International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Original Research Article

Clinico-Pathological Study of Brain Tumors with Special References to Atypical Cases: A Retrospective Analysis of 130 Cases in a Tertiary Care Hospital in India

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ABSTRACT

Context: Brain tumors are heterogeneous group of neoplasms, which can occur at any age. Despite of some published articles regarding pathological pattern of brain tumors from different parts of the world and in India, comprehensive clinic-pathological studies regarding atypical brain tumor cases from Eastern India is lacking.

Aims: Aims of the present study was to study of clinical and histopathological spectrum of brain tumors and discuss the clinical, radiological, squash cytology and histopathological aspects of atypical cases.

Settings and Design: We have approached every cases of brain tumor, diagnosed during the study period. Radiological, clinical and squash cytology data were correlated with histomorphology for correct diagnosis and analysis of atypical cases.

Methods and Material: The study was a cross-sectional observational study involving 130 cases of brain tumor, diagnosed during the three years study period (Jan, 2010-Dec, 2012). Data on clinical, radiological features of the cases were collected from all patients. Histopathological diagnosis was correlated with clinico-radiological diagnosis. Atypical cases were reviewed further with squash cytology and radiological data.

Results: We evaluated 130 cases of brain tumor with a male preponderance. Most common type tumor was neuroepithelial tumor (92 cases, 70.76%), among which, most frequent subtype was astrocytic tumors (54 cases, 41.5%). Second most frequent brain tumor was meningioma (20 cases, 15.3%). We found four atypical cases as rosette forming glioneural tumor, rhabdoid meningioma, primary melanoma of brain and congenital mature teratoma respectively.

Conclusions: Astrocytic tumors are most common subtype. However WHO grade I neoplasms are more frequent brain tumors. Though rare, the atypical cases need radiological, squash cytology, histology and immunohistochemical collaboration for correct diagnosis.

Key-words: Brain Tumors, Incidence, Histopathological Subtypes, Atypical Tumors.

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Article History:

Received: 12-03-2017, **Revised:** 10-04-2017, **Accepted:** 26-04-2017

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2017.3.3.030	

INTRODUCTION

Central nervous system neoplasms are heterogenous group of tumors, which include both benign and malignant lesions.[1] CNS tumors constitute <2% of all neoplasms.[1,2] Statistically, male patients are more affected than female patient except in meningioma. CNS tumors have bimodal age distribution with a peak at childhood and another peak at adult age group of 45-70 years.[1] Clinical presentation of CNS tumors depend on the location, size of the tumor and growth rate of the neoplasm.[1] There is a high morbidity and mortality associated with these tumours irrespective of their histologic grade. According to WHO classification, CNS tumors have extensive classification and subtypes. Glial tumors include astrocytoma, ependymoma,

glioblastoma, oligodendroglioma and others.[1,3] Non-glial tumors include embryonal tumors, choroid plexus tumors, pineal tumors, meningeal tumors, nerve sheath tumors, tumors of sellar region, haematopoietic neoplasm and metastatic tumors.[3] Among these extensive entities, meningiomas, gliomas, nerve sheath tumors and pituitary tumors account more than 85% of all CNS tumors.[3] Accurate diagnosis of CNS neoplasms requires sophisticated modern non-invasive and invasive radiological study as well as intra-operative squash cytology, post- surgical biopsy and histopathology of the tumors.

There are many previous studies on clinicopathological study of common CNS tumors. But some of CNS tumors have very rare incidence, atypical clinical presentation, atypical radiological features and atypical histopathological findings; which have been rarely presented in previous literature. Here we focused the on clinicopathological and squash cytology features of atypical brain tumors in the present study of five years in a tertiary care hospital in India.

SUBJECTS AND METHODS

The present study was undertaken at Department of Pathology in collaboration with Department of Neurosurgery in our hospital from Jan 2010 to Dec 2012. Ethical clearance was obtained from institutional ethical committee. In the three years study period; we studied 130 cases of brain tumor cases. Data on clinical and radiological features of all cases were collected from previous record. In all cases gross features were recorded during grossing. Adequate number of sections was taken from representative area. The tissue sections were processed as standard procedure. Tissue sections were stained by haematoxyline and eosin stain. Squash cytology and immunohistochemistry were used in atypical cases and in cases where were required. Histopathological diagnosis was done depending on the WHO classification and grading (2007). Statistical analysis was done by using SPSS (statistical package for social science). Special discussion and evaluation was done in the atypical/rare cases and clinic-radio-cyto-histopathological correlation was tried.

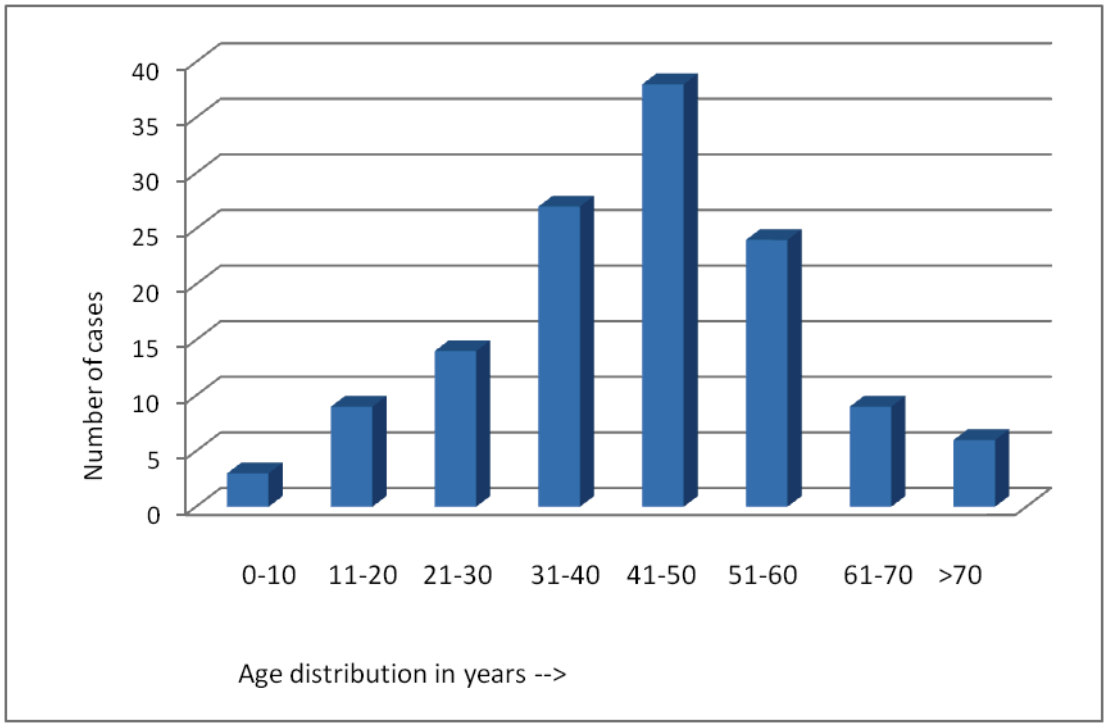

Table 1: Clinical presentations of brain tumors.

Clinical presentations	Number of cases	Percentages
Headache	63	48.46%
Seizure	48	36.92%
Vomiting	32	24.61%
Visual disturbances	11	08.46%
Gait disorder	05	3.84%
Cranial nerve palsy	08	6.15%

RESULTS

We studied 130 cases of brain tumors in three years. We found 73 male patients (56.15%) and 57 female cases (43.84%). We found cases of wide age range (4 years to 78 years) in our series with a mean age of 42.38 years. Age distribution of CNS tumors has been shown in bar diagram (figure 1). Highest number of patients was among 41-50 years (38 cases, 29.23%). Most common presentation of brain tumor in our series was headache (63 cases, 48.46%). Other symptoms were seizure (48 cases, 36.92%), vomiting (32 cases, 24.61%), visual disturbance (11 cases, 8.46%), cranial nerve palsy (8 cases, 6.15%) and gate disturbance (5 cases, 3.84%).

Most of the tumors in our series were neuroepithelial tumor (92 cases, 70.76%). Among the neuro-epithelial tumors most frequent type were astrocytic tumors (54 cases, 41.5%). Second most common group were meningiomas (20 cases, 15.3%).

Histopathological subtypes of brain tumors are shown in table 2. Among the astrocytic tumors, 13 cases were WHO grade I and six cases were grade II. 12 cases (22.22%) were WHO grade III astrocytoma and 23 cases (42.5%) were glioblastoma (grade IV).

Table 2: Spectrum of istopathology subtypes of diagnosed brain tumors (n-130)

Types of brain tumor	Subtypes/specific diagnosis	Number	Percentage
Neuroepithelial tumors	**Astrocytic tumors**	54	41.5%
	Oligodendroglial tumor	11	8.46%
	Ependymal tumors	05	2.3%
	Choroid plexus tumors	03	2.3%
	Neuronal tumor (Lhermitte Duclos)	01	0.76%
	Neuroblastic tumor	07	5.3%
	Pineoblastoma	01	0.76%
	Embryonal tumor	10	7.6%
Nerve sheath tumors	**Schwannoma**	08	6.1%
	Neurofibroma	01	0.76%
Meningeal tumor	**Meningioma**	20	15.3%
Lymphoma	**Primary CNS lymphoma**	01	0.76%
Germ cell tumor	**Germinoma**	01	0.76%
Tumor of Seller region	**Craniopharyngioma**	02	1.53%
	Pituitary adenoma	03	2.3%
Metastatic tumor	**Adenocarcinoma**	02	1.53%

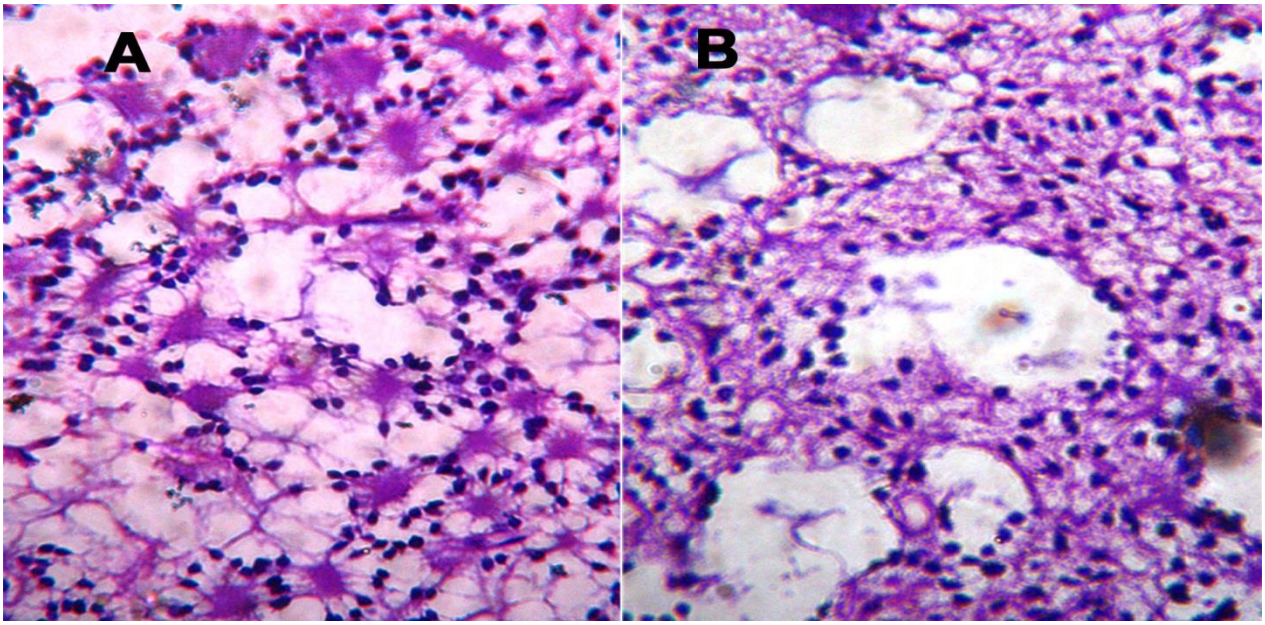

Figure 2: Photomicrograph showing histology of the rosette forming glioneural tumor with different parts: A- rosettes in neurocytic component, B- microcysts of glial component; [H& E stain, 40 X view].

We found four atypical cases of brain tumor in our series. The atypical cases were in presentation, radiological, squash cytology and in histopathology.

CASE 1

21 years male presented with headache, vertigo and gait disorder for last two months. Non-contrast CT scan revealed a mass at cerebellar vermis. MRI brain revealed discrete areas of increased signal intensity in T2 weighted images without any contrast enhancement. Provisional radiological diagnosis was astrocytoma. Squash cytology showed hypercellular containing neoplastic astrocytes in a gliofibrillary background and the diagnosis was diffuse astrocytoma. On histopathology, the tumor had glial components (astrocytes and microcysts) and neurocystic component (rossets) without mitosis and necrosis (figure 2). Final diagnosis was rosset forming glioneural tumor (RGNT) of 4th ventriclular region.

CASE 2

A 11years old girl presented with headache, vomiting and ataxia for last two months. Ophthalmic examination revealed normal visual acuity and right temporal hemianopia. CT brain revealed a large spherical dural based hypodense mass lesion at left occipital area with peri-lesional oedema. Provisional diagnosis of the lesion was infratentorial meningioma. During craniotomy intra-operative finding was a greyish black tumor infiltrating. Intra operative squash cytology was diagnosed as malignant melanoma. In histopathology sections, the tumor was composed of pleomorphic cells arranged predominantly in papillary pattern and having fine brown black pigment in cytoplasm, large round pleomorphic nuclei, prominent macronucleoli and frequent mitosis. The tumor section was negative for immunostaining with synaptophysin. Extensive dermatological, opthalmological and radiological examinations were failed to show any other primary sites. Final diagnosis was given as primary malignant melanoma of brain.

CASE 3

45 year female presented with headache, vertigo and vomiting for last two days and altered sensorium for last one hour. She had past history of posterior fossa tumor and was operated one year back. Histologically it was diagnosed as meningothelial meningioma of posterior fossa (WHO grade I). CT scan revealed a contrast enhancing dural based mass at previously operated site. Clinical and radiological diagnosis was recurrent meningioma. She was undergone surgery and intraoperative squash cytology revealed monotonous meningothelial cells arranged in lobules. Some meningothelial cells had characteristic abundant cytoplasm and round nuclei pushing to periphery (rhabdoid cells). Histopathology revealed a solid mass composed of meningothelial cells in sheets and in whorled pattern with areas of monomorphous sheets of cells with abundant eosinophilic cytoplasm with eccentrically placed vesicular nuclei and prominent nucleoli (figure 3). The cells contained spherical masses of eosinophilic inclusions pushing the nuclei to periphery. Areas of necrosis and psammoma bodies are also found. Mitotic count was 4-8/10high power field. Final histopathological diagnosis was rhabdoid meningioma.

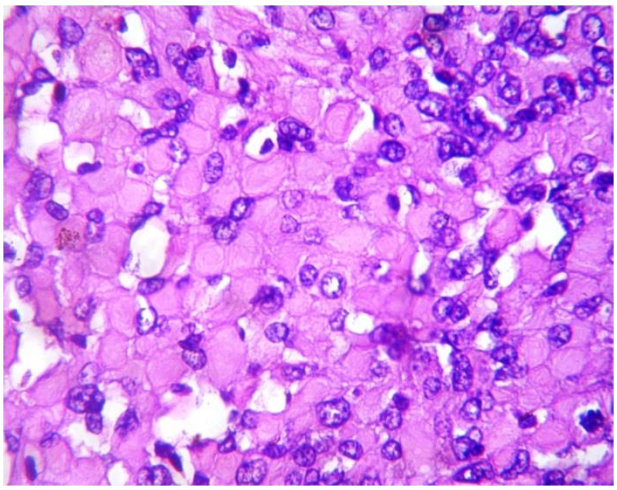

Figure 3: Photomicrograph of histology of rhabdoid meningioma showing monomorphous sheets of cells with abundant eosinophilic cytoplasm, intra-cytoplasmic inclusions, eccentrically placed vesicular nuclei and prominent nucleoli [H & E stain, 40X view].

CASE 4

It was an autopsy case of a intrauterine foetal death of 30 weeks foetus. During autopsy of the foetus we found anencephaly and cranioschisis. On dissection of brain, there was an intracranial mass measuring 4x3 cm dimension. Histopathology of the sections revealed hair follicles, sebaceous glands and cartilage and mucin secreting glands without any immature neuro-epithelium. The case was diagnosed as congenital mature teratoma with cranioschisis.

DISCUSSION

We have studied 130 cases of brain tumor in three years. We found large number of cases (65 cases, 50%) were in the group of 31-50 years. Peak age group in our study was 40-50 years, similar to finding of Masoodi et al and Dhar et al.[1,4] Male versus female ratio was 1.28 but meningioma cases had female predominance. Masoodi et al and Ghanghoria et al found similar sex ratio in their studies.[1,5,6]

Most common symptom was headache, accounting 63 cases (48.46%). Most of the previous studies found headache as the chief complaint in large number of cases.[1,4] Neuroepithelial tumors were the commonest type (92 cases, 70.76%) and astrocytoma was the most common subtype (54 cases, 41.5%) in the present study, supporting the previous studies by Aryal et al and Masoodi et al.[1,3] But Dhar et al found glioblastoma as the most common subtype in their series.[4] Meningiomas (20 cases, 15.3%) were second common type CNS tumor in our series, similar to the findings of other previous studies.[1,3,7,8] But Ghanghoria et al found meningioma as the most common tumor in their study group.[5] Among the astrocytic tumors, commonest type was WHO grade IV (glioblastoma), accounting 42.59% of cases. Dhar et al and Ganghoria et al also found similar finding in their series.[1,4,5,8] Both the metastatic tumors were adenocarcinoma. One was metastasis from colonic adenocarcinoma and another was from ductal carcinoma of breast. Aryal et al found 8 cases of metastatic brain tumor and 87.5% (7 cases) of these were adenocarcinoma.[3] We found higher incidence of oligodendroglial tumor (8.46%) and meduloblastoma (7.69%) in our series than others (Masoodi et al, Ahmed et al and Patty et al).[1,7,8] We found four atypical/rare brain tumor in our series.

Rosette forming glioneuronal tumor is an extremely rare CNS neoplasm. Common sites of involvement are around fourth ventricle, cerebellar vermis, cerebellopontine angle and midbrain. This tumor has indolent growth rate and it presents at late in the course.[9] Typical radiological finding (in MRI- T2) of the tumor is increased signal intensity without contrast enhancement.[9] Squash cytology of RGNT consists of glial cells, neoplastic astrocytes and small cells forming rosettes with central eosinophilic fibrillary material.[10] On cytology, RGNT should be differentiated from pilocystic astrocytoma, dysembryoplastic neuroepithelial tumor (DNT), oligodendroglioma, neurocytoma, pineocytoma and ependymoma.[10] In our case we missed the rosettes and it was diagnosed as diffuse astrocytoma in cytology but on review of the squash cytology smears, we found some rosettoid structures. Similar clinical presentation, radiological findings, predominance of neoplastic astrocytes in a glio-fibrillary myxoid background leaded to misdiagnosis. Histology of rosette forming glioneuronal tumor shows two components; neurocytic component and an astrocytic component. Neurocytic component is composed of

rosettes (like Homer Wright rosettes) formed by neurocytes containing eosinophilic core (synaptophysin positive) and perivascular pseudo rosettes.[9,10] Astrocytic component closely resembles pilocystic astrocytoma. Microcysts, myxoid areas and oligodendroglia like cells, rosenthal fibers may be seen in the tumor. Necrosis and mitosis are absent in the tumor sections. In our case, the tumor had both the components with microcysts, myxoid areas and Rosenthal fibers. On immunohistochemistry staining, RGNTs show positive staining with synaptophysin at core of the rosettes.[1] Glial fibrillary acid protein (GFAP) and S-100 are variably positive at glial component but absent at neurocytic component.[9] Proliferative index by ki-67 labelling is usually low (0-3.8%).[9]

CNS melanomas are rare neoplasm and mostly arise as metastasis from skin or uveal primary.[11,12] After carcinoma of breast and lung, melanoma is third most common malignancy to metastasize to brain.[11,12] But primary intracranial melanoma is a rare tumor.[11,12] Primary CNS melanomas originate from melanocytic elements of leptomeninges (melanoblasts of neural crest).[11] Sites of primary CNS melanomas are hemispheres, cerebellum, medulla oblongata, cervical spinal cord and rarely olfactory bulb.[12]

Primary CNS melanocytic lesions are four types: 1) Diffuse melanosis, 2) Primary isolated intracranial melanoma 3) Meningeal melanoblastoma with cuteneous pigmentation and 4) Discrete spinal cord melanoma.[11] The present case was a primary isolated intracranial melanoma. Melanoma of cerebellum presents with cerebelar symptoms, increased intracranial pressure, cranial nerve palsy and meningism. In our case radiological (CT scan) diagnosis was meningioma because it was a dural based mass. Radiologically differential diagnoses of malignant melanoma are meningioma, meningeal melanocytoma, metastatic tumor and sarcoma.[11] Squash cytology of primary malignant melanoma is indistinguishable from metastatic melanoma. Cytology revealed discohesive sheets of neoplastic cells with abundant intracytoplasmic melanin pigment. The neoplastic cells have dense eosinophilic cytoplasm, large eccentric nuclei, intra-nuclear inclusion and prominent macronucleoli. Mitotic figures are frequent and necrosis is also present.[13] On histopathology, the tumor was composed of polygonal cells in papillae and solid sheets with necrosis. The neoplastic cells had melanin pigmentation, high N:C ratio, pleomorphism and macronucleoli. Depending on location of the tumor and light microscopy of H & E stain, squash cytology, the case was diagnosed as malignant melanoma. Immunohistochemically malignant melanoma of CNS is positive for HMB 45, melan A and S-100. Before diagnosis of primary CNS melanoma, extensive workup should be done to exclude metastasis from extracranial primary.[12] Immunohistochemistry does not help to differentiate primary melanoma from metastatic tumor. Prognosis of primary malignant melanoma of CNS depends on extent of involvement, signs of raised intra cranial tension, neurodeficit, extent of tumor removal and use of adjuvant therapies.

Rhabdoid meningioma is a very rare aggressive variant of meningioma.[14] Most of the meningiomas are among grade I (WHO).[14,15] Only 5-7% meningioma are atypical (grade II) and 3% are anasplastic type (WHO grade III).[14] It was included in WHO classification 2000 as a subtype of meningioma with high risk of recurrence.[15] Most of the cases occur in young and middle age with an equal incidence in male and female.[15] The term rhabdoid refers to resemblance of neoplastic cells to rhabdomyoblast without true skeletal muscle differentiation. Histologically the rhabdoid morphology cells have large round to oval with abundant eosinophilic cytoplasm, eccentrically placed nuclei with prominent nuclei.[15] Para-nuclear cytoplasmic eosinophilic inclusions are frequently found.[15] Most of the cases exhibit rhabdoid morphology with histological evidence of meningothelial differentiation.[15] In our case also, the tumor exhibited typical meningothelial differentiation with areas of rhabdoid morphology. Infiltrating growth and focal necrosis is also associated features and was evident in our case. Differential diagnoses of rhabdoid meningioma include atypical teratoid/rhabdoid tumor, metastatic carcinoma, melanoma, sarcoma and mega cell meduloblastoma.[15] Histological diagnosis depends on evidence of meningothelial differentiation (whorls, nuclear characters, eosinophilic inclusion bodies), IHC findings (EMA, Vimentin & progesterone receptor positive). Recurrence rate is very high approaching about 87%.Median survival is less than three years after surgical resection with adjuvant therapy.[14]

Despite the rare incidence, teratoma is the most common congenital intracranial tumor in foetus and newborn.[16] In contrast to adult counterpart congenital teratomas often contain immature elements but in the present case it was completely mature teratoma. Though most of congenital intracranial teratomas are isolated disease, but sometimes associated with other congenital abnormalities.[17] Prenatal diagnosis is possible by ultrasound and MRI but in our case the patient was from remote area and did not undergone ultrasound before.

In conclusion CNS tumors are common neoplasms but some have atypical presentation, radiological features, atypical histology and rare incidence. These can leads to diagnostic confusion and may affect management protocol. Clinical, radiological (CT scan and MRI), squash cytology and histopathology are very important features to be correlated to provide definitive diagnosis.

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Source of Support: Nil. **Conflict of Interest:** None Declared.

Cite this article as: Rajashree Pradhan, Sajeeb Mondal, Subrata Pal, Shrmistha Chatterjee, Arindam Bandyapadhyay, Debosmita Bhattacharyay. Clinico-Pathological Study of Brain Tumors with Special References to Atypical Cases: A Retrospective Analysis of 130 Cases in a Tertiary Care Hospital in India. Int J Med Res Prof. 2017; 3(3):143-48. DOI:10.21276/ijmrp.2017.3.3.030