Predilection,Tumor location,Comparison with squash and Histological grade in relation to age of embryonal tumors studied.

RESULTS: Out of 1422 cases evaluated in adults embryonal tumors comprised 0.21%(3 cases).Out of 150 cases evaluated in chidren aged 16 years embryonal tumors comprised 20.6%(31 cases).Sex ratio(males to females) 2:1 males outnumbering females.94.11%(32 cases) of embryonal tumors presented as posterior fossa tumors,2.94%(1 case) presented as hypothalamic SOL,2.94%(1 case) presented with multiple lesions in spine and cranium-This was a rare case of Atypical Teratoid /Rhabdoid tumor presented with drop metastasis.5.88%(2 cases) presented as recurrent tumors.82.3%(28 cases) presented histologically as classic medulloblastomas,2.94%(1 case) presented as Anaplastic/Large cell type, 2.94%(1 case) presented as Desmoplastic type,11.76%(4 cases) presented as Atypical Teratoid/Rhabdoid tumor.Most commonly affected age group is 6-10 years comprising 50%(17 cases),20.5%(7 cases) affecting 0-5 years, 20.5%(7 cases) affecting 11-16 years.

CONCLUSION: Embryonal tumors are highly malignant tumors affecting children from early infancy to adolescence .Because of efforts to avoid craniospinal irradiation in an attempt to lessen treatment related neurotoxicity,diagnosis and management is very important.

KEYWORDS : Embryonal tumors,Medulloblastoma,Atypical Teratoid/Rhabdoid tumor

INTRODUCTION

Embryonal brain tumors are a heterogenous group of neoplasms primarily occurring in infants and young children[1].They are highly cellular tumors with brisk mitotic activity and they share a propensity for dissemination throughout neuroaxis. The tumors may be malignant or benign . Most CNS embryonal tumors in children are malignant[2]. Malignant brain tumors are likely to grow quickly and spread into other parts of the brain.They are the second most common CNS neoplasms after Astrocytomas in paediatric age group[3]. Age group commonly affected are less than 10 years.

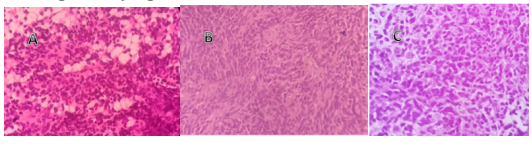
Classified according to the World Health Organisation 2016 classification of CNS tumors into
Medulloblastoma
Embryonal tumor with multi-layered rosettes
Medulloepithelioma
CNS Neuroblastoma
CNS Ganglioneuroblastoma
CNS Embryonal tumor
Atypical Teratoid/Rhabdoid tumor
CNS Embryonal tumor with rhabdoid features

MEDULLOBLASTOMA:

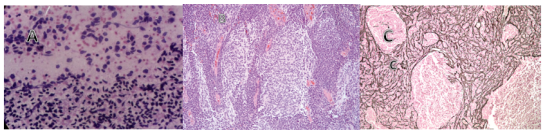
Most common embryonal tumor of childhood.Of all paediatric neoplasms medulloblastoma is second in frequency only to pilocytic astrocytoma accounting for 25% of all intracranial neoplasms[4].Most common age group affected is between 3 and 7 years.Grows into fourth ventricle,cerebellar hemisphere.Since they cause increased intracranial pressure by exerting mass effect and blocking cerebrospinal fluid pathways ,patients present with short history of headache,frequent nausea and vomiting[5].

Classified histologically as Classic
Desmoplastic
Medulloblastoma with extensive nodularity
Large cell/Anaplastic

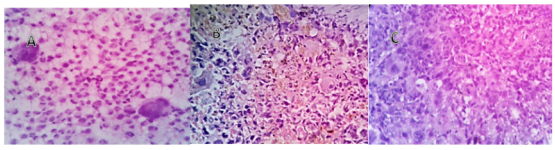
- Figure1:H&E Staining-Classic medulloblastomaA)Squash10x-Round to oval cells with dark staining nuclei arranged in sheets,clustersB)4X-Typical syncytial arrangementC)10X-Sheets of cells with round/oval hyperchromatic nuclei and scanty eosinophilic cytoplasm



- Figure2:Desmoplastic medulloblastomaA)Squash10X-Monotonous, homogenous nuclei with stippled chromatinB)H&E Staining-10x-Pale nodular areas surrounded by densely packed hyperchromatic cellsC)IHC 10X-Reticulin silver impregnation showing reticulin free pale islands



- Figure3:Large cell/Anaplastic MedulloblastomaA)Squash10x-Sheet like pattern with high degree of cytologic atypia and larger cell sizeB)C)H&E Staining10x-Increased nuclear size,pleomorphism,prominent nucleoli.Tumor cell wrapping is evident



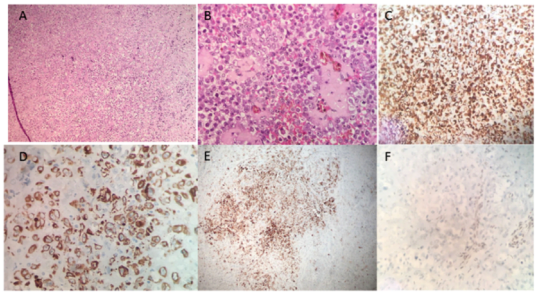
ATYPICAL TERATOID /RHABDOID TUMOR:

Central nervous system (CNS) Atpical teratoid/Rhabdoid tumor (AT/RT) is a very rare, fast-growing tumor of the brain and spinal cord6. It usually occurs in children aged three years and younger, although it can occur in older children and adults[7].

About half of these tumors form in the cerebellum or brain stem. The

cerebellum is the part of the brain that controls movement, balance, and posture. The brain stem controls breathing, heart rate, and the nerves and muscles used in seeing, hearing, walking, talking, and eating[8]. AT/RT may also be found in other parts of the central nervous system (brain and spinal cord).A case of AT/RT with history of weakness both limbs and drop metastasis was encountered.

Figure4:A)4xTumor comprises two main elements sheets of large cells and amall more primitive appearing cellsB)40X-Rhabdoid cells with vesicular chromatin,prominent nucleoliC)Vimentin-PositiveD)EMA-PositiveE)CK-PositiveF)INI1-Negative



AIM OF STUDY :

Our aim of the study was to assess the age wise incidence, various histomorphological variants and recurrence rate in our institute and compare it with national and international literature.

MATERIALS AND METHODS

It is a retrospective study for a duration of three years from January 2015 to December 2017 received in our department of neuropathology, Institute of neurosurgery Madras Medical College Inclusion criteria: Of all CNS tumors, only cases of embryonal tumors during the period 2015 – 2017 were included.Embryonal tumors in all age groups, sites and both the sexes were included .

Exclusion criteria: Other CNS tumors were excluded.

Sample size: 34 cases of Embyonal tumors

Methodology:

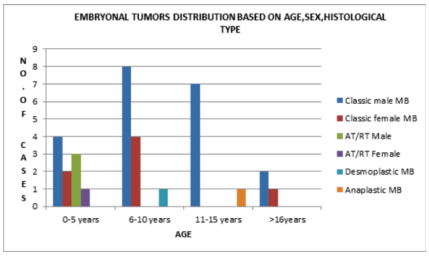
Based on Histological, IHC features and WHO 2016 classification embryonal tumors were classified . various parameters were studied and compared with national and international data on embryonal tumors

Specimens were received from the Institute of neurosurgery , fixed in 10% formalin and processed as per specified guidelines. The clinical features, imaging and per operative findings were analysed . Histological subtyping were done as per WHO classification 2016 ..

RESULTS

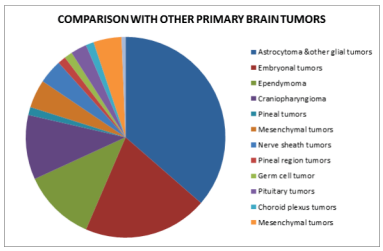
Overall incidence: In our Institute out of the 1572 cranial and spinal tumors, the incidence of embryonal tumors is 2.16%(34)Among children incidence is 20.6%(31) and among adults incidence is 0.21%(3)

Figure5:Distribution based on Age,Sex,Histological type



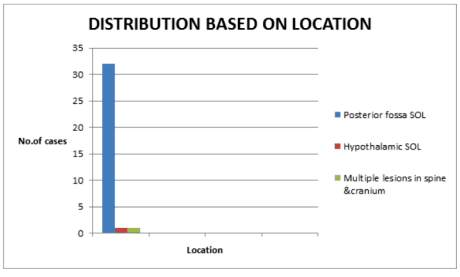
The cases were subdivided into four age groups,0-5 years,6-10 years,11-15 years,>16 years.On analysis there were 14 patients(41.17%) in 6- 10 years age group,followed by 9 patients (26.47%)in 0-5 years age group,8 patients(23.52%) in 11-15 years age group,3 patients(8.82%) in >16 years age group.In all age groups males outnumbered females.

Figure6:Comparison with other primary brain tumors in paediatric population



Nearly a quarter of all tumors within paediatric population were Astrocytomas & other glial tumors(37.33%) followed by embryonal (20.6%) and ependymal tumors(12%).Together these 3 tumor types constituted more than 60% of all paediatric tumors.Within the embryonal tumors about 87.09% were Medulloblastomas and 12.90% were Atypical Teratoid/Rhabdoid tumors.Comparatively other neoplasms like craniopharyngiomas,mesenchymal tumors ,nerve sheath tumors constitute 10.66%,4.66%,4%,1.33% respectively.

Figure7:Distribution based on location



94.11%(32 cases) of embryonal tumors presented as posterior fossa tumors,2.94%(1 case) presented as hypothalamic SOL,2.94%(1 case) presented with multiple lesions in spine and cranium-This was a rare case of Atypical Teratoid /Rhabdoid tumor presented with drop metastasis.

TABLE1:COMPARISON WITH SQUASH

Distribution of cases	Number
Total number of cases	**34**
Complete correlation in cases	**32**
Partial correlation in cases	**1**
Discrepant cases	**1**
Overall accuracy	**94.11%**

Complete correlation was obtained in 94.11% cases.The cases with the same diagnosis and grade on cytology and histopathology were considered as complete correlation.Deviations of grade of tumor with lesser grade on squash smear cytology were included in partially correlated cases.The cases where intraoperative cytological diagnosis did not correlate with the histological examinations were categorized as Discrepant cases.

TABLE2:COMPARISON WITH OTHER STUDIES[2]

Study	Frequency
Present study	**20.6%**
AIIMS	**16.8%**
NIMHANS	**19.7%**
TMH	**29%**
CMC VELLORE	**10.3%**

TABLE 3:COMPARISON WITH DIFFERENT COUNTRIES[2]

COUNTRY	Frequency
INDIA(Present study)	20.6%
Germany	25.7%
Korea	19.8%
Sweden	17%
Japan	10%

Tables 2& 3 compares the frequency of embryonal tumors in various hospitals of India and also among different developing and developed countries.

DISCUSSION:

Embryonal tumors include a constellation of neoplasms that most commonly arise during childhood[9].The prototypical tumor is Medulloblastoma-nomenclature of which is in part dependant on the location of the lesion.Cerebellar tumors which most commonly manifest as with gait disturbances,truncal ataxia and with symptoms related to increased intracranial pressure are generally medulloblastomas.

Another important embroyonal tumor which is currently in the rise with increasing incidence is Atypical Teratoid/Rhabdoid tumor which usually have varied presentations[10].All embryonal tumors are round cell tumors capable of demonstrating divergent patterns of differentiation.Tumors are associated with prominent mitotic activity and apoptosis.AT/RT patients have a grave prognosis.Most patients die within one year of diagnosis.

CONCLUSION:

In this study about Embryonal tumors in our Institute for a period of 3 years Embryonal tumors in different age groups-Most common in the age group of 6-10 years,Sex predominance-Males outnumbering females,Histological grade-Medulloblastomas predominate with currently Atypical Teratoid/Rhabdoid tumor seen with increasing incidence,Location predominance-Mostly presenting as posterior fossa tumors,Comparison with squash-91.17% with complete accuracy were all studied.This study is significant because identification of specific subtype earlier in accordance with squash may help in further treatment of the patient without exposing them to unnecessary craniospinal irradiation.Histopathological diagnosis is necessary for the formulation of further management after neurosurgery.Our study gives a current outlook of various subtypes of embryonal tumors in differing age groups , their clinical presentation and their outcome.

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