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RESEARCH ARTICLE

STUDY OF THE MORPHOLOGICAL PATTERNS OF INTRACRANIAL LESIONS IN A TERTIARY CARE HOSPITAL IN HARYANA: A CLINICOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL STUDY

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ABSTRACT: Introduction: Central nervous system tumors comprise 1-2% of all tumours and constitute a heterogeneous group which shows a spectrum of morphological features. Although the mainstay of diagnosis including its grading remains conventional Hematoxylin-Eosinstained histopathology but it is not always straightforward and the pathologist faces diagnostic dilemmas due to overlap in morphological features and divergent differentiation within the same tumor. Immunohistochemistry (IHC) plays a major role in the differential diagnosis and in improving the diagnostic accuracy. The present study was done to determine the utility of IHC in the diagnosis and grading of brain tumors. **Patients and Methods**: Thestudy was carried out between January-September 2019. The demographic, clinical and imaging details of all the cases were noted. Brain tumors were diagnosed based on examination of H&E stained sections. IHC markers were applied in difficult cases for an accurate diagnosis. **Results:** Out of 40 cases, 95 %were primary and 5%were metastatic tumors. Headache was most common symptom and most common site was the anterior fossa. Astrocytoma was the most common diagnosis. Grading of tumors was done as per the universal grading system. IHC was done on problematic cases to reach the final diagnosis and grading. **Discussion and Conclusions**: This study was carried out to highlight the importance of IHC in identifying the tumor cell type and its origin in case of metastasis. IHC also helps in assessing the proliferation index of the tumor cells, excluding reactive processes,evaluating the tumor margins and as a prognostic indicator of different types of CNS tumors.

KEYWORD: CNS Tumors, Immunohistochemistry, Radiology, Astrocytoma, Meningioma

INTRODUCTION :

Central nervous system tumors comprise 1-2% of all tumors and constitute a heterogeneous group which differ in histogenesis and show a spectrum of morphological features**.** Location of tumors is of paramount importance in formulating histological diagnoses. Majority of pediatric neoplasms occur in posterior fossa while in adults anterior cranial fossa is commonest location. CNS tumors have a guarded prognosis because of their location.[1] Clinical features of CNS neoplasms depends on location, size and growth rate of tumor. Low grade neoplasms progress to high grade depending on genetic and morphological features of the tumor.

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Immunohistochemistry (IHC) plays a crucial supplementary role in resolving diagnostic dilemmas in the routine practice of neurosurgical pathology. The principle of IHC was known since 1930s, but first IHC study was reported in1942.FITC- labelled antibodies were used to identify pneumococcal antigen in infected tissue. IHC is based on localizing specific antigens in tissues or cells which are recognize by means of specific antibodies. Once Ag-Ab binding occurs, it can be visualized either by light microscopy or by ultraviolet light (if florescent antibodies are used).[2,3]Common methods applied in IHC are avidin-biotin method and peroxidase antiperoxidase immune complex method.Glial fibrillary acidic protein (GFAP) is a member of class III of intermediate filament proteins and is expressed mainly in neuroglia including astrocytes and ependymal cells. Positive staining for GFAP can firmly establish the astrocytic origin and differentiation of a CNS neoplasm.

The present study aimed to provide morphological patterns with clinicopathological spectrum of intracranial lesions in a tertiary care hospital in Rohtak, Haryana, India and to determine the utility of IHC in the diagnosis of brain tumors.

PATIENTS AND METHODS:

The study was conducted over a period of 9 months from January to September 2019 in the Department of Pathology, Pandit B.D. Sharma PGIMS, Rohtak, Haryana. A total of 40 cases of intracranial lesions were included and morphological patterns along with IHC were evaluated. Only histopathological proven cases of intracranial tumours with total or gross total excision were included in study while cases diagnosed on stereotactic biopsy, inadequate biopsy specimen, hematoma and bony lesions of skull were excluded from the study. A serial number was assigned to each one to ensure the confidentiality. Ethical approval for this study was obtained from the institutional ethics committee.

The tissue was fixed in 10% formalin for histopathological examination. Then paraffinembedded blocks were made in the usual manner and thin sections of 5 microns were cut using a microtome. Sections were stained by hematoxylin & eosin stains and histological andimmunohistochemical analysis was performed to diagnose and classify the various brain tumors according to the World Health Organization classification (2016). IHC was performed on problematic cases where the final diagnosis could not be reached on H&E stained sections alone. Using 3µm thick sections on Poly-l-lysin coated slides, antigen retrieval was done using decloaking chamber in citrate buffer at PH 6. Selected markers from a panel including glial fibrillary acidic protein (GFAP), epithelial membrane antigen (EMA), vimentin(VIM), Progesterone receptor (PR), Neuron specific enolase(NSE), cytokeratin (CK), synaptophysin, Ki-67, thyroid transcription factor-1, (TTF-1) and P63 were used for antigen detection by standard avidin biotin kit.

RESULTS:

In the current study, a total of 40 CNS tumors were studied. Tumors were classified after H& E staining of slides. Astrocytoma (grade II and III) formed the major group, constituting about 40 % of all the tumors, followed by Glioblastoma multiforme (17.5%), Meningioma (12.5%) and Ependymoma (7.5%). (Table 1)(Figure 1,2,3,4)

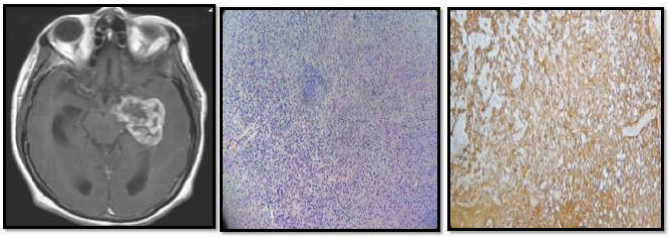

Figure 1: Anaplastic Astrocytoma A) MRI showing left temporal lobe space occupying lesion, B) H& E Section shows pleomorphic astrocytic cells, C) On IHC- tumor cells are positive for GFAP

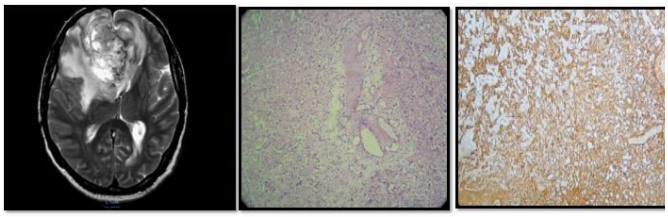

Figure 2: Glioblastoma multiforme A) MRI showing bilateral Fronto-parietal lobe space occupying lesion. B) H& E Section shows pleomorphic astrocytic cells and serpentine necrosis. C) On IHC- tumor cells are positive for GFAP

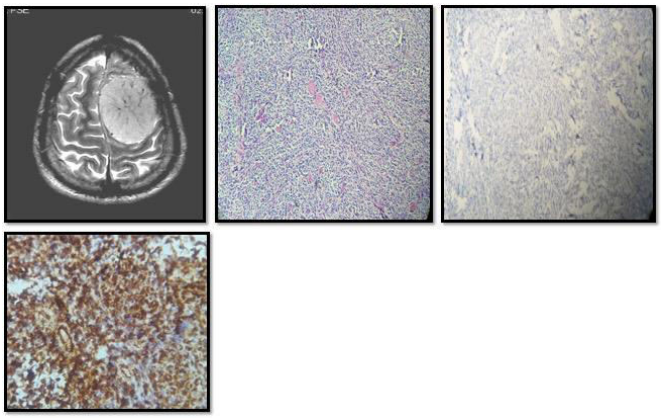

Figure 3: Meningioma A)MRI showing Fronto-parietal space occupying lesion B) H& E Section shows tumours cells in whorls and sheets C) On IHC : Tumor cells negative for GFAP D)On IHC: Tumor cells positive for Vimentin

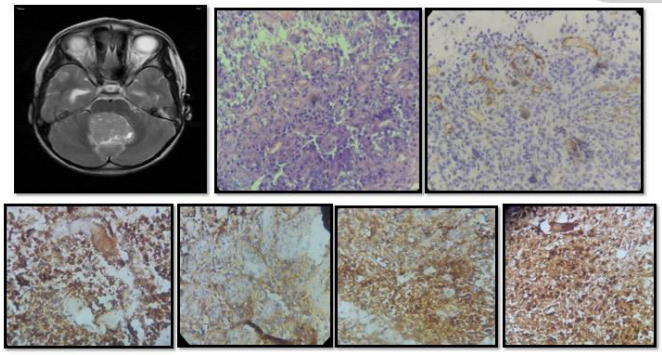

Figure 4: Ependymoma- A) MRI showing space occupying lesion in cerebellar vermis. B) H& E Section shows perivascular pseudorosettes. On IHC positive for C) CD31 around vessel wall. D) GFAP E) EMA F) CD99 G) S100

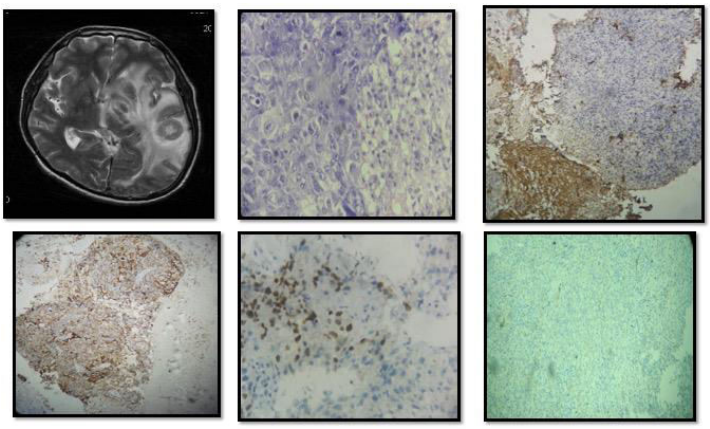

Figure 5: Metastasis- A) MRI showing space occupying lesion in Parietal lobe, B) H& E Section shows metastatic tumour deposits. On IHC C) GFAP positive in brain tissue D) CK positive E) P 63positive F) TTF-1 negative

CNS tumors were classified as primary and secondary (metastatic) which constitute 95% (38/40) and 5% (2/40) respectively in our study (Figure 5).Out of a total of 40 cases, 25 were males, with Male: Female ratio being 1.6:1. (Table 1) Majority of cases were in the 3rd decade of life. (Table 2). The most common location of these CNS tumors was Frontal lobe i.e. 15 (37.5 %) out of 40 cases. (Table 3) Headache was the most common presenting symptom in 26 (65 %) of cases, followed by vomiting, visual disturbances and gait disorders in 4(10%) of cases in each category. (Table 4) Out of 40 cases, 12 cases were referred to IHC section for confirmation of morphological patterns identified on H & E sections details of which are shown in Table 5.

Table 1: Gender wise distribution of cases

Histopathological Pattern	Male	Female
Astrocytoma	10	6
Oligodendroglioma	3	1
Ependymoma	2	1
Medulloblastoma	1	1
Meningioma	1	4
Glioblastoma Multiforme	6	1
Choroid Plexus Papilloma	1	-
Metastatic Tumours	1	1
Total	25	15

Table 2: Age-wise distribution of cases

Histopathological Pattern	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80
Astrocytoma	1	2	5	4	3	1	-	-
Oligodendroglioma	-	-	2	-	1	1	-	-
Ependymoma	1	-	1	1	-	-	-	-
Medulloblastoma	1	1	-	-	-	-	-	-
Meningioma	1	-	-	-	1	1	1	1
Glioblastoma Multiforme	-	-	2	1	2	2	-	-
Choroid Plexus Papilloma	-	-	1	-	-	-	-	-
Metastatic Tumours	-	-	-	-	-	-	2	-
Total	4	3	11	6	7	5	3	1

Table 3: Site wise distribution of cases

Site	Number of Cases	Percentage (%)
Frontal	15	37.5%
Temporal	7	17.5%
Parietal	8	20%
Posterior fossa	4	10%
Intraventicular	4	10%
Thalamus	2	5%
Total	40	100%

Table 4: Clinical features

Clinical Features	Number of cases	Percentage%
Headache	26	65%
Vomiting	4	10%
Visual disturbance	4	10%
Gait disorder	4	10%
Seizure	2	5%

Table 5: IHC markers on 12/40 cases of intracranial space occupying lesion

Histological types	GFAP	VIM	EMA	PR	NSE	SYN	CK	TTF1	P63
Astrocytoma (5/16)	+	-	-	-	-	-	-	-	-
Ependydoma (2/3)	+	+	+	-	-	-	-	-	-
Medulloblastoma (1/1)	-	+	-	-	+	+	-	-	-
Meningioma (2/5)	-	+	+	+	-	-	-	-	-
Metastasis (2/2)	-	-	-	-	-	-	+	+	+

DISCUSSION:

We analyzed 40 cases of CNS tumors which share various clinical and histopathological features published in the literature. Maximum number of cases were observed in 31-50 years of age while Madabhushi[4] observed peak incidence in 4th decade and Mondal [5] observed peak in 5th decade.Males were more in our study and this corroborates with the existing literature of Bhati[6]and Desai [7] who also reported the male preponderance in their studies.Majority of the tumors were located in the frontal lobe (37.5 %) followed by temporal lobe and parietal lobe (12.5%). Similar results were shown in other studies done by Andrews[8] and Torres[9].

Astrocytoma was the most common CNS tumors(57.5 %) in our study,out which 43.4% (10/23) were WHO Grade II,26.0% (6/23) Grade III and30.4% (7/23)Grade IV (Glioblastoma Multiforme). Grading of gliomas are important as it predicts the survival, prognosis and treatment plan of the patient. Mondal[5], Bhati[6], and Anadure[10]also reported similar incidence of various grades of astrocytoma in their studies while Aryal[11]reported a higher incidence of Grade IV astrocytoma in his study. He stated that late presentation of his patients to the hospital could be the possible cause.

The second most common type of primary CNS tumour in our study was meningioma (12.5%), followed by oligodendroglioma (10%) and ependymoma (7.5%). There were two cases of medulloblastoma (5%) and one case of choroid plexus papilloma (2.5%). Two cases (5%) diagnosed as metastatic deposits from squamous and adenocarcinoma. The findings were comparable with Bhati[6], Aryal[11] and Pradhan[12]while Ghanghoria[13]reported meningioma as the most common tumour followed by astrocytoma.

Out of 40 cases, 12 cases were referred to IHC section which helped in making final diagnosis by corroborating the morphology and IHC findings.

GFAP is done for confirmation of glial differentiation while Ki 67 was used for grading of astrocytoma. Most of our cases were WHO grade II. Ependymoma were positive for GFAP, Vimentin and EMA while medulloblastoma were positive for Vimentin, NSE and synaptophysin. Meningiomas were positive for vimentin EMA and PR.

In the present study two cases of brain metastasis were reported with a frequency of 5%. These cases were negative for GFAP but positive for CK and TTF1 and P63 each. On further investigations of primary site, one case was metastasized from adenocarcinoma lung and another case metastasized from squamous cell carcinoma. Metastatic nodules are usually sharply circumscribed with pushing margins and reflect the histology of the donor lesions.

The diagnosis of intracranial space occupying lesion is sometimes difficult morphologically due to small size specimen, non-availability of complete clinical and radiological findings. In these cases, IHC helps in establishing the origin of the tumour as emphasized in our study. However, there are certain limitations of our study like small sample size and lack of follow up of these patients.

CONCLUSIONS :

The present work shows that histopathologic examination is the gold standard in the diagnosis and grading of majority of brain tumors, but IHC plays an important role in identifying the tumor cell type and its origin in case of metastasis, in assessing the proliferation index of the tumor cells, in excluding reactive processes, in evaluating tumor margins and as a prognostic indicator. Clinical, radiological, and morphological correlation is mandatory for accurate interpretation of any study on immunohistochemistry.

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