Section: Pathology

Original Research Article

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

Garima Sharma[1], Chayanika Kala[2], Suman lata Verma[3]

[1]Assistant Professor Department of Pathology, Ganesh Shanker Vidyarthi Medical College, Kanpur, Uttar Pradesh, India.
[2]Associate Professor Department of Pathology, Ganesh Shanker Vidyarthi Medical College, Kanpur, Uttar Pradesh, India, India.
[3]Professor Department of Pathology, Ganesh Shanker Vidyarthi Medical College, Kanpur, Uttar Pradesh, India.

Received : 18/02/2023
Received in revised form : 24/03/2023
Accepted : 06/04/2023

Keywords:
CNS tumors, grading, diagnosis, histopathology, Immunohistochemistry.

Corresponding Author:
Dr. Garima Sharma
Email: drgarima321@gmail.com

DOI: 10.47009/jamp.2023.5.3.8

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (3); 33-36

Abstract

Background: CNS tumors are a heterogeneous group and differ in histogenesis with a broad spectrum of morphological features. Many tumors pose diagnostic challenges because tumors of varying histogenesis show divergent differentiation and overlap in morphological features. So, the application of immunohistochemical markers has become necessary for an exact diagnosis and grading. **Materials and methods:** This study was conducted retrospectively in the Department of Pathology, GSVM Medical College, Kanpur, from January 2020 to December 2022. Based on histopathological examination of Hematoxylin and Eosin stained sections, total of 106 brain tumors were diagnosed. Out of which, immunohistochemical markers were applied on 22 cases for accurate diagnosis and grading. **Results:** In adults, astrocytomas occurred most frequently in the study, followed by meningiomas, Ependymal tumors, Schwannoma, and Craniopharyngioma followed by metastatic deposits. Age and sex incidence of various tumors were studied. The tumors were graded as per the newly revised World Health Organization criteria. The results of an immunohistochemical study in 22 cases were analyzed. **Conclusion:** The present study shows the utility of histopathological examination with IHC play as a vital tool for diagnosis and grading in most tumors, and IHC plays an essential role in complex cases where diagnosis and grading are not possible only on a histological basis.

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

ISSN (O): 2687-5365; ISSN (P): 2753-6556

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-1-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 1: Frequency of brain tumors in our study

Brain tumors	No of tumors (n)	Percentage (%)
Astrocytic tumors	32	30.18
Meningioma	29	27.36
Ependymal tumor	17	16.03
Schwannoma	8	7.55
Craniopharyngioma	4	3.77
Oligodendroglial tumors	1	1.0
Oligoastrocytic tumors	1	1.0
Neuronal and mixed neuronal-glial tumors	2	1.88
Hemangioblastoma	2	1.88
Metastatic tumors	3	2.83
Others	3	2.83
TOTAL	**106**	**100**

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 as trocytoma 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 1:3, 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-L1 was done in 7 cases for grading and in 5 cases GFAP was also applied to confirm glial differentiation.

MIB-L1 in grade-1 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-L1 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

ISSN (O): 2687-5365; ISSN (P): 2753-6556

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 gliosarcoma. Literature shows that sarcomatous change occurs in approximately 2% of glioblastomas.[22,23] In one case of oligodendroglioma Olig2 was positive and MIB- LI was 20-25%. Glial protein may be focally present in oligodendroglioma due to the presence of mature reactive astrocytes. (David N Louis et al. 2007.[19] 2 cases of oligoastrocytoma were positive for GFAP, IDH1, Ki67(7-8%), and MIB-LI value of about 4%. GFAP is expressed in astroglial component and variably expressed by the oligodendroglial 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 4-5%. 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.

CONCLUSION

The present study showed that histopathological examination is a mainstay for the diagnosis in of 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.

REFERENCES

1. Pieter Wesseling Johan M. KrosJudith W.M. Jeuken. Diagnostic Histopathology, Volume 17, Issue 11, November 2011, Pages 486-494.
2. Antonio MP Omuro, Claudia C Leita, Karima Mokhtari, Jeans-yves Delattre; Pitfalls in the diagnosis of brain tumors; lancetneurol 2006,5;937-948.
3. Takei H, Bhattacarjee MB, Rivra A, Dancer Y, Powell SZ. New immunohistochemical marker in the evaluation of central nervous tumors. Archpathol lab med 2007 feb;131(2):234-41.
4. JA Ramos-vara. Technical aspects of immunohistochemistry. Vet pathol 2005;42;405-426.
5. Stacey E Mill, Darry L Carter (et al). Sternberg's diagnostic surgical pathology -5th edition; section III; page no 351.
6. David N Louis, Arie Perry, Pieter Wesseling, Daniel J Brat, Ian A Cree, Dominique Figarella-Branger, Cynthia Hawkins, H K Ng, Stefan M Pfister, Guido Reifenberger, Riccardo Soffietti, Andreas von Deimling, David W Ellison, The 2021 WHO Classification of Tumors of the Central Nervous System: a summary, Neuro-Oncology, Volume 23, Issue 8, August 2021, Pages 1231–1251.
7. Bhati Sanju et al JMSCR; Volume 06; Issue 03; page 1138-1146; March 2018
8. Sajeeb Mondal, Rajashree Pradhan, Subrata Pal, Biswajit Biswas, Arindam Banerjee, Debosmita Bhattacharyaya. Clinicopathological pattern of brain tumors: A 3-year study in a tertiary care hospital in India;2016,5(5):437-40.
9. Khaled R Zalata, Dina A El-Tantawy,Azza Abdel-Aziz, Abdel-Wahab M Ibraheim, Ahmed H Halaka, Hasan HGawish, Mohamed Safwat, Nabil Mansour, Mohammad Mansour, Abdelhadi Sheb. Frequency of central nervous system tumors in delta region, Egypt; Indian Journal of Pathology and Microbiology-2011;5 4(2):299- 306.
10. Venugopal Madhubhusi, RenukaInuganti Venkata, Sailabala Garikaparthi, Satya Varaprasad Kakarala, Seshadri Shekhar Duttaluru. Role of immunohistochemistry in diagnosis of brain tumours: A single institutional experience. Journal of DrNTR university of health sciences 2015;4(2) 103-111.
11. Bondy M, Ligon BL. Epidemiology and etiology of intracranial meningioma: a review. J Neurooncol 1996;29(3):197-205.
12. Yong-Hyun Chai, Shin Jung, Jung-kil Lee, In-Young Kim, Woo-youl Jang, Kyun-Sub Moon, Jae-Hyoo Kim, Kyung-Hwa Lee, Seul-kee Kim, Tae-Young Jung. Ependymoma: Prognostic Factors and Outcome analysis in a Retrospective Series of 33 Patients; Brain Tumor Res Treat.2017 oct;5(2):70-76.
13. Scheithauer BW, Louis ON, Hunter S, Woodruff JM, Antonescu CR: Schwannoma. In: Louis ON, Ohgaki H, Wiestler OD, Cavenee WK,ed. WHO classification of tumours of the central nervous system. Lyon: IARC; 2007. p. 152-5.
14. Niki Karavitaki, Simon cudlip, Christopher BT Adams, John AH Wass. Craniopharyngioma. Endocrine review. 2006,27(4):371-397.
15. Kenneth E. Livingston, Gilbert Horrax, Ernest Sachs JR. Metastatic brain tumors. Surgical clinics of North America,1948; 28(3):805-810.
16. McNeill KA: Epidemiology of brain tumors. Neural Clin. 2016, 34:981-998. 10.1016/j.ncl.2016.06.
17. Baxter DS, Orrego A, Rosenfeld JV, Mathiesen T: An audit of immunohistochemical marker patterns in meningioma. J Clin Neurosci. 2014, 21:421-426. 10.1016/j.jocn.2013.06.008.
18. Louis DN, Perry A, Reifenberger G, et al.: The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol. 2016, 131:803-820. 10.1007/s00401-016-1545-1.
19. 14. Louis DN, Ohgakih, Wiestler OD, Cavenee WK (Eds.). WHO classification of tumours of central nervous system. IARC; Lyon 2007.
20. Giannin C, Scheithauer BW, Burger PC, Cristensen MR, Wollan PC, SeboTJ. Cellular proliferation in pilocytic and

ISSN (O): 2687-5365; ISSN (P): 2753-6556

diffuse astrocytomas. J Neuropathol Exp Neurol, 1998;58 (1):4 6-53.
21. Johannessen AL, Torp SH. The clinical value of Ki-67/MIB-1 labeling index in human astrocytomas. Pathol Oncol Res. 2006; 12 (3):143–147.
22. Rosenblum MK. Central Nervous System. In: Rosai J, editor. Rosai and Ackerman's Surgical Pathology. 10th ed. St Louis: Mosby; 2011.P.2307-410.
23. Meis JM, Martz KL, Nelson JS. Mixed glioblastoma multiforme and sarcoma. Aclinicopathologic study of 26 radiation therapy oncology group cases. Cancer 1991;67:2342-9.
24. Rama Goyal, Satyavir Kumar Mathur, Sumiti Gupta, Rahul Goyal, Sanjay Kumar, AshimaBatra, Sonia Hasija, RajeevnSen. Immunohistochemical expression of glial fibrillary acidic protein and CAM5.2 in glial tumors and their role in differentiating glial tumors from metastatic tumors of central nervous system. J Neuroscience Rural Pract 2015;Oct-Dec;6(4):499-503.
25. Kunishio K, Shiraishi T, Mishima N, Satoh T, Matsumoto K, Nishimoto A, Taguchi K.Immunohistochemical study for choroid plexus papilloma and ependymomas. Neurol Med chir (Tokyo). 1991Dec,31(13):859-66.
26. Prayson RA.Clinicopathological study of 61 patient with Ependymoma including MIB-1 immunohistochemistry; Annals of diagnostic pathology 1999;volume 3 (1):11-18.
27. JMTheaker, KC Gatter, MM Esiri, KA Fleming. Epithelial membrane antigen and cytokeratine expression by meningiomas: An immunohistological study. J ClinPathol 1986:39:435-439.
28. Shih –Ming Jung and Tseng-tong kuo. Immunoreactivity of CD10 and inhibin alpha in differentiating hemangioblastoma of central nervous system from metastatic clear cell renal cell carcinoma. Modern pathology (2005)18,788-794.
29. Frank TS, TrojanowskiJQ, Robert SA, Brooks JJ. A detailed immunohist-ochemical analysis of cerebellar henagioblastoma: an undifferentiated mesenchymal tumor. Mod pathol 1989 Nov;2(6):638-51.
30. Posner JB. Neurologic complications of cancer. Philadelphia, F.A. Davis; 1995.
31. Wesseling P, von Deimling A, Aldape KD. Metastatic tumors of the CNS. In: Louis ON, Ohgaki H, Wiestler OD, Cavenee WK, editors. WHO classification of tumours of the central nervous system. Lyon: IARC; 2007. p. 248-51.

ISSN (O): 2687-5365; ISSN (P): 2753-6556