IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 1 Ser. 19 (January. 2019), PP 01-05
www.iosrjournals.org

Histopathological analysis of PediatricBrain Tumors in correlation with Ki-67 labelling index

Dr.Martina.V[1],Dr.S.Jenita Christiana Ranjana[2]
[1] *(Assistant professor, Department of Pathology, Madras Medical College,Chennai, India.)*
[2]*(Associate professor, Department of Pathology, Govt KAPV Medical College,Trichirapalli, India.)*
Corresponding Author: Dr.S.Jenita Christiana Ranjana

Abstract:*The Central Nervous System tumors arethe second most commontumors occurring in children following Acute lymphoblastic leukemia. These areless frequently analysed due to relatively low incidence of occurrence of these tumors compared to cancers of other organs like aero-digestive tract, cervix and breast. The objective of this study was to correlate the histological grade and Ki 67 expression in various CNS neoplasms and provide a benchmark for future studies assessing data in continuum. This was a retrospective study carried out in our institution on 13 CNS neoplasms arising in children from a total of 100 cases . There was positive correlation between the Ki-67 expression and histological grade showing a proportionate rise in the labelling index with the corresponding histological grade.*

Keywords: *Childhood brain tumors, Ki 67, labelling index***.**

Date of Submission: 18-01-2019 Date of acceptance:02-02-2019

I. Introduction:

The CNS tumors especially in the children is one of the most devastating forms of human cancers and a cause of considerable concern due to their relatively high mortality andmorbidity and the enormous cost of care especially in the developing world where the financial burden is on the poor parents. Grading of CNS neoplasms is fundamental for optimal prognostication and deciding on the choice of therapy. Histological grading of CNS tumors can be challenging despite criteria given by WHO more often due to limited tumor material provided. The number of mitosis is of paramount importance but can be hard to identify in the haematoxylin and eosin stained sections. Ki -67 is a novel non histone nuclear protein that is expressed in the active phases of the cell cycle and thus labelling with the monoclonal antibody against this antigen readily identifies cells that are actively proliferating.

II. Materials And Methods:

This study was carried out in the department of Pathology over 29 months. About 100 cases of CNS tumors were studied and of which 13 cases of childhood brain tumors occurring between the age groups of 0-16 years were included.All the tumors were graded according to the WHO criteria.**Exclusion criteria:**1.Reactive lesions 2.CNS infections 3.Non neoplastic cystic lesions. All the specimens were fixed in 10% neutral formalin and were subjected to histopathological examination. Sections of 3-5 micron thickness were made and routine staining with haematoxylin and eosin was done. Immunohistochemistry was done with Ki 67 based on the peroxidise method with a standard HRP kit.

III. Results:

Table -1 shows the age distribution of the braintumors that occurred in in this study. Table -2 shows the various brain tumors that occurred in the age group between 0-16 years. The maximum number of cases were contributed by the medulloblastoma followed by astrocytoma. Table -3 shows the distribution of Ki-67 expression in the tumors."Fig" -1 shows the histopathology of the glioblastoma with palisading necrosis and ki 67 labelling index of 80 %. "Fig"- 2 shows the histology of rhabdoid meningioma with Ki 67 index of 20 %. "Fig" -3 shows medulloblastoma with characteristic elongated cells with scant cytoplasm and Ki 67 labelling index of 5 percent.

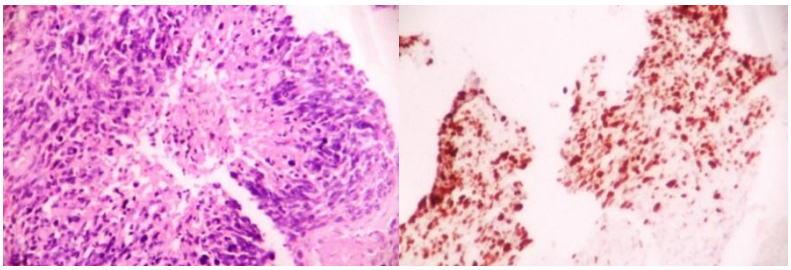


Figure – 1 Astrocytoma grade IV, ki-67 labelling index - > 80 %

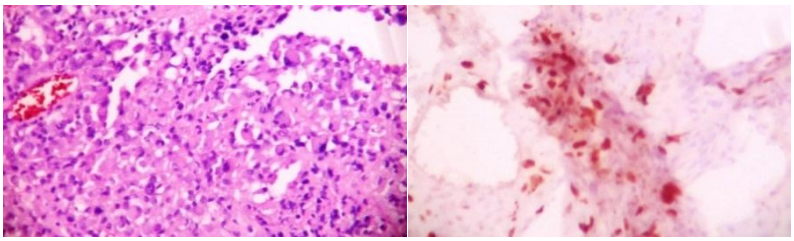


Figure 2 RhabdoidMeningioma grade III, Ki- 67 labelling index 20 %

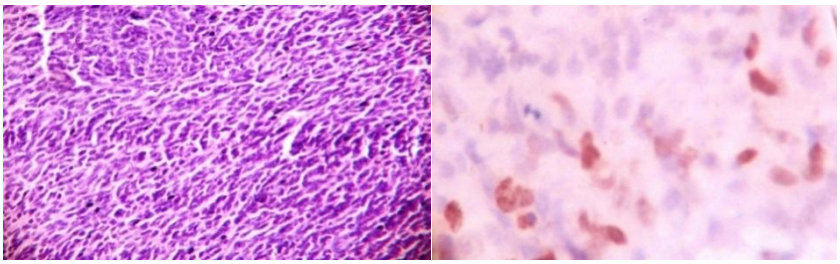


Figure -3Medulloblastoma ki-67 labelling index -5 %

Table – 1 . Age Distribution of Various CNS Neoplasms

Tumor	1-10 yrs	11-20 yrs	21-30 yrs	31-40 yrs	41-50 yrs	51-60 yrs	61-70 yrs	71-80 yrs	Total
Astrocytoma	-	3	10	11	11	7	1	1	45
Meningioma	1	-	2	7	4	5	3	1	23
Nerve sheath tumor	1	-	2	3	3	1	1	-	13
Medulloblastoma	3	4	-	-	-	-	-	-	7
Pituitary adenoma	1	-	-	2	-	-	1	-	4
Ependymoma	-	-	-	1	-	1	-	-	2
Hemangioblastoma	-	-	1	-	1	-	-	-	2
Metastasis	-	-	-	1	1	-	-	-	2
Ganglioglioma	-	-	-	-	1	-	-	-	1
Oligodendroglioma	-	-	1	-	-	-	-	-	1
Total	**6**	**10**	**16**	**25**	**21**	**15**	**6**	**2**	**100**

Table – 2 . Age Distribution of Various Childhood Brain Tumours

S.no	Age/sex	Histological diagnosis	SITE	grade
1	16/M	Medulloblastoma	Posterior fossa	IV
2	7/M	Medulloblastoma	posterior fossa	IV
3	14/M	Medulloblastoma	Posterior fossa	IV
4	11/M	Medulloblastoma	Posterior fossa	IV
5	10/F	Medulloblastoma	Posterior fossa	IV
6	6/F	Medulloblastoma	Posterior fossa	IV
7	9/F	Neurofibroma	D1-D3	I
8	12/M	Medulloblastoma	Posterior fossa	IV
9	13/F	Gliblastoma	Frontal lobe	IV
10	15/F	Gliosarcoma	Frontal lobe	IV
11	15/F	Gliosarcoma	Frontal lobe	IV
12	10/F	Rhabdoid meningioma	Temporal lobe	III
13	10/M	Pituitary adenoma	Suprasellar	I

Table -3 Ki 67 Labelling Index In Various Childhood Brain Tumors

S.NO	HPE Diagnosis	MIB INDEX
1	Astrocytoma – grade - IV	80%
2	Gliosarcoma	60%
3	Meningioma- grade- III (Rhabdoid)	20 %
4	Medulloblastoma	5 %
5	Pituitary adenoma	Negative
6	Neurofibroma	Negative
15.	Ependymoma	1%

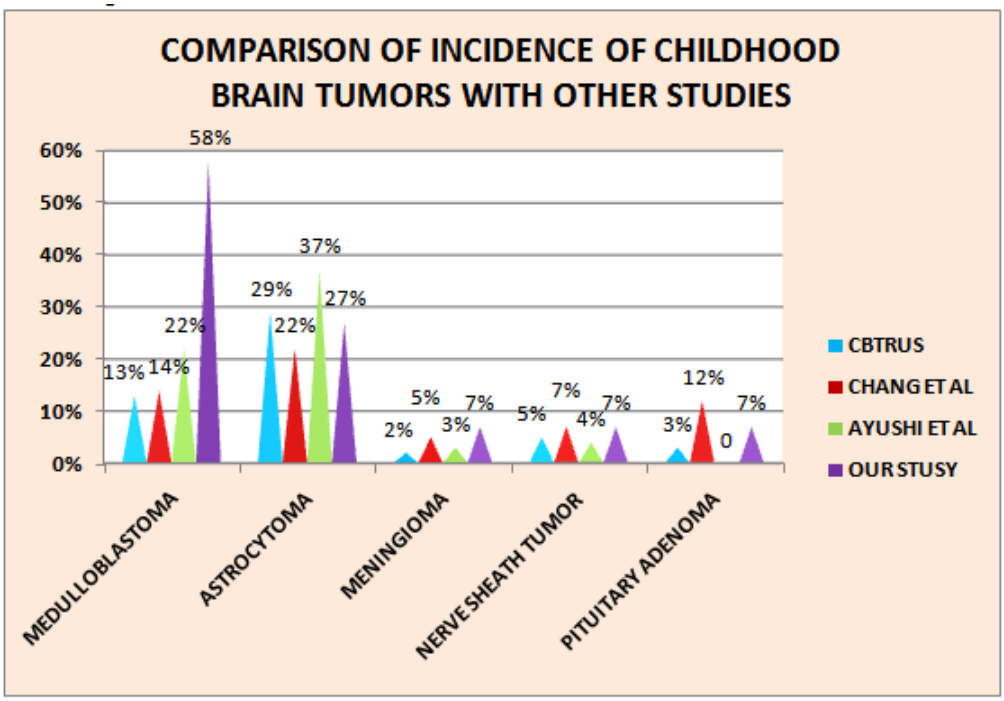
IV. Discussion:

An estimated 2400 children between the ages of 0-19 years are diagnosed with invasive primary central nervous system tumors in the United 100,000 person years (CBTRUS report 2009)[1] . Brain tumors are second only to acute lymbhoblasticleukemia (ALL) in children. The incidence of CNS tumors in children as stated by Smith, Freidlin et al was found to have increased by 35 % between the years 1975-1984. This increase was attributed to the introduction of magnetic resonance imaging (MRI) brain growth occurs rapidly during gestation and peaks around 4 months after birth but continues until 3-4 years thereafter. Hence it is more vulnerable to genotoxic damage and neoplastic transformation than any other organ in the body, due to the relatively longer course of development both in utero and post natal life during which the rapidly dividing cells become susceptible to exposure to potential environment toxins and DNA damage.It appears that fetal brain is less able to efficiently repair DNA alkylation induced by various mutagenic agents. The blood brain barrier is also not complete in the fetal brain and facilititates free transfer of carcinogens into the vulnerable neural tissue.

Only about 5 % of the CNS tumors are the direct consequence of a specific gene defect. Ron, Modan et al has stated that occurrence of majority of these neoplasms are multifactorial due to the interplay of both genes and the environment. One known environmental cause of brain tumors is ionising radiation and can induce both benign and malignant gliomas or occasionally primitive neuro-ectodermal tumors (PNET)

A total of 13 cases(13%) of pediatric brain tumors occurred in our study. A similar incidence was reported in the study of Manoharan et al[2] (9.3%) According to the CBTRUS[1] data (2009) about 7 % of the reported brain tumors occurred in children. The following were the distribution of various groups of CNS tumors in children in comparison with various studies."Fig"-4

Figure -4



The spectrum of childhood brain tumors in the present study "fig"-4 showed a predominance of medulloblastoma which seem to contrast with all theinternational studies (CBTRUS[1], Chang et al[2] (korea),Mehidi et al [11](Morocco),) including the Indian study of Manoharan et al[2] who showed a predominance of Astrocytomas. The overall male to female ratio in all the studies of Cho KT et al[3], Farinotti et al[6], Mehrazin et al[12], , indicated that pediatric brain tumors are more common in males than in the females, which is in contrast with our study where females predominated (61.5%).

Over 90 % of the medulloblastoma typically arise from the superior medullary velum, grows and fills the cavity of the fourth ventricle. Dissemination to leptomeninges occurs in 10 -30 % and spread to the neuraxis occurs in < 10 %. Medulloblastoma is the most common malignant brain tumor in children. About 400 children are diagnosed with this tumor each year in the United States.The peak age of onset is between 5 -9 years of age.

Most common malignant childhood tumor according to the studies of and Rosalva et al[18] is medulloblastoma (28.9%) with the peak incidence in the 5 -9 years age group. Out of the 13 cases of pediatric brain tumors in our study there were 7 cases of meduloblastomas. The mean age of occurrence of the tumor was in the 10 years. Pediatricgliomas accounted for 52.6% of all brain tumors in children in the studies of Chang et al[2]. High grade gliomasincluding grade III and grade IV constitute about 14% in the study of Sri Gururangan et al[19], whereas GBM contributes to only 3% in the study of Chang[2] and CBTRUS[1]. In our study GBM accounts for 23.3 % of all childhood brain tumors. We reported 3 cases of high grade gliomas in our study out of which 2 cases of gliosarcoma was reported .

Most common age of occurrence is the fourth – sixth decade.Age and sex incidence of gliosarcoma shows a peak in the first and second decade in the females following which the males show a predominance In our study two cases(2%) of gliosarcoma were reported which was in accordance with the study P.Koul et al[16] who showed an incidence of <2% of all gliomas. Both cases occurred in 15 years age group and both cases were females. Pediatricgliosarcoma has been described with no difference in morphology or clinical features. It is more common in infants with previous history of radiotherapy. In his study Michael Karremanet al[13] showed a median age of occurence of gliosarcoma to be 11 years. As per the literature the gliosarcomas showed a strong predilection for the cerebral hemispheres in our study also. In gliosarcoma the sarcomatous element resembled fibrosarcoma: the tumor cells were elongated and spindly and they organised into fascicles of parallel cells. Reticulin stains demonstrated a single cell pattern of reticulin positivity, whereas the pure glial areas of the same tumorwasreticulin negative but stained positively for GFAP.

Malignant meningiomas are uncommon comprising between 1 -2.8 % of meningiomas(Mahmood et al[9], Jass et al[12]). Rhabdoid variant is an apparently recent addition to meningioma family. Rhabdoid meningioma was first described in 1998 as an unusual variant of meningioma and it is an histological indication of increased proliferation activity.Histologically the descriptor rhabdoid refers to both the cytoplasm and nuclear configuration wherein gemistocyte appearing eosinophilic cytoplasm often shows displacement of nucleus by spherical mass of intermediate filaments. This change may be present diffusely throughout the lesion or focal int he background of a more classical meningioma pattern. The pattern often emerges during tumor progression and is therefore more obvious in recurrences than in the initial specimen.However Maier et al[10] have stressed that unless the rhabdoid cells constitute half or more of the lesion it does not meet he WHO 2007 criteria for the diagnosis of rhabdoidmeningioma.As per Douglas C Muller[5] and Perry et al[17], pediatricmeningiomas are distinctly rare but are more likely than adult counterpart to manifest aggressive behaviour or aggressive variant histologically and they lack any female predominance. Predisposing factors often include NF-2 or history of prior radiation, although half are still sporadic. In comparison with adult cases, clinical behaviour is more difficult to predict.

Pituitary adenomas in children are relatively infrequent occurrences .most studies report the incidence of these tumors to be between 1 % and 10 % of all surgically treated adenomas. Despite the rarity of these tumors they can have a significant effect on the quality of life of the patient, especially during childhood, when the growth rates and development are at a peak. Christopher web et al[4] suggested the fact that most of the pituitary adenomas are secretory with prolactinomas being the most common type. They also reported that in there study 60 % were macroadenomas.

The clinical presentation of prolactinomas is sexually dimorphic with females presenting at a younger age with microadenomas, because they have a prolactin responsive breast and endometrial tissue, whereas the

males present at a much older age group with macroadenomas with compressive symptoms like headache or visual problems . Kane LA et al[17] and MindermanTwilson et al[14] in their studies have evaluated that adenomas occurring in children are usually PRL or ACTH producing. In accordance , in our study we have reported one case of pituitary adenoma in a 10 years old child that presented as a macroadenoma (> 1cm) and was already evaluated outside as prolactinoma. Pediatric pituitary adenomas are quiet variable in their presentation.

V. Conclusion:

Hence we conclude that the pediatric brain tumors are on therise and any little data related to the statistical analysis of these tumors would be a valuable contribution to literature and aid in the diagnosis and grading of these tumors, keeping pathologists and surgeons aware of the incidence of rare variety of central nervous system tumors occurring in children. Ki 67 labelling index helps in easily grading the tumorsand thus aids in accurate diagnosis and further management of pediatric brain tumors.

References

[1]. Central Brain Tumor Registry of the United States: Statistical report: Primary Brain and central nervous system tumors diagnosed in the United States in 2004- 2007, published February 2011.
[2]. Chang –Hyun Lee,Kyu Won Jung, HeonYoo, Sohee Park SeungHoon Lee. Epidemiology of primary brain tumors in Korea. *J Korean NeurosurgSoc* 2010;48:145-152.
[3]. Cho KT, Wang KC, Kim SK,Shin SH, Chi JG (2002) Pediatric brain tumors : statistic of SNUH, Korea (1986- 2000). Childs NervSyst 18:30-37.
[4]. Christopher Webb, Richard A Prayson. Pediatric pituitary adenomas. 2008; 132: 77-80.
[5]. Douglas M Miller Modern surgical pathology of the central nervous system. ; Third edition; vol 2. Pg 439- 450
[6]. Farinotti M, Ferrarini M, Solari A, Filippini G (1998) Incidence and survival of childhood brain tumors in the region of Lombardy, Italy. Brain 121: 1429 -1436.
[7]. JaasKelainen J, H altia M, Servo A. Atypical and anaplastic meningioma :radiology,surgical and radiotherapy outcome. Surg. Neurol 1986;25:233-242.
[8]. Kane LA, Leinung MC Scheithauer BW et al, Pituitary adenoma in childhood and adolescence, J. Clinical Endocrinolmetab. 1994;79: 1135-1140.
[9]. Mahamood A, Caccamo DV, Tomechk FJ et al Atypical and malignant meningioma: clinicopathologic review .Neurosurg ,1993;33:955-963.
[10]. Maier H Ofner D Hittmair A Kitz K. Classic ,atypical and anaplastic meningioma: Three histopathological subtypes of clinical relevance. J .neurosurg 1992;77:616-623.
[11]. Mehdi karkour i,SadiaZafad, Mohammed Khattab, Sana Sefiani, et al. Epidemiologic profile of paediatric brain tumours in Morocco.Childsnervsyst 2010; 26 : 1021-1027.
[12]. Mehrazin M, Yavari P (2007) Morphological pattern and frequency of intracranial tumors in children. Childs NervSyst 23: 157-162.
[13]. Michael Karremann, Ulrike Rausche, GardranFleischback et al. Clinical and epidemiological characreristics of pediatricgliosarcomas.*Jneurooncol*. 2010 ; 97: 257 -265.
[14]. Mindermann T Wilson CB Pediatric pituitary adenoma. Neurosurg. 1995; 36: 259-268;discussion 269.
[15]. N.Manoharan , PK Julka, GK Rath. Descriptive Epidemiology of Primary brain and CNS tumors in Delhi, 2003-2007. *Asian Pacific Journal of Cancer Prevention 2012*;13: 637 – 640.\
[16]. P Koul, P Tai, ADubey. Five patients with gliosarcoma. J HK collRadiol 2008;11: 116-121.
[17]. Perry A et al ,Rhabdoid meningioma an aggressive vriant. Am J SurgPathol.1998 ;22(12) 1482 -1490.
[18]. RosalvaTherezaMeurer, Daniele Tondolo Martins, ArleteHilbig, Marlise de Castro Ribeiro.Immunohistochemical expression of markers Ki 67,NeuN, Synaptohysin, p53 and Her 2 in medulloblastoma and its correlation with the clinicopathological parameters. *ArqNeuropsiquiatr* 2008;66:385-390.
[19]. Sri Gururangan, the Preston Robert Tisch Brain tumor centre. Chapter 5 ;99-130.