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Original Research Article

WHO Grading of Central Nervous System Tumours

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Abstract

Background: Central Nervous System tumours are diverse group of neoplasms affecting brain and spinal cord and are graded from WHO grade I to IV from less to more severity. The incidence of CNS tumours has increased in recent years in both developed and developing countries. ***Materials and Methods:*** A total of 100 CNS cases were studied and evaluated from July 2014 to July 2016 in the Department of Pathology, K S Hegde Charitable Hospital. Patient's data was retrieved from the records. The operated specimen was histopathologically evaluated and diagnosis of CNS tumour was made with WHO grading. The data collected was analysed using statistical tools by SPSS software version 21.0. ***Results:*** The study group consisted of 100 cases of CNS tumours. Intracranial tumours accounted for 84% and spinal cord tumours were 16%. The age distribution of the patients with CNS tumours ranged from 21 days to 78 years with mean age of 47.16 years. Males (59%) were commonly affected with male to female ratio of 1.44:1. Adults (93%) were more commonly affected than paediatric age group. In the study period from July 2014 to July 2016, a total of 7800 specimens were received in histopathology, among which 100 CNS tumours were encountered. Majority of them were in WHO grade I (66.67%). Local invasion and recurrence was seen in 22.2% (4 cases each). Metastasis (6 cases) (6%) was equally distributed between brain (50%) and spinal cord (50%).They were WHO Grade IV. The primary of the metastatic tumours to brain encountered were from breast, renal cell carcinoma and colon. Metastasis to spinal cord was from lung carcinoma and plasmacytoma. 20% were WHO Grade II and remaining 7.33% was WHO Grade III. ***Conclusion:*** The incidence of metastasis to CNS has been increasing in recent years. A general awareness of clinical manifestations of CNS tumours, along with usage of advanced radiological techniques lead to early precise diagnosis and proper management.

Keywords: CNS tumours, WHO grading, Histopathology.

INTRODUCTION

Central nervous system (CNS) tumours are quite heterogeneous; vary widely by site of origin, morphologic features, growth potential, and extent of invasion [1]. The incidence of CNS tumours has increased in recent years. CNS tumours accounts for 1–2% of tumors in body [2]. The incidence rates are higher in developed countries (5.1 per 100,000) than in developing countries (3 per 100,000) [3]. In India, incidence of brain tumours is 1.84% [4]. Majority of CNS tumours (80%) involve the brain and 20% involve the spinal cord. Males are more affected than females [5]. In adults age group affected is 40-50 years which usually occurs in the cerebral hemispheres [6-8]. CNS tumours account for 20% of all childhood cancers, of which 70% arise in the posterior fossa.

The first edition of the World Health Organization Classification of Central Nervous System tumours was first edited by Zulch and was published in 1979.The 2007 (4th edition) WHO classification of tumours of the central nervous system emphasizes on tumours of the central nervous system which includes tumours of cranial and paraspinal nerves [10].

The 2016 World Health Organization classification of tumors of the CNS uses molecular parameters in addition to histology to define many tumor entities. They present major restructuring of the diffuse gliomas, medulloblastomas and other embryonal tumors and incorporates new entities that are defined by both histology and molecular features, including glioblastoma, IDH-wild type and glioblastoma, IDH-mutant; diffuse midline glioma, H3K27M– mutant; RELA fusion–positive ependymoma; medulloblastoma,

WNT-activated and medulloblastoma, SHH- activated and embryonal tumour with multilayered rosettes,C19 MC-altered. The 2016 edition has added newly recognized neoplasms and has deleted some entities, variants and patterns that no longer have diagnostic and/or biological relevance.

Major restructuring of diffuse gliomas, with incorporation of genetically defined entities, Major restructuring of medulloblastomas, with incorporation of genetically defined entities, Major restructuring of other embryonal tumors, with incorporation of genetically defined entities and removal of the term "primitive neuroectodermal tumor", Incorporation of a genetically defined ependymoma variant, Novel approach distinguishing pediatric look-alikes, including designation of novel, genetically defined entity, Addition of newly recognized entities, variants and patterns IDH-wildtype and IDH-mutant glioblastoma (entities) Diffuse midline glioma, H3 K27M–mutant (entity), Embryonal tumour with multilayered rosettes, C19MC-altered (entity), Ependymoma, RELA fusion–positive (entity) Diffuse leptomeningeal glioneuronal tumor (entity) Anaplastic PXA (entity), Epithelioid glioblastoma (variant), Glioblastoma with primitive neuronal component (pattern) Multinodular and vacuolated pattern of ganglion cell tumor (pattern), Deletion of former entities, variants and terms, Gliomatosis cerebri, Protoplasmic and fibrillary astrocytoma variants Cellular ependymoma variant,"Primitive neuroectodermal tumour" terminology, Addition of brain invasion as a criterion for atypical meningioma, Restructuring of solitary fibrous tumor and hemangiopericytoma, (SFT/HPC) as one entity and adapting a grading system to accommodate this change, Expansion and clarification of entities included in nerve sheath tumors, with addition of hybrid nerve sheath tumors and separation of melanotic schwannoma from other schwannomas, Expansion of entities included in hematopoietic/lymphoid tumors of the CNS (lymphomas and histiocytic tumors).

WHO GRADING OF CNS TUMORS

WHO classification of tumors includes grading CNS tumours into grade I, II, III, IV. CNS tumours with WHO grade I includes lesions with low proliferative potential and the possibility of cure following surgical resection alone. Neoplasms with WHO grade II are usually infiltrative in nature and low-level proliferative activity which often recur. Few WHO II tumours may progress to higher grades of malignancy. CNS tumours with WHO grade III include lesions with histological evidence of malignancy, which includes nuclear atypia and high mitotic activity. Most of patients with grade III tumours will require adjuvant radiation and/or chemotherapy. A CNS tumour with WHO grade IV is histologically malignant, high mitotic activity, neoplasms associated with necrosis and is associated with rapid pre- and postoperative disease evolution and fatal outcome. Grade IV neoplasms infiltrate surrounding tissue and may cause craniospinal dissemination.

METHODOLOGY (MATERIAL AND METHODS)

Source of Data

Specimens of central nervous system tumours received at Department of Pathology, K S Hegde Charitable Hospital during the period July 2014 to July 2016.

Study Design

A descriptive study.

Study Setting

K S Hegde Charitable Hospital during the period July 2014 to July 2016.

Sample Size

A two year time bound study with a minimum of 50 cases.

Inclusion Criteria

All operated cases of central nervous system tumours specimens which were sent to the department of Pathology, K S Hegde Medical Academy, Mangalore.

Exclusion Criteria

- Inadequate biopsy.
- Bony lesions of skull.
- Non - neoplastic lesions of central nervous system.

Method of Collection of Data

Patient's data regarding clinical history, examination, investigations and diagnosis were retrieved from hospital records. Patients with CNS and neurological complaints were clinically examined and radiologically evaluated with CT/MRI scan. Those patients with radiological evidence of CNS tumours were operated by neurosurgeons, after receiving an informed consent from the patient in their local language. The excised specimens were fixed in formalin (10% solution of formaldehyde in buffered alcohol) and sent to the department of pathology for histopathological examination and final diagnosis.

Procedure

Formalin fixed specimens were processed. Paraffin blocks were prepared from which sections of 3-6 micrometer were mounted on a clean glass slide and stained with hematoxylin and eosin (H&E) stain. Special stains and immunohistochemistry were done wherever required.

Outcome Measures

Based on the histological diagnosis, classification and grading of tumour, patient treatment stratification and prognosis can be planned.

Statistical Analysis

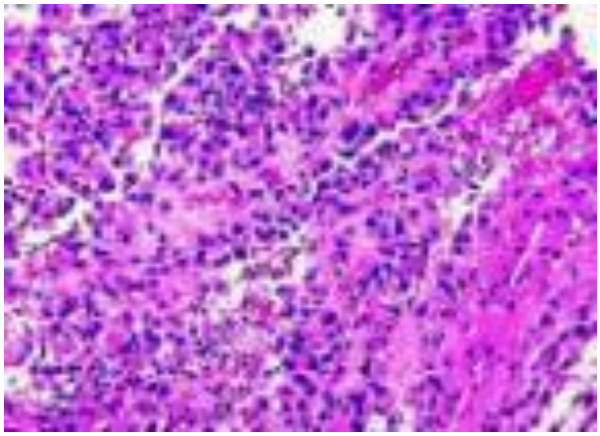
Data obtained will be analysed using SPSS software version 21.0.

RESULTS

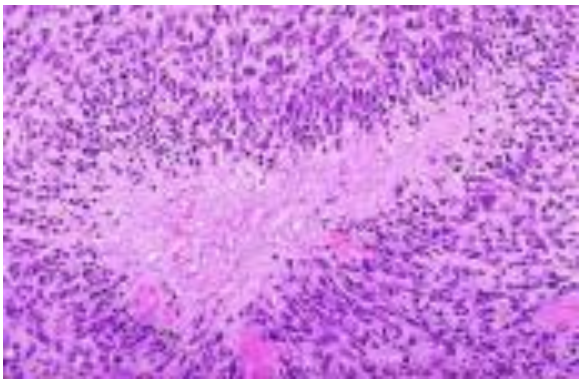
The study group consisted of 100 cases of CNS tumours. Intracranial tumours accounted for 84% and spinal cord tumours were 16%. The age distribution of the patients with CNS tumours ranged from 21 days to 78 years with mean age of 47.16 years. Males (59%) were commonly affected with male to female ratio of 1.44:1. Adults (93%) were more commonly affected than paediatric age group. In the study period from July 2014 to July 2016, a total of 7800 specimens were received in histopathology, among which 100 CNS tumours were encountered.

- Majority of them were in WHO grade I (66.67%). Local invasion and recurrence was seen in 22.2% (4 cases each).
- Metastasis (6 cases) (6%) was equally distributed between brain (50%) and spinal cord (50%).They were WHO Grade IV.
- The primary of the metastatic tumours to brain encountered were from breast, renal cell carcinoma and colon. Metastasis to spinal cord was from lung carcinoma and plasmacytoma.
- 20% were WHO Grade II and remaining 7.33% was WHO Grade III.

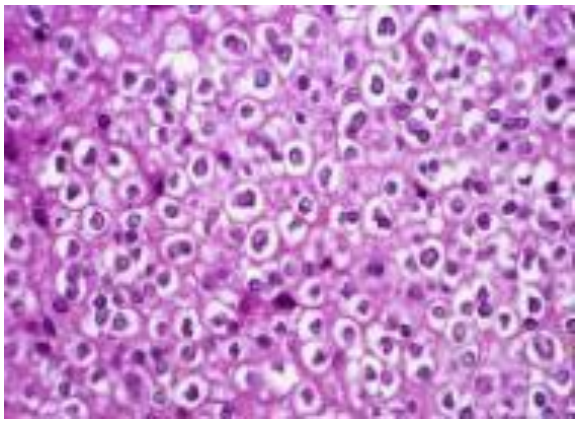
Colour plate: Gross of papillary meningioma showing grey white lesion and attached nerve



Colour plate: Microscopy of papillary meningioma with perivascular papillary pattern (H&EX100)



Colour plate: Microscopy of glioblastoma showing geographical necrosis with palisading tumour cells (H&EX 100)



Colour plate: Microscopy of oligodendroglioma'fried egg pattern' (H&EX100)

DISCUSSION

CNS neoplasms represent a heterogenous population of tumours that has high morbidity and mortality irrespective of their histological grading. Histopathologic evaluation was done in 100 patients with CNS tumours in this study.

Clinical Features of CNS Tumours

Clinical features of patients with CNS tumours included headache (42%) as the common symptom, followed by, difficulty in movement (31%), visual disturbances (18%), giddiness (12%), sensory loss (10%), seizures (9%), mental alterations (9%), gait disturbances (8%), loss of memory(6%), sphincter disturbances(3%) which is in comparision with studies done by Kushal *et al.,* (2015). Most paediatric tumours are sporadic and some have complicate multisystem congenital abnormalities like Turcots syndrome and Gorlin syndrome. One case of medulloblastoma had associated cleft lip and palate in the present study Spinal cord tumour patients presented with complaints of difficulty in movement (93.75%) as common symptom followed by sphincter disturbances and sensory loss (12.5% each) and gait disturbances (6.25%). This is in comparision with study done by Tamkeen *et al.,* (2012).

Histopathological Spectrum of CNS Tumours

Histopathologically, neuroepithelial tumours formed the major part of CNS tumours in present study which accounted for 41%. Other tumours encountered were nerve sheath tumour (19%), meningioma (18%), metastatic tumours (6%), pituitary adenoma (6%), lymphoma (4%), craniopharyngioma (3%), and hemangioblastoma (3%). These are in comparision with the studies by Deshpande *et al.,* (2010). However, Meningioma is the 2nd most common CNS tumour in the studies done by Deshpande *et al.,* (2010). Incidence of pituitary tumours (6%) in our study is at par with American publications (6.3%). All of the pituitary tumours were non-functional tumours. Majority of CNS tumours are primary tumours and accounted to 92% and remaining 8% are metastatic tumours. This is in comparision with studies done by Zalata *et al.,* (2011) and Intisar *et al.,* (2008). Brain metastasis is found in 20% to 40% of cancer patients and occur commonly in the cerebral hemispheres (80%), followed by cerebellum (15%) and brain stem (5%). Most of them are multiple metastases (70%) than solitary metastasis. Brain metastasis is commonly from lung cancer (50%), followed by breast cancer (20%), unkown primary cancer (15%), melanoma (10%) and colon cancer (5%).

Metastatic tumours to CNS have been increased in recent years as per the worldwide studies. In present study, Metastasis (6 cases) was equally distributed between brain (50%) and spinal cord (50%). (Table 26) Metastatic tumours encountered in brain were 3 cases of poorly differentiated carcinoma, the primary tumour of which was from infiltrating ductal carcinoma breast, renal cell carcinoma and adenocarcinoma colon respectively. One case of metastatic adenocarcinoma from lung and 2 cases of plasmacytoma were seen in the s Spinal cord. The common primary tumour site of metastasis to CNS in the studies done by Yeon *et al.,* (2002), Intisar *et al.,* (2008) Jesalpura *et al.,* (2015) are from lung, breast, gastrointestinal tract, kidney, liver and melanoma.

The prognosis of CNS tumours varies depending upon the location, histological grade local extension and metastasis. Most of the higher grade neuroepithelial tumours have bad prognosis. Embryonal neuroepithelial tumours respond well to chemoradiation. Meningioma, nerve sheath tumours have good prognosis following excision. Recurrent and metastatic tumours have bad prognosis.

CONCLUSION

The incidence of CNS tumors has been increasing in recent years worldwide. They have a high morbidity and mortality. CNS tumours affect predominantly intracranial location than spinal cord. Multilobe of cerebrum and frontal lobe are commonly affected. Majority of CNS tumours affect elderly population, predominantly affecting males than females. They usually present with headache and difficulty in movement as the commonest manifestation. Neuroepithelial tumours are the commonest CNS tumours followed by nerve sheath tumours and meningiomas. In the paediatric age group, embryonal neuroepithelial tumours are most common. Most of the neuroepithelial tumours will be usually of higher grade due to late onset of clinical manifestations. Nerve sheath tumours are the common spinal cord tumours. The incidence of metastasis to CNS has been increasing in recent years. Therefore, thorough knowledge of clinical presentations and radiological investigations like Computed Tomography and Magnetic Resonance Imaging helps in early precise diagnosis and localizing the tumour. Histopathology is the gold standard in diagnosing and grading of CNS tumours. Further it can be enhanced by immunohistochemistry, molecular and genetic studies for early precise diagnosis, proper management and prognosis.

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