Histomorphological spectrum of lesions of the central nervous system including the brain, spinal cord and vertebrae

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ABSTRACT

INTRODUCTION: Lesions of the central nervous system including the brain, spinal cord and vertebrae cause profound morbidity and mortality as they occur within the tight confines of the rigid cranium and vertebral column. They constitute both primary tumors and secondary tumors spread from tumors outside the central nervous system and also many infective and parasitic infections that may simulate space occupying lesions. This retrospective study analyzed the neurosurgical specimens that were sent to us by the only National Neurosurgical Referral Centre located in Bir Hospital in five years starting from January 2007 to December 2012. This study will give a broad prospective of the lesions and tumors of the central nervous system in our country during the studied period.

METHODS: All the slides of the central nervous system, spinal cord and vertebrae from the Department of Pathology, Bir Hospital, Kathmandu, Nepal of five years between Jan 2007- Jan 2012 were retrieved and evaluated. Demographic data including age, sex and clinical presentation were retrieved from the histopathology record.

RESULT: A retrospective evaluation of slides of 357 representative biopsy samples of five years duration were conducted and it constituted 2.23% of the total specimens received for histopathology. Out of these, 338 were lesions, twelve cases were of normal glial tissue and seven cases were inadequate. In spite of suspicion of neoplasm in the brain it is not always possible to get the tumor tissue due to deep site of the lesion and poor general condition of the patient which allows only burr holing and minimal low yield of tmour mass. A slight male predominance was observed with the male to female ratio of 1.31:1. Neoplastic lesions comprised the majority of cases (82.0%) followed by non-neoplastic lesions (13.60%) and inflammatory lesions (4.43%). WHO grade I neoplasm comprised 127 cases (45.84%) followed by grade IV neoplasms 67 cases (24.18%), 48 cases (17.32%) of grade II, 13 cases (4.69%) of grade III neoplasms and 24 cases (8.66%) of all the neoplastic lesions comprised of neoplasms which were not categorized in any of the grades in the WHO classification. Out of the neoplasias, low-grade neoplasia and high-grade neoplasia comprised 42.58% and 20.60% respectively. Low-grade neoplasms occurred in the 2nd to 4th decades of life and high-grade neoplasms occurred in the 4th to 6th decades of life.

CONCLUSION: The lesions of the central nervous system including the brain, spine and vertebrae showed that neoplastic lesions comprised the majority of cases followed by non-neoplastic lesions and inflammatory lesions.

KEY WORDS: Central nervous system, inflammatory, neoplasm, non-neoplasm.

INTRODUCTION

The lesions from different parts of the central nervous system including the brain, spinal cord and vertebrae are common and specimens from these lesions were sent to the Pathology Department of Bir Hospital to assert their nature. Once the labeled sample reached us, they were fixed in 10% formalin processed and Haematoxylin and Eosin stained. These slides are diagnosed by senior consultant pathologists and interpretated in correlation with patient's age, clinical presentation and radiological findings. Neoplastic lesions are graded according to WHO criteria and then reports dispatched. However, the need for an expert neuropathologist is becoming crucial in reviewing the cases before commencing on treatment.1,2,3

Histopathological grading predicts the biological behavior of a neoplasm in clinical setting and it also influence choice of therapy. Different grading systems are used like Broder's, Kernohan and Sayre, St' Anne/ Mayo or Daumass-Duport system depending on nuclear atypia, mitoses, endothelial proliferation and necrosis.

Nowadays, WHO classification of tumors of the central nervous system have gained popularity and neoplastic

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lesions are graded from I to IV and this forms the corner stone for subsequent planning, management and treatment of these lesions.

Grade I lesions generally presents include tumors with low proliferative potential and possibility of cure following surgical resection alone. Lesions designated grade II are generally infiltrative in nature and, despite low level of proliferative activity, often recur. Some grade II tumors tend to progress to higher grades of malignancy, for example, low-grade diffuse astrocytoma and glioblastoma. The designation grade III is generally reserved for lesions with histological evidence of malignancy, including nuclear atypia and brisk mitotic activity. In most settings, patients with grade III tumors receive adjuvant radiation and/or chemotherapy. The designation grade IV is assigned to cytologically malignant, mitotically active, necrosis prone neoplasms often associated with rapid pre and post operative disease evolution and a fatal outcome.4

Inflammatory lesions could be either tuberculomas, brain abscess or chronic inflammatory process. Non-neoplastic lesions could be either congenital or cystic in nature.

Ependymal cysts are benign and lined by ciliated ependymal cells.5 These are cysts of the lateral ventricle or juxtaventricular region of the temporoparietal region and frontal lobe and infrequently in the subarachnoid spaces, brainstem, and cerebellum.

Arachnoid cysts comprise 1% of all intracranial masses and are benign, congenital, intra-arachnoidal space-occupying lesions that are filled with clear cerebrospinal fluid. The incidence is somewhat higher in men. Fifty to 60% are found in the middle cranial fossa, anterior to the temporal lobes.6 Microscopically, the cyst walls are made of a vascular collagenous membrane lined by flattened arachnoid cells.

Colloid cysts account for 0.2-2.0% of all brain lesions rare, benign mucin-containing cysts.7 These originate when ectopic endodermal elements that migrate into the velum interpositum during embryogenesis.

Dermoid and epidermoid cysts are dysembryogenic tumors representing 1% of all intracranial tumors. They are characterized by slow growth, localization to the middle in relation to the basal cisterns and their benign course.8 The epidermoid cysts, by definition is devoid of cutaneous-type adnexal structures and filled by friable, often laminated keratinous debris that radiates a pearly sheen as viewed through the thin, fibrous lesional capsule. Dermoid cysts are endowed with skin appendages, including pilosebaceous units, eccrine and occasionally apocrine glands, as well as mural adipose tissue foreign to the epidermoid type.9

Neuroenteric cysts are congenital, benign, malformative endodermal lesions in the central nervous system. They are approximately three times as common in the spine, compared with the brain.10

The notochord and foregut fail to separate, causing primitive endodermal cells to be incorporated into the notochord. These displace alimentary cells ultimately give rise to the cyst.

Cysticercosis is the most common, most widely disseminated parasitic infection in the world. Neurocysticercosis occurs in 60% of all cases of systemic cysticercosis.11

Brain involvement with hydatid disease occurs in 1-2% of all Echinococcus granulosus infections.12 Cerebral hydatid cysts are usually supratentorial, whereas infratentorial lesions are quite rare.

METHOD

This retrospective cross-section study was done on slides retrieved from the Department of Pathology, Bir Hospital, of a total duration of 5 years between Jan 2007 to Jan 2012. Demographic data including age, sex and clinical presentation were obtained from the histopathology records.

All patients diagnosed with the lesions of brain, spinal cord and vertebrae were included. The criteria for selection of cases were mainly based on history and clinical examination. Detailed history, clinical examination, necessary radiological findings and other laboratory parameters were also documented. Biopsies were sent for histopathological examination to confirm the diagnoses.

The biopsy samples were received in 10% formalin, routinely processed for histopathological examination and stained by Haematoxylin and Eosin (H&E) and examined by junior pathologists followed by senior consultant pathologists.

RESULTS

Table: 1 Incidence of inflammatory, non-neoplastic and neoplastic lesions

Type of mass	Incidence	Percentage	Male	Female
Inflammatory	15	4.43	10	5
Non-neoplastic	48	13.60	34	12
Neoplastic	277	82.00	148	129
Total	338		192	146

Table :2 Distribution of lesions according to age

Age (Years)	Non-neoplastic	Low-grade neoplasms	High-grade neoplasms	Neoplasms not graded by WHO
<10	21	18	10	1
11-20	9	31	11	4
21-30	8	34	9	5
31-40	3	36	7	5
41-50	3	24	12	5
51-60	2	15	12	4
>60	2	17	19	
Total	48	175	80	24

Table:3 Non-neoplastic lesions

Lesions	Incidence	Percentage	Male	Female
Vascular lesions	7	14.58	5	2
Subdural hematoma	7	14.58	5	2
Cysts	16	33.33	14	2
Meningoceles	13	37.50	8	5
Encephaloceles	3	6.25	2	1
Meningomyelocele	2	4.16	2	
Total	48	100	36	12

Table: 4 Cystic lesions

Nature of cysts	Incidence	Percentage	Male	Female
Arachnoid	5	33.33	4	1
Epidermoid	2	13.33	2	
Dermoid	2	13.33	2	
Colloid	1	6.25	1	
Hydatid	2	13.33	2	
Neurocysticercosis	3	18.75	2	1
Endodermal	1	6.66	1	
Total	**16**	**100**	**14**	**2**

Table:5 Incidence of neoplastic lesions according to gender.

Grade	Male	Female	Total
Low-grade (I and II)	87	86	173
High-grade (III and IV)	45	35	80
Miscellaneous	16	8	24
Total	148	129	277

Table: 6 Grade I neoplastic lesions according to WHO.

Grade I	Incidence	Percentage	Male	Female
Meningioma	46	37	10 (18.51%)	36 (53.73%)
Schwannoma	35	28	23 (42.60%)	12 (17.91%)
Pilocytic astrocytoma	22	18.0	9 (16.6%)	13 (19.40%)
Subependymal giant cell astrocytoma	2	1.6	1 (1.85%)	1 (1.50%)
Hemangioblastoma	2	1.6	1 (1.85%)	1 (1.50%)
Angiocentric glioma	1	0.80		1 (1.50%)
Pleomorphic xanthoastrocytoma	2	1.60	1(1.85%)	1 (1.50%)
Subependymoma	1	0.80		1 (1.50%)
Myxopapillary ependymoma	2	1.65	2 (3.70%)	
Craniopharyngioma	12	10	9 (16.66%)	3 (4.47%)
Choroid plexus papilloma	2	1.65	2 (3.70%)	
Total	**127**	**100**	**58**	**69**

Table:7 Grade II neoplastic lesions according to WHO

Grade II	Incidence	Percentage	Male	Female
Meningioma	3	6.0	2	1
Diffuse astrocytoma	12	25.0	8	4
Oligodendroglioma	16	33.0	11	5
Oligoastrocytoma	4	8.0	3	1
Ependymoma	10	21.0	5	5
Hemangiopericytoma	1	2.0	1	
Central neurocytoma	2	4.0	1	1
Total	**48**	**100**	**31**	**17**

Table: 8 Grade III neoplastic lesions according to WHO

Grade III	Incidence	Percentage	ale	Female
Meningioma	5	38.46	2	3
Anaplastic astrocytoma	4	31.0	2	2
Anaplastic oligodendroglioma	2	15.38	1	1
Anaplastic oligoastrocytoma	2	15.38	2	
Choroid plexus carcinoma	1	7.69	1	
Total	**13**	**100**	**7**	**6**

Table: 9 Grade IV neoplastic lesions according to WH

Grade IV	Incidence	Percentage	Male	Female
Glioblastoma	27	40.29	11	16
Gliosarcoma	1	1.49	1	
Medulloblastoma	15	22.38	9	6
Supratentorial PNET	2	3.0	2	
Malignant Lymphoma	2	3.0	2	
Metastasis	20	30.0	15	5
Total	**67**		**40**	**27**

A total of 357 slides from representative biopsy samples of five years duration were examined, which constituted 2.23% of the total specimens received for histopathological examination during that period. A slight male predominance was observed with the male to female ratio 1.31:1. Neoplastic lesions comprised the majority of cases (82.0%) followed by non-neoplastic lesions (13.60%) (Table 1).

Non-neoplastic lesions were most common in the age group less than ten years old (43.75%). All cases of low-grade, high-grade and neoplasm that are not graded by WHO were most common in age group 21-40 years of age (Table 2).

The vascular lesions comprised seven cases including four cases of arteriovenous malformations and three cases of cavernous hemangioma.

The spinal cord and vertebral lesions, the neural tube defect cases constituted meningoceles, myelomeningoceles and encephaloceles which constituted thirteen cases (37.50%), two cases (4.16%) and three cases (6.25%) respectively. Cystic lesions comprised 16 cases i.e 33.33% (Table 3).

Arachnoid cysts comprised 5 cases (33.33%) of all cystic structures followed by 3 cases (18.75%) of neurocysticercosis. Out of 15 inflammatory cases, there was one case of tuberculoma and one case of brain abscess and remaining cases showed just chronic inflammation.

Of all the neoplastic lesions, low-grade comprised 175 cases (63.17%), followed by 80 cases (28.80%) of high-grade neoplasm and 24 cases (8.66%) were neoplasms not graded by WHO. The male to female ratio observed was 1.14:1. Grade I neoplasm comprised 127 cases (45.84%) followed by grade IV neoplasms of 67 cases (24.18%), 48 cases (17.32%) of grade III, 13 cases (4.69%) of grade III neoplasms and miscellaneous neoplasm comprised 24 cases (8.66%). Grade I meningiomas comprised 46 cases (38%) with female predominance. Oligodendroglioma outnumbered all cases of grade II neoplasm and comprised 16 cases (33.33%) followed by 12 cases (25%) of diffuse astrocytoma of grade II neoplasm. Out of the grade III neoplasm, grade III meningiomas comprised 5 cases (38.46%) followed by 4 cases (31.00 %) of anaplastic astrocytoma. Of grade IV neoplasms, glioblastoma multiforme comprised 27 cases (40.29%), followed by 20 cases (30.0%) of metastases and 15 cases (22.35%) medulloblastoma.

DISCUSSION

In our restrospective evaluation of specimens from Neurosurgery Department of Bir Hospital, neoplasias comprised 82.00%, followed by non-inflammatory 13.60% and inflammatory 4.43%. Out of all the neoplasias, low-grade neoplasia and high-grade neoplasia comprised 42.58% and 20.60% respectively. Male : female ratio being 1.31:1.

Our observation showed 2nd to 4th decades of life are the most vulnerable period for development of low grade neoplasm whereas high-grade neoplasia were common in 4th to 6th decades of life.

Most common neoplasias in this observation were meningioma (19.49%), schwannoma (12.63%), glioblastoma (9.74%), pilocytic astrocytoma (7.94%), metastases (7.22%) and oligodendroglioma. Similar type of observation was also made by Jazayeri SB et al, in Iran where male:female ratio was 1.48:1 and common histopathologies were meningioma, astrocytoma, glioblastoma and ependymoma.13

Similar type of male to female distribution of neoplasm

and histopathologically confirmed types were also seen.14 Our study also showed that the following tumors, oligodendroglioma, diffuse astrocytoma, craniopharyngioma, pituitary adenoma, schwannoma, medulloblastoma and metastases had significant male preponderance. Similar type of male dominance pattern was observed by Katchy KC et al.15

Malignant tumors of the brain are lethal and directly destroy brain tissue, raise intracranial pressure and cause secondary changes. Even benign tumors can be lethal because they impinge on the limited space comprising the skull and may press the vital centers with fatal consequences.

Meningioma represent the most common primary brain tumor and comprise from grade one to grade three of World Health Organization (WHO) grades, the most frequent being WHO grade one (90%). In our observation, grade I meningioma comprised highest i.e. 37% of all WHO grade I neoplasm, followed by grade III meningioma which comprised 38.36% of all grade III meningioma and grade II which comprised 6% of all grade II neoplasms. Mostofi also found similar male to female ratio in his study.16 He found meningioma comprised 38% of total cases of grade I WHO neoplasm. Grade one meningioma variants comprised meningothelial twenty five, transitional nine, psammomatous five, fibrous three, microcystic two, metaplastic and lymphocytic one each case. Out of all WHO grade II neoplasias, grade II meningioma comprised variants like atypical meningioma two and chordoid one.

Grade III meningioma comprised following variants like papillary one, rhabdoid two and anaplastic two cases.

Out of 35 cases of Schwannoma, ancient schwannoma and infected schwannoma comprised one case each. In this study, schwannoma comprised 96.15% of the cerebellopontine angle tumours whereas Hassepass F et al found cerebellopontine angle schwannoma comprised 80% of the tumours of the cerebellopontine angle.17 Our observation showed right sided cerebellopontine angle schwannoma comprised fifteen, left sided comprised ten and intradural and extramedullary comprised ten cases. Out 10 cases of intradural exramedullary schwannoma, cervical (C3-C4) lesion three, C7 lesion two, thoracic (D10-11) two and lumbar (L4-5) three cases.

Craniopharyngioma comprised 10 % of all grade I WHO neoplasm and only 4.33% of all neoplastic lesion in this study. All cases belonging to an adamantinomatous type. Similar morphological type prevailed in the study done by Gupta DK et al where an adamantinous pattern was seen in 81.4% of cases and a papillary pattern was seen in 18.6% in 243 craniopharyngioma that were reviewed.18

Hemangioblastoma are WHO grade I lesions that comprise 1-2 % of primary nervous system tumors. They commonly occur in young adults with a peak incidence corresponding to the fourth decade of life. Although most hemangioblastoma are sporadic, they are associated with the autosomal dominant von Hippel-Lindau disease in approximately 25 % of cases. In our observation also, it was sporadic ones and it comprised two cases only and were seen in cerebellum. The average age at presentation in our case was 40 years. In the study done by Dwarakanath S et al the average age was 34.5 years similar to the age distribution in our cases, and their tumor was also located predominantly in cerebellar hemisphere(60%) followed by vermian (28%) and brainstem regions (12%).19 Similar average age and location was found by Galabert G in study of twenty-four patients.20

Pilocytic astrocytoma comprised twenty cases (44%) of all astrocytoma. Similar observation was also made by El-Gaidi MA where pilocytic astrocytoma constituted 55% of all astrocytoma and 19.3% of all brain tumors, only slightly ahead of medulloblastomas.21

Diffuse astrocytoma comprised twelve cases out of which one case was gemistocytic astrocytoma, rest being fibrillary type. Of the ependymoma cases, two cases were cellular ependymoma rest being conventional ependymoma.

We observed sixteen cases of oligodendroglioma and it constituted 17% of all the glioma in our study. Our observation was slightly less than that seen by authors Coons SW, Johnson PC, Scheithauer BW, Yates AJ, Pearl DK where oligodendrogliomas constituted 25% of all the gliomas.2

Choroid plexus tumors are rare intraventricular tumors and they represent 2-4% of brain tumors in children. In this study of 277 neoplastic lesions, choroid plexus tumors account 1.08% of brain tumors. Due-Tonnessen B, Helseth E, Skullerud K, Lundar T in their retrospective study observed consecutive thirteen cases of choroid plexus papillomas and three carcinomas and male predominant pattern.22 In our case two cases were of choroid plexus papilloma and one case was a choroid

plexus carcinoma. All three cases were males and in the second decade of life.

WHO grade IV lesion were seen predominantly in 5-6th decade of life with male to female ratio 1.48:1. Tanaka S, Meyer FB, Buckner JC, Uhm JH, Yan ES, Parney IF also found similar age predilection for high grade gliomas.23 In this present study, high-grade neoplasm i.e. WHO grade IV constituted 24.18% of all the neoplastic lesions. Glioblastoma multiforme comprised 40.29%, followed by 25.37% of metastases and 22.38% of medulloblastoma.

Primary central nervous system lymphoma comprised approximately 0.7% of all primary brain tumors in our retrospective study. Doucet S, Kumthekar P, Raizer J in their study found primary central nervous system lymphoma 5%. This figure is higher as compared to us may be due to variation in sample size and geographic location.24

According to WHO, metastatic tumors are the most common central nervous system neoplasm and therefore continue to be major cause for mortality and morbidity. Macroscopic features and corresponding radiological findings can be diagnostic in majority of the cases, however, microscopic evaluation would be necessary when the differential diagnosis includes a primary CNS tumor, unknown primary tumor site, and when the resection of the tumor is either considered therapeutic or palliative. The first step in the diagnosis of a metastatic brain lesion is to exclude a primary CNS tumor, followed by verification or identification of the primary tumor and the site. When morphological features are not enough to establish a definitive diagnosis, additional studies including immunohistochemical stains are applied.25

In this retrospective study of five years duration, we found twenty cases of brain metastases. These comprised two cases of papillary carcinoma and metastatic urothelial carcinoma each, five cases of metastatic poorly differentiated adenocarcinoma, three cases of metastatic carcinoma, three cases of metastatic small cell carcinoma. Two cases were also designated as metastatic lesions but the exact morphogenesis of these tumors could not be ascertained and immunohistochemistry was recommended to clinch the diagnoses. There were three cases of secondary lymphomas. Although the metastases of papillary carcinoma of thyroid to the brain is rare, there was a case with unequivocal metastasis in the brain and another case with papillary configuration was suggested to arise from either the thyroid, ovary or urinary bladder and needed further investigations to assert the etiopathogenesis. Similar observation was found by Tahmasebi FC, Farmer P, Powell SZ, Aldape KD, Fuller GN, Patel S, et al.26

Both the primary and secondary lymphoma cases were of non-Hodgkin's lymphoma type. Two cases of primary malignant lymphoma were of diffuse mixed large and small cell type i.e. Intermediate grade, according to International Formulation for major classification schemes of non-Hodgkin's lymphoma.

Similar morphology was appreciated in three cases (1.08%) of metastases of NHL i.e. diffuse mixed large and small cell lymphoma. Microscopic examination of these cases showed mixed population of atypical small monotonous cells and large cells arranged in diffuse sheets and even angiocentricity and crushing artifacts in some areas. The areas showing normal looking glial tissue with evidence of infiltration by tumors cells were also seen in the sections examined.

A large group of tumors constituting 7.10% of all the specimens submitted and 8.66% of all the neoplastic lesions comprising of pituitary adenoma, germinoma, eosinophilic granuloma were seen. These tumors are not categorized in any of the groups of WHO grading system. These comprised pituitary adenoma twenty cases, germinoma and eosinophilic granuloma comprised two cases each. Both the pituitary adenoma and germinoma had male dominance and were seen in adults. Eosinophlic granuloma were located extracranially in the skull with no intracranial attachment.

CONCLUSION:

The lesions of the central nervous system including the brain, spinal cord and vertebrae could be neoplastic, non-neoplastic or inflammatory conditions. The neoplastic lesions should be distinguished from non-neoplastic and reactive processes and it is of utmost importance to distinguish the various primaries from secondaries in the brain. Duration of illness, symptoms and signs with imaging modalities definitely help to make a presumptive diagnosis but still sine-qua-non will be histopathological examination. Only after the tentative histopathologic diagnoses, correct and timely interventions can be done for the alleviation of the patients' conditions. From this study we came to a conclusion that neoplasia constituted the predominant lesions in our centre so proper and timely evaluation

of the patient's symptoms and signs and thorough histopathological examination followed by definite treatment management will ameliorate his conditions and improve his survival status as well.

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