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THE HISTOPATHOLOGICAL STUDY AND EXPRESSION OF IMMUNOHISTOCHEMICAL MARKERS IN CENTRAL NERVOUS SYSTEM TUMOURS – AN INSTITUTIONAL STUDY

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ABSTRACT

INTRODUCTION: Central Nervous System Tumours are not frequent tumours but still the primary CNS tumours continue to be among the top ten causes of cancer related deaths in the world .The GMC ,Kota being the biggest draining hospital in the Kota region, with a well known neurodisorder service, but lacking an accurate data on the CNS tumour epidemiology ,mandates the need for this study.

AIM: To provide the histopathological spectrum of CNS tumours in the Institute with respect to age , sex & clinical presentation and utility of IHC.

MATERIAL AND METHODS: Material comprised of all the CNS tumours.The 3 year study comprising a total of 200 specimens formed the basis of this study. The histological and the Immunohistochemistry findings were correlated.

RESULTS: Primary CNS tumours accounted for the majority of the CNS tumours comprising 96.5% of the cases, rest 3.5% being metastatic Glial tumours comprised the largest category.Among the glial tumours,astrocytomas were the commonest (31.5% of all CNS tumours), of which 36.5% were GBM, followed by meningiomas (18.5%), peripheral nerve sheath tumours, ependymal tumours, embryonal tumours, craniopharyngiomas, Mixed tumours, gliosarcomas, choroid plexus tumours, Oligodendroglioma and hemangioblastomas.Metastatic tumours, that constituted 3.5% of all the CNS tumours were most common in the sixth and seventh decades of life. Immunohistochemistry played an instrumental role in the diagnosis and evaluation of certain lesions.

CONCLUSION: This study has highlighted the relative frequency of different intracranial space occupying lesions in the region.

KEYWORDS : Tumours,intracranial,histopathology,astrocytomas, Metastasis

INTRODUCTION

The term 'Central Nervous System Tumours' refers to a mixed group of neoplasms, originating from intracranial and intraspinal tissues, including the meninges and Schwann cells .These range from benign to malignant and show varying degrees of aggressive behaviour.

Each type of tumour has its own cell of origin, morphological appearance, biological behaviour, mode of treatment and prognosis. Even benign tumours can be lethal due to their location in some vital part of the brain.Their ability to infiltrate locally and their propensity to transform into malignancy, makes the classification of brain tumours a difficult one. Sometimes the diagnosis fails to distinguish between different tumour subtypes. Although treatment and prognosis may vary, the functional neurological consequences are frequently similar . The CNS tumours constitute only about 2 % of all malignancies,[1] but they are disproportionately more common in children, in whom they rank second after neoplasms of haematopoeitic system .The CNS is affected by both primary and the metastatic tumours .Approximately 85% of all Central Nervous System tumours are intracranial and 15% are intraspinal.[2],[3] These tumours also have a distinct age difference in their location. While upto three quarters of the brain tumours in adults occur in the supratentorial region, almost the same proportion of them in children is in the infratentorial location .

The Institute under study is the biggest draining hospital in the region, with a well known neurodisorder service, where, the major patient population comes from the urban middle class . The types of brain tumours encountered in this social class are not well documented till now,& no significant data is available on the frequency of various types of central nervous system neoplasms in our institute . Moreover, the role of immunohistochemistry in the diagnosis of CNS tumours has not been systematically examined in this hospital.

MATERIALS & METHODS

Material comprised of all the brain tumours biopsies and respective specimens examined in the department of histopathology at our Institute from Jan 2014 to Dec 2017(a three year study). A total of 200 specimens formed the basis of this study.

Clinical history of all cases were collected in a pretested proforma meeting the objectives of the study. Informed consent was obtained from all the patients who underwent surgery. Tumours of CNS tabulated according to the classification and grading of World Health Organisation. Statistical analysis was performed using Microsoft Excel Software and the Standard Stastistical Package for the Social Sciences (SPSS) version 20.0 for windows. This study was approved by institution ethical committee.

OBSERVATIONS & RESULTS

There were two hundred (200) cases of space occupying lesions in the CNS, one hundred and ninety (190) cases were neoplastic,and ten (10) cases were non-neoplastic, which were analysed and classified based on the morphology following WHO classification. Immunohistochemical staining was used in those cases where morphology alone could not categorise the tumour. These cases were also correlated with the CT/MRI findings and were clinically observed.

The clinical presentation of the patient was mainly attributed to the site where the tumour was located. Age and Sex distribution of the histopathological types of the lesions were tabulated ,shown in Table No.1 Based on the site , the tumour was divided broadly into cranial and intraspinal.Of the 200 cases , 172 were intracranial and 28 were intraspinal. Of the 200 cases,193 were primary and 07 were metastatic constituting 96.5% and 3.5% of the total cases respectively, shown in [Figure No. 1]

TUMOURS OF NEUROEPITHELIAL CELLS : ASTROCYTOMAS :

Astrocytic tumours were the most common group comprising of 31.5% of all primary CNS tumours (63 of 200 cases) and 67.7%.of the neuroepithelial tumours (93of200cases).

The astrocytic tumours were graded, based on nuclear atypia, mitotic activity, microvascular proliferation and necrosis. In the presence of increased cellularity and nuclear atypia, they were graded as Grade II (Diffuse Fibrillary Astrocytoma). If in the presence of nuclear atypia, mitosis was seen, they were graded as Grade III (Anaplastic Astrocytomas) and Grade IV (Glioblastoma multiforme) when in

addition to Grade III there was necrosis and/ or microvascular proliferation. Pilocytic astrocytomas are generally circumscribed than diffuse and are graded as Grade I.

Of the 63 astrocytic tumours, 23 were glioblastoma multiformes comprising of 36.5% of the astrocytic tumours, followed by Astrocytoma Grade II (22.2%)(14of 63 cases),and Astrocytoma Grade III (22.2%)(14 of 63cases) and the low-grade gliomas (pilocytic type) 19.0% (12of 63 cases). Distribution of all astrocytic tumours as shown in [Figure No. 2]

Pilocytic Astrocytoma (Grade I Tumours)

A total of 12 cases comprised the Pilocytic Astrocytoma, which is a low grade glioma and occured, mainly in the first three decades of life and comprised the19.0 % (12 of 63 cases) Pilocytic Astrocytoma were the most common gliomas (75%) i.e 3 of 4 gliomas in children and a common tumour comprising 25% (3 out of 12cases) of all CNS tumours in children.

Of the 12 cases, 3 were in the males and 9 in females, making M:F ratio 0.3 : 1 Of the 12cases, 11 were found to be intracranial and only 1was intraspinal, making the intracranial to intraspinal ratio as 11:1. The most common site of occurrence was the cerebellum (٣٣,٣٪)ie 4 out of 12cases.

Morphology of all the cases were studied and 12 out of 63 astrocytic tumours were categorised as pilocytic.These showed a biphasic pattern in which compact pilocytic areas were interspersed with microcystic loose areas, variably cellular with bipolar cells & long hair-like (piloid) process. Mitotic activity were low,hence WHO grade I . Only one case that was intraspinal (C3-C4), a GFAP and S-100 was done to rule out schwannoma. GFAP was positive,S-100 negative, confirming the glial nature of the tumour.

Diffuse Fibrillary Astrocytoma (Grade II)

Fibrillary Astrocytoma comprised of 7.0% of all primary CNS tumours (14of 200 cases) and 22.2.% of astrocytic tumours (14of 63cases). The peak incidence was in the fourth decade of life comprising42.8% of the cases (6out of 14) Of the 14 cases, 8 were in males and 6 were in females, giving a male to female ratio of 1.3:1 Fibrillary Astrocytoma were found to be the most commonly in the cerebral hemispheres comprising of 78.6% of cases (11 of 14cases). Of these, 7 were in the frontal region, 2 in the temporal, 1 in the parietal.

3 of the 14 cases were present intraspinally in the cervical segment. Morphology of all the cases were studied and were graded as diffuse fibrillary astrocytomas based on increased cellularity and pleomorphic nuclei (grade II), Photomicrograph :[Figure No. 1]

Two cases were reported Pleomorphic Xanthoastrocytoma, on the basis of large pleomorphic, some bizzare nuclei and nuclear pseudoinclusions. Multinucleated giant cells were also seen.Reticulin silver stain was helpful. Graded WHO II.Photomicrograph: [Figure No.3]

Anaplastic PXA WHO Grade – III, was given to one case which showed increased proliferative activity, areas of necrosis and microvascular proliferation.

Immunostaining for GFAP showed strong positivity.EMA, S100,Ki-67 were also done in the case, ultimately favouring the histopathological diagnosis Two cases of Diffuse Astrocytomas showed high mitotic activity (3-30/hpf) and high percentage on Ki-67 thereby changing the grade from II to III.Photomicrograph :[Figure No 2].

Anaplastic Astrocytoma (Grade III)

Anaplastic astrocytoma accounted for7.0% of all the primary CNS tumours (14 out of 200) and 22.2% (14 out of 63) of the astrocytic tumours. Most of the cases occurred in the third and fourth decade of life comprising, of 50% of the cases, (7 of 14) Most of the anaplastic astrocytomas were located in the cerebral hemispheres accounting for 57.1% (8 of the 14cases), of which the most common site were in frontal lobes (5 cases), followed by temporal, parietal and occipital lobes. Of these 14 cases 3 were in cerebellum & brain stem.

Morphology of all cases were studied and 14 of the 63 astrocytic cases were diagnosed as Anaplastic Astrocytomas. They were distinguished by increased cellularity, pleomorphism & increased mitotic activity. Microvascular proliferation and necrosis were absent. One fibrillary astrocytoma was categorized to grade III on the basis of proliferation marker.

3 cases of diffuse astrocytoma had protoplasmic features.

GFAP, Vimentin and Ki-67 were done in 5 cases, showing varying positivities and proliferative indices.

Glioblastoma multiforme (WHO Grade IV)

The total Astrocytic tumours were 63. GBM were the most common astrocytic tumours accounting to 36.5% , (23of 63 cases) and the most common primary CNS tumours-11.5.% (23of 200 cases). Majority of the cases occurred in the fourth and fifth decades of life comprising of 50.8% of all cases(32 of 63 cases).

Of the 23 cases,13 were males and 10 were females, giving a male to female ratio 1.3:1.

The most common site that was affected by these tumours were the cerebral hemispheres comprising of 78.2% of the cases,(18 of 23). Of these 7 were in the frontal lobe, 4 each in temporal and parietal and 6 in occipital lobe. After the cerebral hemispheres, the next common site was the thalamus constituting 13.0% of the cases (3/23). Two cases were also seen in the cerebellum 8.7% (2of 23).

Morphology of all the cases were studied and 27 of 63 were categorised as GBM, as they showed increased cellularity, necrosis (many showing geographical necrosis or pseudopallisading of tumour cells around the necrotic area), mitosis, microvascular proliferation (some forming glomeruloid bodies) and nuclear atypia (some having prominent giant cells), Photomicrograph:[FigureNo 4] No immunohistochemistry was required to classify them as GBM. However, immunostaining with GFAP & Ki-67 was done in 12 GBM cases. These 12 cases were those which showed morphological features suggestive of either primary or secondary GBM. The ones which showed features of secondary were those which had areas of low grade to high grade transition,(4 cases), those with gemistocytes (6 cases) and the ones which favoured more of primary were those which had massive necrosis without pseudopallisading (4 cases).

One case showed feature of Giant cell Glioblastoma,one had features of GBM and Oligo compoment.

Of the 23cases,15 cases were prospective. On MRI, in 8 cases possibility of high grade glioma was given, in 5 cases metastatic tumour was considered and in 2 cases low grade glioma was kept.

Gliosarcomas WHO Grade IV

Of the 200 cases, 4 were gliosarcomas, constituting 2% of CNS tumours . All the cases were in males, three in the frontal lobe and one in the temporal lobe within the age group of 50 - 70 year old men.Morphological diagnosis of gliosarcomas (on H&E section) showed a biphasic pattern with alternating areas displaying glial and mesenchymal differentiation. However a strong positive stain for reticulin and a positive immunostain for GFAP confirmed the diagnosis. Vimentin was also positive in the sarcomatous components.

OLIGODENDROGLIOMA WHO Grade II & III

12 cases of oligodendroglioma were reported, that comprised 6% (12 out of 200 cases) . 9 cases were in males, 3 were in females, M:F 3:1. Most of the cases belonged to the third and fourth decades comprising of 5 out of 12 cases, (41.7%). Frontal lobe was involved in 7 of the cases 58.3%, Parietal lobe in 3 cases(25%) and one each in temporal lobe and the thalamus .

H & E sections showed lesions chiefly comprising of cells resembling oligodendroglia giving a honeycomb appearance and ' fried egg appearance', with increased vascularity and focal calcification, Photomicrograph: [Figure No 6]. 4 cases were Anaplastic Oligodendroglioma (Grade III) of which 2 were confirmed on IHC using Ki-67.

OLIGOASTROCYTOMAS (Mixed) (WHO Grade II & III)

Of the 200 cases, 2 were oligoastrocytomas, constituting 1% of all primary CNS tumours. Both the cases occured in the first decade of life .One occured in the temporal lobe and the other in the posterior

fossa.

The H & E stained sections showed a tumour composed of a conspicous mixture of two distinct neoplastic cells resembling the tumour cell in the oligodendroglioma and diffuse fibrillary astrocytoma. One was WHO Grade II other one had Grade III, on the basis of high mitotic index,endothelial hyperplasia & pallisading necrosis.

EPENDYMAL TUMOURS (WHO GradeII)

Ependymomas accounted for 5 % of all primary CNS tumours (10 of 200 cases). In our study, all the ten cases were distributed in all age groups, and had equal male to female distribution making the M:F =1:1. Preferred locations were the ventricles, Posterior fossa and cerebellum.

The morphology of Ependymoma was studied.The key histological features were perivascular rossetes and ependymal rossetes.
Of the 10 cases,3 were Myxopapillary WHO Grade I, 2 cases were classical ependymomas WHO grade II, one was Anaplastic WHO Grade III .

Also, 2 each cases were seen of Clear cell ependymoma and Tanycytic ependymomas respectively . One of the myxopapillary ependymomas resembled metastatic adenocarcinoma, on which immunostain for GFAP and CEA was done.GFAP positivity and CEA negativity confirmed diagnosis. One patient,18 month old /F, showed CSF seeding too .

CHOROID PLEXUS TUMOURS

Of the 200 cases, 2 were Choroid plexus Papillomas comprising 1% of all primary CNS tumours . However, they are common in age group upto 10 years of age, our study showed 2 cases,both age 35 years and 40 years respectivelely. One was located in ventricles and other located in the posterior fossa

A morphological diagnosis was made on H & E as the tumour was papillary and composed of fibrovascular connective tissue fronds covered by a single layer of uniform cuboidal to columnar epithelial cells with round to oval basally placed monomorphic nuclei . Occassional mitotic figures were seen, both the cases were graded WHO Grade I . Immunohistochemical stains were not required.

EMBRYONAL TUMOURS

WHO Grade IV Eleven cases out of 200 cases were embronal tumours, amongst which majority were medulloblastoma (9 cases), (2case)were primitive neuroectodermal tumours (PNET).

MEDULLOBLASTOMAS :

Medulloblastomas accounted for 81.8% (9 out of 11cases) of all embryonal tumours and the second most common in children. However,they accounted for only 4.5% (9 out of 200 cases) of all primary CNS tumours in all age groups. All the 9 cases, occured upto 30 years age. Out of 9 patients,6 were males and 3 were females making the M:F ratio 2:1 . Most of these cases (7cases)were present in post. Fossa. Only 2 cases were present in the cerebellum.

Morphology of all the medulloblastoma were studied, Classical Medulloblastoma were diagnosed,in those showing a patternless sheet of small tumour cells with hyperchromatic nuclei and minimal cytoplasm,with inconspicous nucleoli, Photomicrograph:[Figure No 5]. Three cases were found to have astrocytic differentiation. Two were classified as desmoplastic medulloblastoma,which showed nodular,reticulin free zones(pale islands) surrounded by densely packed,highly proliferative cells that produced a dense intercellular reticulin fibre network.These were confirmed by a retic stain.

In other medulloblastomas,synaptophysin positivity and chromogranin negativity helped to confirm the diagnosis.Areas of astrocytic differentiation were confirmed by GFAP stain . On MRI,in 3 cases a diagnosis of medulloblastoma was made and in one possibility of low grade astrocytoma was considered.

PRIMITIVE NEUROECTODERMAL TUMOURS (PNET)

These comprised of the rest of the embryonal tumours,(2 of 11 cases). PNET s accounted for 1% of all the CNS tumours (2 of 200 cases) . One of the case was found in the lumbar region of the spinal cord and in the second decade of life,while the other was located in the thalamus,and in a 60 year old female. Morphologically, both the cases presented as small round cell tumours. Thus immunohistochemical positivity with CD99 and NSE supported the diagnosis. LCA was also done in one of them to rule out the possibility of Lymphoma. Both the cases were retrospective.

PERIPHERAL NERVE SHEATH TUMOURS

Of the 200 cases, 26 were diagnosed as peripheral nerve sheath tumours (13%). Of these most common were the schwannomas (22 out of 200) constituting 11.0% of all the CNS tumours, followed by neurofibromas (4 out of 200 cases)(2 %) and MPNST no case was seen.

SCHWANNOMAS :

Schwannomas accounted for 11.0 % of all primary CNS tumours (22 of 200 cases). Majority of cases occured in the third and fourth decades of life constituting 50% of cases (11 of 22 cases) . Of the 22 cases 12 were in males and 10 were in females, giving a male to female ratio of 1.2:1. Most of the cases ie 90.9% (20of 22)were intraspinal and9.1% were intracranial (2 out of 22). They were the most common spinal tumours accounting for 81.5% of all tumours in the spine (22 of 27). The thoracic segment was the most commonly affected site 41% (09 cases), then lumbar 32% (7 cases) and cervical 18.2% (4 cases)region respectively. The only site that was affected intracranially was the CP angle 9%(2 cases) Of the 22 schwannomas, 20 did not need any immunohistochemistry. Their morphology on H&E was quite characteristic i.e the tumours composed of spindle shaped neoplastic Schwann cells with alternating areas of compact elongated cells with occassional nuclear pallisading (Antoni A pattern) and less cellular, loosely textured (Antoni B). One of the schwannomas resembled neurofibroma . A strong S100 positive immunostain for most of the tumour cells confirmed the diagnosis of schwannoma. Of the 22 cases, 11 cases were prospective,. in 9 cases a diagnosis of schwannoma was made, in 1 case a diagnosis of neurofibroma and in 1 a diagnosis of meningioma was kept in mind on MRI.

NEUROFIBROMAS :

Neurofibromas accounted for 2.5% of all CNS tumours (5 out of 200 cases). There was almost equal distribution of the cases in all age groups.Of the 5 cases, 3 males and 2 in females, making M:F ratio,1.5:1.

All the neurofibromas were present intraspinally. Of these 2 were in the cervical region and 3 in thoracic . In 3 cases, S100 was done to rule out schwannoma. . On MRI, in 2 a diagnosis of neurofibroma was made and in one a possibility of schwannoma was made.

TUMOURS OF THE MENINGES:

MENINGIOMAS :

They were the second most common tumours (Astrocytoma, being the most common) constituting 18.5% of all the primary cases,(37 out of 200 cases) The most common age group found to be affected by meningiomas was the fifth and sixth decades of life,accounting for 29.7% cases (11 out of 37 cases) These were the only group of tumours which were more common in females (25 of 37 cases) making the female to male ratio 2.08:1 . Of the 37 cases, 30 (81.1%) were found to be intracranial and 7 (18.9 %)were intraspinal.

Of the 30 cases,19 were cranial, 6 were cerebellar, 5 of which were in the parasaggital area. Of the 7 cases, which were in the spinal cord,5were in the thoracic region and 1 each were in dorsal & lumbar regions respectively.

Most common presentation was headache (48.6%) 18 cases,seizures (27%) 10 cases, and sensory deficits (10.8%) 4 cases. Vertigo and confusion in 2 cases each (5.4%),one case had drowsiness (2.7%) All the 37 cases were studied morphologically,showed predominent architectural features, showing fascicles of spindle cells & meningiothelial cells (whorls pattern) .

Amongst them 11 were meningothelial, 9 were transitional, 8 were fibroblastic, 7 were psammomatous .

1 case was atypical and 1 was anaplastic on the basis of increasesd cellularity and mitotic figures > 4 / 10HPF and >20 / HPF respectively. The 2 of the fibroblastic meningiomas resembled schwannomas. IHC staining with EMA and S100 were done. Strong EMA positivity and very weak S100 positivity confirmed the diagnosis of meningiomas. EMA also helped to confirm the diagnosis in all the 6 meningiomas

with metaplastic changes. Of the 37 cases 26 were prospective and MRI in 21 cases gave a diagnosis of meningioma.

MENINGEAL - HEMANGIOPERICYTOMA : (WHO Grade II,III)

Two cases (1%) of all the CNS tumours,both in males and in fourth to sixth decade. One case belonged to retrospective group and could not be followed appropriately. The case that occured in the 45 year old male with post. Fossa mass, Histomorphology of the case was studied . The monomorphous cellular spindle cell lesion,showed storiform pattern,and staghorn vessels were highlighted by the Reticulin stain. IHC pattern with Vimentin and CD34 helped in diagnosis.

HAEMANGIOBLASTOMA : WHO Grade I

One case of haemangioblastoma (0.5%) was diagnosed based on the morphology i.e a capillary rich neoplasm, containing variably lipidised interstitial or stromal cells . It was present in the cerebellum of a 27- year –old male patient . On MRI, first possibility of pilocytic astrocytoma was considersd with the second possibilty of hemangioblastoma.

GFAP was negative in stromal cells favouring Haemangioblastoma.

TUMOURS OF THE SELLAR REGION :

PITUITARY ADENOMAS :

Pituitary tumours accounted for 5 % of all the CNS tumours (10 of 200 cases) .In our study,all lodged in the sellar /suprasellar space and M:F was 1:1.

Most of the cases belonged to age group 50-70 years,comprising of 60% (6 out of 10),followed by fourth decade and fifth decade. Pituitary adenomas are uncommon in pediatric age group.

Histologically, these tumour displayed a diffuse, papillary or trabecular arrangements similar to that of other neuroendocrine tumours. The hormone type of the tumour was not possible due to inavailability of the corresponding IHC marker.

CRANIOPHARYNGIOMAS (WHO Grade I).

The diagnosis of craniopharyngioma was made in 2 cases out of 200 cases, constituting 1% of all primary CNS tumours. One case occured in a 8 year old and the other in a 56 years old female. Both the cases occured in suprasellar region.

Morphologically the cases were of adamantinomatous type i.e . the tumour showed broad strands, cords and bridges of a multistratified squamous epithelium with peripheral pallisading of nuclei,showed the typical nodules of compact (wet keratin) and dystrophic calcification. No IHC staining was required for the diagnosis.One of the case was prospective and MRI same diagnosis was done.

METASTATIC TUMOURS :

7 out of 200 cases were diagnosed as metastatic tumours constituting 3.5% of cases.The most common age groups affected by metastasis were in the sixth and seventh decades of life, comprising all the cases .Not a single case was found below the age of 30 years. Of the 7 cases, 3 were males and 4 were females, making the male to female ratio of 0.75:1

Of the 7 cases that metastatized to the CNS, all were intracranial (100 %) Cerebral hemispheres were the most common site for metastasis, Frontal lobe constituting 57.1%(4out of 7) .The parietal,occipital and the cerebellum showed one case each.

Morphology of all the cases were studied . The 5 cases were metastasis of Adenocarcinomas and rest 2 cases of Squamous cell carcinoma.

The panel of IHC that included pan CK, CEA, GFAP, Vimentin,favoured the metastatic morphology.

DISCUSSION

The present study was conducted with the objectives mentioned and as all these aspects have been studied by many other authors, comparision of results in the present study with results recorded in the literature have been done. It is to be pointed ,that our sample size was quite small and the epidemiological data differed in a few tumours in comparision with the literature that was reviewed.

The age distribution of CNS tumours is said to be bimodal, one peak in children and second in 50-70 years.[4] Our study showed peak in the third decade comprising of 22% cases comparable to the study conducted by Masoodi T et.al. 2012, that showed peak incidence in the third decade [5].

There is, in general, a male preponderance in most parts of the world including Indian subcontinent where sex ratio has been found to be 2.2:1 .[6] In our study, out of the 200 cases, we recorded, 52% were males, rest 48% females (Ratio 1.08:1). Data is very much compatible with that of the study done in Australia, Chang et.al,2003 in which a total of 1361 CNS tumour cases had 58.2% males and rest 41.8% females.[7][Table No.1]

Most common symptom was headache (69.6%) in the intracranial tumours followed by seizures (35.9%), according to the study by Masoodi T et.al.2012,[8] while, in our case ,headache was present in 29% followed by vertigo in 9.5% .Of the intraspinal lesions, our study had weakness of extremities as most common symptom (53.6%), but the study by Masoodi had 85.7%.

According to Masoodi T et.al 2012 study,the majority of tumours were intracranial (86.8%),remaining were intraspinal (13.2%). Our study showed, intracranial lesion 65.5% and intraspinal 13.5%.

The CNS can be affected by both the primary and metastatic tumours. Primary CNS tumours account for 85-90% of all CNS tumours,[9] rest being metastatic (10-15%). However, in the study by Butt et. al 2015 at Rawalpindi,[10] metastatic tumours comprised 4.9%, that is comparable to that of metastatic cases in our study. Of the 200 cases, 193 were primary,constituting 96.5% of the cases, and metastatic being 3.5%

The one year study conducted by Chawla N et.al,2014 at the PGIMS,Rohtak,[11] astrocytic tumours constituted the largest category accounting for 55.84% of CNS tumours followed by meningiomas (18.18%) and pituitary adenomas (7.8%). Out of Astrocytomas, 13.95% were Grade I, 44.18% were grade II while grade III & IV constituted 20.9% each . [Table No.2]

In the study by Sumathi V et.al 2015,[12] the histopathological spectrum comprised of Astrocytomas 49%, meningiomas 16.1%, neural tumours 8.4%,metastatic tumours 6.3%. In the pediatric population, medulloblastoma were the commonest tumour comprising 4.8%.[12]

The 5 year study spectrum by Nibhora S et. al. 2015,[13] the tumours of neuro-epithelial tissue comprised mainly of astrocytic tumours (39.32%), followed by oligodendroglial tumours (4.5%), mixed gliomas (2.25%), ependymal tumours (2.25%), choroid plexus tumours (2.25%), and embryonal tumours (1.12%).

It was hard to compare the different studies due to the difference in the case material and prevalances of the lesions, but our study showed Astrocytomas as the most common tumour comprising of 31.5% of all CNS tumours. Among Astrocytomas, GBM constituted 36.5% of astrocytic neoplasms. Meningiomas were the second prevalant with 18.5%, that followed Schwannoma (11%), Oligodendrogliomas were 6%, Ependymal tumours 5%, Pituitary adenomas 5%, Medulloblastomas 4.5%. Metastatic lesions were 3.5%. Rest included Neurofibroma 2.5%, ChoroidPlexus tumours,Craniopharyngiomas, Round cell tumours, Hemangiopericytoma-like, and the mixed oligo-astrocytomas each having 1% incidence, Hemangioblastomas were 0.5% of total cases.[Table No 1]

The complete spectrum of this study is comparable and tabulated with the study by Aryal G,Nepal 2011[14].[Table No 2] Due to unknown reasons , we found that our study was far away from the statistics published by the CBTRUS 2004-2008 survey.

ROLE OF IHC :

In our study, **GFAP** turned out to be a sensitive and specific marker for glial differentiation and its demonstration was very helpful in firmly establishing the astrocytic origin of tumour. As all the astrocytic tumours, on whom GFAP was done,all showed positivity, including the cases of GBM., however degree decreased with high grade.

Positive reaction, although, variable was also seen in the ependymomas.

Hemangioblastoma showed positivity with GFAP & **CD 34**, whereas, Meningeal hemangiopericytoma demonstrated CD 34 positive and **ER-PR** negative.

Vimentin was useful to us in the case of confirming the histopathological diagnosis of Gliosarcoma, where, it showed positive mesenchymal component of the tumour.
An interesting case of PXA, showed strong positive GFAP, **CK, EMA** along with **Ki-67** index 30%, favouring the diagnosis of Anaplastic PXA with composite component of anaplastic Meningioma.

S-100, was one consistent marker positive in all the cases of Schwannomas.

CEA, was used in case of the secretory Meningioma, where the hyaline globules showed positive.

The Proliferative Index marker Ki-67 was helpful in all the cases where it was confusing to grade,especially in the absence of necrosis .

EMA was helpful along with vimentin and negativity of GFAP,in cases of Meningiomas.

Pan –CK, EMA, CEA, GFAP, were helpful in confirming the metastais in brain in our study.

SUMMARY AND CONCLUSIONS

The present study on CNS tumours was conducted inour Institute , included the epidemiological analysis of CNS tumours, correlation with the clinical picture, and CT/MRI findings, classification of CNS tumours following the WHO and the utility of immunohistochemistry in their diagnosis. All the findings were comparable to other studies after reviewing the literature.

Table No 1 : Comparative studies of spectrum of CNS neoplasms

Histological type	Aryal G	Masoodi et.al	Chawla et.al.	CBTRUS2004-2008survey	Present study
Astrocytoma	38.6%	41.5%	55.84%	23.1%	31.5%
Meningioma	14%	19.81%	18.18%	34.7%	18.5%
Schwannoma	5.2%	11.32%	8.9%	8.5%	11%
Metastasis	14%			20%	3.5%
Pituitary adenoma	5.2%		7.8%	13.5%	5%
Medulloblastoma	3.5%	3.78%		1.1%	4.5%
Craniopharyngioma	3.5%	0.94%	1.3%	0.9%	1%
Round cell tumour	3.5%	1.89%		2.3%	1%
Neurofibroma	3.5%				2.5%
Ependymoma	1.8%	4.72%	3.9%		5%
Hemangioblastoma	1.8%	0.94%	2.6%		0.5%
Hemangiopericytoma	1.8%		1.3%		1%
Oligodendroglioma		2.84%		1.9%	6%
Mixed Oligo-Astro		0.94%		5.0%	1%

Table No 2 : Comparative study of the Grades of Astrocytoma in different studies

WHO Grade	Aryal G. %	MasoodiT et.al %	Butt.et.al %	Chawla et.al %	Present study %
Grade I	27.3	4.5	21%	13.9	19.0
Grade II	27.3	27.2	17.8	44.1	22.2
Grade III	13.6	27.2	5.6	20.9	22.2
Grade IV	31.8	40.9	40.4	20.9	36.5

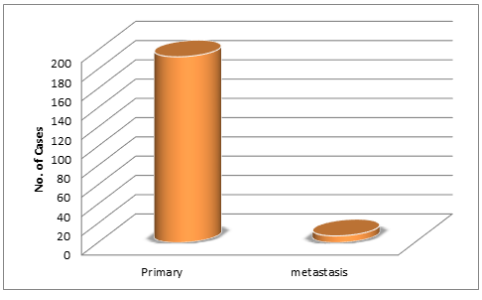

Figure 1: Distribution of tumours of central nervous system

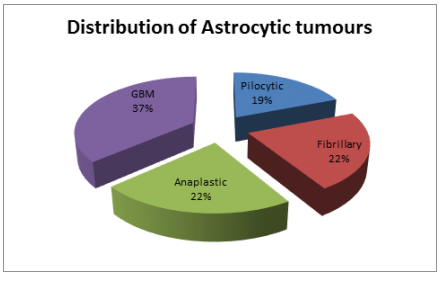

Figure 2: Astrocytic tumours

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