ROLE OF IMMUNOHISTOCHEMISTRY IN DIAGNOSIS AND GRADING OF CNS TUMORS: A SINGLE INSTITUTIONAL EXPERIENCE

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INTRODUCTION

Brain tumors are a heterogeneous group and also they differ in histogenesis and show a wide spectrum of morphological features.[¹] Though clinical data, radiology techniques, and perioperative findings offer some valuable clues to all the diagnostic possibilities, histopathologic examination is the primary necessity of diagnosing brain tumors. Histological diagnosis of brain tumors is not easy due to overlap in morphological features among different categories, divergent differentiation within the same tumor, and the non-neoplastic lesion can also mimic tumor.[²] Hence, in spite of clinical data, radiological techniques and preoperative findings, the application of immunohistochemical markers has become imperative for an exact diagnosis and subtyping. In the last two decades, diagnostic neuropathology benefited from the incorporation of immunohistochemistry (IHC).[³] The fundamental concept behind IHC is the demonstration of antigens within tissue sections by the means of specific antibodies. Once Ag-Ab binding occurs, it is visible by light microscopy or fluorochromes by ultraviolet light.[⁴] Recently, the approach to diagnosis relies principally on histopathological evaluation of H&E stained sections with the incorporation of smear preparations, histochemical stains, electron microscopy, and immunohistochemical preparation as a supplemental aid in diagnosis.[⁵] This present study was taken up in our institution, planned to determine the proportion of occurrence of types of brain tumors and to assess the efficacy and utility of immunohistochemistry (IHC) as a rational supplementary technique in the diagnosis and grading of brain tumors.

MATERIALS AND METHODS

The present study was a hospital-based retrospective study in the Department of Pathology, GSVM Medical College, Kanpur, from January 2020 to December 2022. Brain tumor specimens were...
received from our institution's Department of Neurosurgery. Pertinent clinical data, including details of radiology investigations and perioperative findings, were obtained in all the cases. A total of 108 specimens were received, which were classified according to “WHO Classification for Central Nervous System Tumors 2021”.[6] The tissue was fixed in 10% formalin for histopathological examination, then paraffin-embedded blocks were made in the usual manner, and thin sections of 5 microns were cut using a microtome. Sections are stained by hematoxylin & eosin stains and histological analysis was performed to diagnose and classify various brain tumors. IHC was performed on problematic cases where differential diagnosis was given on H and E sections. Using 3-µm-thick sections on poly-L-lysine coated slides; antigen retrieval was done using high pressure in citrate buffer at pH.[6] Required markers were used for antigen detection. Autolysed specimens were excluded.

RESULTS

In the present study, a total of 106 brain tumors were diagnosed. Astrocytic tumors were found in the highest frequency (30.18%), followed by meningioma (27.36%), schwannoma (7.55%), and craniopharyngioma (3.77%) as show in table no 1.

<table>
<thead>
<tr>
<th>Brain tumors</th>
<th>No of tumors (n)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astrocytic tumors</td>
<td>32</td>
<td>30.18</td>
</tr>
<tr>
<td>Meningioma</td>
<td>29</td>
<td>27.36</td>
</tr>
<tr>
<td>Ependymal tumor</td>
<td>17</td>
<td>16.03</td>
</tr>
<tr>
<td>Schwannoma</td>
<td>8</td>
<td>7.55</td>
</tr>
<tr>
<td>Cerebral parenchymal tumor</td>
<td>4</td>
<td>3.77</td>
</tr>
<tr>
<td>Oligodendrogial tumors</td>
<td>1</td>
<td>1.00</td>
</tr>
<tr>
<td>Oligoastrocytic tumors</td>
<td>1</td>
<td>1.00</td>
</tr>
<tr>
<td>Neuronal and mixed neuronal-glial tumors</td>
<td>2</td>
<td>1.88</td>
</tr>
<tr>
<td>Hemangioblastoma</td>
<td>2</td>
<td>1.88</td>
</tr>
<tr>
<td>Metastatic tumors</td>
<td>3</td>
<td>2.83</td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>2.83</td>
</tr>
<tr>
<td>TOTAL</td>
<td>106</td>
<td>100</td>
</tr>
</tbody>
</table>

The highest age incidence of all brain tumors was observed in the age group 31-50 years (41.67%), followed by 11-30 years (24.07%), >50 years (19.44%), and <10 years (7.40%). Overall M:F ratio observed was 0.95:1. The highest astrocytic tumors were observed in the age group 21-30 years (43.33%) followed by 31-50 years (33.34%). The highest meningioma was observed in the age group 31-50 years (57.14%) and >50 years (32.14%) as show in . The most common variant was fibroblastic meningioma followed by transitional meningioma and psammomatous meningioma. Most cases of schwannoma seen in the 4th and 5th decades (75%) and craniopharyngioma in the 1st and 2nd decades (62.5%).

DISCUSSION

A total 106 cases of brain tumors were studied. Out of 106 cases, 30 cases (28.3%) were astrocytoma followed by meningioma (26.41%) which is similar to the study done by Bhati Sanju et al. (2018).[7], Sajeeb Mondal et al. (2016).[8], Khaled R Zalata et al. (2011).[9] and M: F ratio of brain tumors was 0.95:1 which is consistent with Bhati Sanju et al. (2018) [7] Peak incidence of brain tumors was noted in 30-50 yrs (41.67%) which is similar to Bhati Sanju et al. (2018).[7], Sajeeb Mondal et al. (2016),[8] and Venugopal Madabhushi et al. (2015).[10] Among 32 cases (30.18%) of astrocytoma, grade IV astrocytoma was the most common subtype, which is consistent with Bhati Sanju et al. (2018).[7] and Sajeeb Mondal et al. (2016).[8] 29 cases (27.36%) of meningioma were found in the present study, and M: F ratio was 1:1, which is very consistent with Bhati Sanju et al. (2018).[7] and Bondy M et al. (1996).[11] 17 cases of Ependymal tumors were found in the present study, and M: F ratio was 1:1, which is consistent with the study of Yong-Hyun Chai (2017).[12] In the present study, schwannoma was comprising of 8 cases (7.55%). Schwannoma, the most common variant of nerve sheath tumors in the central neuraxis, occurs in adults in the cerebellopontine angle or lumbosacral spinal extramedullary space.

Incidence of craniopharyngioma was 3.77% in the present study, which is consistent with Niki Karavitaki et al. (2006).[14] (2.5%). 2.83% of tumors were metastatic brain tumors, which is consistent with Kenneth E Livingston et al (1948).[15] Out of 106 cases, 22 cases were referred to IHC section for grading and diagnosis. For 11 cases of astrocytoma, IHC was used. Grading of gliomas is done as per the revised WHO criteria. Circumscribed lesions of low proliferative potential are graded as Grade I and infiltrative tumors are graded as Grade II, whereas infiltrating tumors with increased cellularity and mitotic activity are designated as Grade III. Grade IV is assigned to histologically malignant, mitotically active, and necrosis-prone tumors. The final diagnosis was made by correlating histopathology and immuno-histochemistry findings.[16,17,18] MIB-LI was done in 7 cases for grading and in 5 cases GFAP was also applied to confirm glial differentiation.

MIB-LI grade-1 in grade was typically <1% (David N Louis et al. 2007),[19] but can vary from 0 to 3.9% (Giannini C et al. 1999).[20] MIB-LI value varied from 1%-4% for grade II, 8-10% for grade-III, and 15-60% for grade-IV astrocytoma, which was consistent with the study of David N Louis et al. (2016).[19] (in our study, grade II MIB-LI is upto
The present study showed that histopathological examination is a mainstay for the diagnosis in most tumors, but immunohistochemistry plays an important role in difficult cases where there is a diagnostic dilemma, and grading is not possible only on histological basis in the routine practice of neurosurgical pathology.

**CONCLUSION**

4%, for grade III 5-10% and for grade IV>10%) but MIB-LI has overlapped values so cannot be used alone as diagnostic factor, it should be used with combination of established histological criterias (Johannessen et al 2006).[21] In one case of glioblastoma in our study showed biphasic tissue pattern comprising neoplastic astrocytes admixed with pleomorphic spindle-shaped cells and increased mitotic activity. IHC revealed patchy GFAP expression and diffuse vimentin positivity leading to the diagnosis of giosarcoma. Literature shows that sarcomatous change occurs in approximately 2% of glioblastomas.[22,23] In one case of oligodendroglionioma Olig2 was positive and MIB-LI was 20-25%. Glial protein may be focally present in oligodendroglionioma due to the presence of mature reactive astrocytes. (David N Louis et al. 2007).[19] 2 cases of oligoaestrocytoma were positive for GFAP, IDH1, Kif6(7-8%), and MIB-LI value of about 4%. GFAP is expressed in astroglial component and variably expressed by the oligodendrogial component (David N Louis et al. 2007).[19] and Rama Goyal et al. 2015,[24] and the average value of MIB-LI is less than 6% for grade II (David N Louis et al 2016).[19] 2 cases of Ependymoma were positive for GFAP and EMA. Ependymoma shows immunoreactivity for GFAP and EMA (Kunishio K et al. 1991).[25] MIB LI <4% has greater survival, and >5% has poor survival (Prayson RA et al. 1999).[26] Out of 29 cases of meningioma, only 4 cases were sent to IHC section. EMA and vimentin were positive in different cases. MIB was applied on 1 case, value was 4%. Meningioma shows EMA and vimentin (JM Theaker et al. 1986).[27] and MIB-LI >4% have increased recurrence rate (David N Louis et al. 2016).[19] One case of hemangioblastoma was positive for EMA and S-100. According to Shih Ming Jung et al. (2005)[28] hemangioblastoma show immunoreactivity for inhibin, whereas a study by Frank TS et al. (1989).[29] shows that few cases may be immunoreactivity for S-100 and GFAP (negative in our case). In adults, brain metastases usually derive from lung and breast carcinomas, followed by malignant melanomas, renal carcinomas, and colorectal adenocarcinomas.[30,31] Out of 2 cases of metastatic adenocarcinoma 1 case was positive for Pan CK, CK7 and CK 20 and another case was positive for EMA, TTF-1 and CK 7 which were consistent with Sushila Jaiswal 20163.

**REFERENCES**

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20. Giannin C, Scheithauer BW, Burger PC, Cristensen MR, Woolan PC, SeboTJ. Cellular proliferation in pilocytic and