ORIGINAL RESEARCH PAPER

Volume-7 | Issue-4 | April-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# HISTOPATHOLOGICAL STUDY OF CP ANGLE TUMOURS WITH CLINICAL FEATURES AND OUTCOME IN TERTIARY HEALTH CARE CENTRE

**Pathology**

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## ABSTRACT

**INTRODUCTION:-** Tumors of the CP angle account for 5% to 10% of all intracranial neoplasms. VSs are the most common CP angle tumor then, followed by meningiomas and the epidermoids. Much rarer primary tumors are schwannomas of other cranial nerves: of the trigeminal nerve, of the facial nerve, or of the caudal cranial nerves; paragangliomas, chordomas, chordosarcomas, arachnoid or neurenteric cysts, dermoid tumors, and metastases. The CP angle could be secondarily involved by tumors extending from the brainstem or fourth ventricle: gliomas, ependymomas, choroid plexus papillomas, medulloblastomas, or lymphomas.

**Material And Methods:-**Clinical data and histopathological evaluation of 55 patients were studied who presented with CP angle mass and retrospectively reviewed.

**RESULT:-** In our study of 55 cases majority of them were benign with 51 cases and four cases were malignant. Most common cp angle tumor diagnosed histopathologically in our set up was Vestibular Schwanomma. Age group varied from 1st decade to 7th decade.

**Conclusions:-** A large variety of unusual lesions can be encountered in the CPA and should be differentiated from acoustic neuromas or meningiomas.Histopathology plays a key role in differentiating different CPA lesions and is primarily based on the site of origin of the masses and their variable clinical presentation

## KEYWORDS

**Introduction:-**

CP angle tumors are accounting for 5-10% of all intracranial masses in adults. Cerebellopontine angle (CPA) tumours are classified accordingly extra-axial tumours, intra- axial tumours, extradural tumours and petrous apex lesions. Vestibular schwannomas (VS) are by far the most common extra-axial tumour followed by meningiomas and cysts of the posterior fossa mainly (epidermoid and, arachnoid, deltoid, neurentric cysts and cranial nerve neuromas) along with aneurysms, malformations.

Intra-axial tumours mainly comprise of parenchymal lesions such as astrocytomas, ependymomas, papillomas, haemangioblastomas and metastases. Extradural tumours include glomus tumours and bone lesions while petrous apex include cholesterol granulomas, epidermoid cysts, mucoceles and aneurysms of the carotid artery.

In adults, common tumors at the CPA are vestibular schwannoma, meningioma, and epidermoid. Bonneville et al.observed that vestibular schwannoma account for 70–80 % of all CPA lesions, 10–15 % meningiomas, and 5 % epidermoid in adults [1], however these tumors are rare in pediatric age group population.

Cerebellopontine angle masses may present in a patient with hearing loss, tinnitus, and vertigo. Other clinical features are hemifacial spasm, trigeminal neuralgia, diplopia, vocal cord palsy and hydrocephalus. The most common type of mass found in this location is a vestibular schwannoma, commonly referred to as an acoustic neuroma. The patients may present with symptoms typically of insidious onset, but sudden hearing loss or vertigo may occur. These tumors are generally located within the cerebellopontine angle (CPA) and may involve the significant number of closely associated vital neurological anatomical structures or embryological remnants. The complications from cranial nerve damage and brainstem compression increases with delay in diagnosis and treatment and results in more morbidity,recurrences and mortality. Pre-operative imaging may not distinguish the point of origin, but this can be determined by the histological typing which plays a role in differentiating the tumors and their spread and grading along with, intraoperative observation, and post-operative imaging [2]. Prognosis of the lesions may vary according to different aspects like patient age, specific tumor growth rate and pathologic behaviour . Histopathology along with radiology plays an important role and guideline for treatment of various lesions. It plays an important part in grading the various lesions along with planning the mode of treatment. Surgical resection is considered for any patient in good medical condition with a benign or malignant lesion in the CPA if the boundaries of the tumor are resectable and not involving any vital structures. Surgical removal of a benign lesion with free margins resection renders the opportunity of complete tumor eradication of the vast majority of CPA lesions.

In most of the cases cause of vestibular schwannomas is unknown. Cushing (1917) and Revilla (1948) believed trauma may be a etiology, as in some observations there was association of occipital trauma with tumors of the cerebellopontine angle [3,4]. The risk factor for developing an acoustic neuroma may be due to genetic condition called neurofibromatosis type 2 in many cases . Meningiomas are significantly more common in women than in men; they are most common in middle-aged women. Other neoplasms that may involve the cerebellopontine angle include metastatic disease, facial nerve schwannoma, exophytic brainstem glioma, haemangiopericytomas ,lipomas and hemangioma. Non-neoplastic lesions that may occur include aneurysms arising from the vertebrobasilar arteries, arachnoid cysts,epidermoid cysts,dermoid cysts and neurenteric cysts. The most common complaints at the time of the initial evaluation are due to involvement of eighth cranial nerve presenting with unilateral hearing loss, vertigo or imbalance and tinnitus.They may also involve the fifth cranial nerve presenting with hemifacial spasm altered sensation and facial pain.

**Material And Methods:-**

Clinical data and histopathological evaluation of 55 patients were studied who presented with CP angle mass and retrospectively reviewed. All had histologically and radiologically verified CPA/CMF lesion and underwent surgical resection through craniotomy except for eight cases in which biopsy was only obtained. History, clinical features and histopathological distributions and grading was studied along with their incidence and management. Biopsies for the study were obtained from patients were attending the clinics at TMMC & RC.We performed a retrospective and prospective study conducted at TMMC& RC ,Histology Lab, during the period from January 2017 to December 2017. The data were collected from the referral sheets.

The procedures were approved by the local ethics committee.

Patients having vascular pathology and tumors other than CPA were excluded. Data of the involved cases was then collected on a designed proforma from the hospital records, radiology and histopathology reports.

**Result**:-

In our study of 55 cases, majority of them were benign with 51 cases and four cases were malignant. Most common cp angle tumor diagnosed histopathologically in our set up was Vestibular Schwanomma.Age group varied from 1st decade to 7th decade(Table 2)

Acoustic neuroma constituent of about (53%), and meningioma (29%) preceded by Ependydomas with(5%) of lesions. Three cases of epidermoid cyst were also reported after histopathlogical confirmation. 2 cases of astrocytoma were reported out of which one was primary while other was due to diffuse spread. Only single case of arachnoid cyst and choroid plexus papilloma were present in the CP angle location(Table 4). Most of the lesions were benign with 93% cases. Females predominated over males with ratio of 1:1.6(Table 1). The most common presentation was hearing loss followed by headaches and irritability. Tinnitus and vertigo were the next common presentation followed by nerve dysfunction, diplopia and gait disturbances. Of the 55 patients, 44 presented with unilateral hearing loss,36 of the patients had complaint of intermittent headache off and on. Tinnitus was the next common complain followed by vertigo with 19 and 18 patients respectively.08 patients presented with cranial nerve dysfunctions preoperatively;(Table3)facial weakness in 2, facial pain in 2.Out of operated 47 cases recurrence was seen in seven cases.

Acoustic neuromas (vestibular schwannomas), arising from the neurilemmal junction of the vestibular nerve,generally constitute about 80%–90% of these tumours [5,6,7]. Histopathological examination in the acoustic neuroma presents two distinctive microscopic patterns, showing Antoni A and Antoni B areas along with fibrocollagenous tissue, spindle cells with elongated nuclei and fibrillated cytoplasm, predominantly those of Schwann cells. The two tissue patterns differ in cellular arrangement and density. Antoni A tissue is compact, with a prominence of interwoven fascicles. Antoni B tissue is porous and less structured. The cells are dispersed randomly surrounding blood vessels, microcysts, collections of xanthomatous cells and areas of previous hemorrhage. Most of them were benign. Three of the patients showed features of neurofibromatosis. Most of them were resected completely except 5 of them in which sub total resection was performed due to adherence of nearby structures while recurrence was seen in 4 cases.

Meningiomas were next tumors in our setup with 29% cases and female preponderance. All of them were generally benign and patients presented in the middle age group with facial symptoms and headache. Three of the patients presented with recurrence after excision of the tumor while rest others had complete recovery. Among 16 patients with meningiomas, 9 were females and seven males with a median age of 45 years. Median duration of symptoms was 10 months. About half the patients had signs of cerebellar ataxia at presentation, with only a third presenting with subjective hearing loss and headache. According to histopathology, meningiomas may be further categorized into grade(I), atypical grade(ii) and anaplastic grade(iii). Generally variants seen were meningothelial, transitional, fibroblastic, psammomatous and angiomatous. All of them in our study were grade(I).

Next to meningioma the lesions seen were epidermoid cysts. The cysts were generally seen in middle age and excised after radiological confirmation. In our cases all were benign,with female predominance .General complaint was hearing loss and facial nerve involvement.In all cases complete resection was performed and there was complete recovery.

Epidermoid cysts (IECs) are benign and slow growing lesions accounting for about 1% of all intracranial tumors [8-9]. Radiologically on MRI scan they have a similar signal to acoustic neuromas but do not enhance and are more irregular so they can be distinguished from arachnoid cysts which have smooth surface.On gross appearance epidermoid cysts have a pearly white appearance.On histopathological examination, an epidermoid cyst is comprised of benign keratinizing stratified squamous epithelium lining [10] with a low proliferative index and desquamated cellular debris. Next incidence of cp angle tumor was of ependymomas equal in percentage as of epidermal inclusion cyst with 5% cases. Generally the patients presented with female preponderance and in adult age. General presenting chief complaints of vomiting and headache were reported with involvement of lower cranial nerves.On radiological examination general features were multiloculated CPA lesion, isointense on T1, hyperintense on T2 and enhancing on contrast. The histopathology revealed two cases of grade1 and a single case gradeII ependymoma showing perivascular pseudorosettes with a small component of rare foci of few bizarre cells with hyperchromatic nuclei. Few areas of necrosis without palisading were encountered in ependymomas presenting with grade ii.On immunohistochemistry GFAP positivity was mainly seen in the perivascular regions. All the cases were seen in the adult age group in second to fourth decade interval.

Percentage of astrocytomas was (4%). Both were male patients and in older age group with two to four month history of giddiness, blurred vision, and difficulty in walking. They had worsening headaches, vomiting, and gait disturbances.

In adult patients brainstem gliomas can manifest as asymmetric expansion of the brainstem with a peduncalated mass protruding into the CPA and even they may resemble other lesions like acoustic neuroma [11][12]. Gliomas may appear as hypoattenuating masses at CT with variable enhancement depending on the their grading. These tumors arise in all age groups. Infantile tumors suggest the possibility of intrauterine origin as congenital glioblastoma. Among anaplastic astrocytomas and glioblastomas, a biphasic presentation is generally noted.

Diffuse astrocytomas, in most of the cases have a characteristic appearance of increased cellular density associated with modest nuclear pleomorphism, increased intercellular edema showing collections of fluid known as "microcysts. On histological examination of the removed tumor specimens showed a cellular tumor with elongated, spindle-shaped cells with irregular, moderately pleomorphic nuclei, as well as proliferative blood vessels and necrosis. The presence of glial fibrillary acidic protein (GFAP) in immunohis tochemistry staining confirmed the glial origin of the neoplasm.

Arachnoid cysts are benign developmental cysts that occur in the cerebrospinal axis in relation to the arachnoid membrane. Only single case was reported in a young adult complaining of headache and hemifacial spasm. The lining epithelium as seen in our cases shows collagen and meningothelial cells. The cysts contain clear, colourless fluid resembling normal CSF as seen in our case. No proper etiology of its cause and its formation was made in our patient. Despite several studies, the mechanism of formation of these cysts is not completely understood[13].

Only single case of choroid plexus papilloma was reported in our set up in an adult female patient. Main features of presentation were vertigo and intracranial hypertension. along with intermittent headache.

Choroid plexus papillomas may occur in children but also occur in adults. These tumors derive from the neuroepithelial cells of the choroid plexus and recapitulate the structure of normal choroid plexus when benign. [14].Choroid plexus papillomas can be encountered wherever choroid plexus is.present In adults, choroid plexus papillomas often arise in the fourth ventricle and extend to the CPA through the foramen of Luschka, but they can also primarily develop in the CPA [15].

**Discussion:-**

Of these benign tumors, 75–90% are vestibular schwannomas (these tumors are also called acoustic neurinomas). Brackmann and Bartels (1980)[16] in their studies observed that out of 1354 cerebello-pontine angle tumors treated in their hospital, 90% were acoustic neuromas.

The majority of the cerebello-pontine angle tumors are benign representing approximately 96–98% of the cases . In our study, acoustic neuroma constituent of about (53%), and meningioma (29%) and those readings are nearly concordant with the study made by Thaba BK et al. BSMMU, Dhaka where acoustic neuroma represents 77% and Meningioma 15 %. These findings are compatible with a study in which the acoustic neuroma accounts for 70-90% , meningioma 5-10% and epidermoid 3-7%. [17]

Vertigo and tinnitus are the main presentations in our study, 76.6% and 46.6% respectively as most of our patients 70% referred from both neurologist and otolaryngologist. In the literature, reports of balance disorder in vestibular schwannoma vary widely. Some authors maintain it may be the presenting symptom in 15% of cases. Continuous or intermittent tinnitus with concomitant hearing loss is present in approximately 90% of cases, and is nearly always unilateral [18].

In our study also the symptoms seen in cases of schwannoma were generally from the involvement of eighth cranial nerve with unilateral hearing loss-24 patients, vertigo or imbalance-16 patients, tinnitus-12patients, and the fifth cranial nerve altered sensation-in 4 patients.

The most frequent presenting symptoms of cerebello-pontine angle tumors including intracanicular vestibular schwannomas are unilateral hearing loss (95%) and tinnitus (80%) with vertigo and/or impaired balance observed in half of the cases [19].

Cerebellopontine angle (CPA) meningiomas constitute about 1% of intracranial meningiomas. The clinical findings were correlated with other studies where surgically confirmed CPA meningiomas are analyzed. The most common symptoms at the time of the initial evaluation were from the eighth cranial nerve mainly unilateral hearing loss. A report of female preponderance was documented by Marin *et al*., with a female to male ratio of 2.5:1 [20]. Gabriela *et al*.[21] reported 100% cerebellar origin meningiomas histologically as being fibrous alone, although most of the angiomatous subtypes originated from the cerebellopontine angles.In our case various variants seen were fibrous meningothelial, transitional, fibroblastic, psammomatous and angiomatous,Histologically, the fibrous and transitional meningioma subtypes had microscopic features of fibroblast found in the deeper layers of the arachnoid, close to the subarachnoid space, whereas, the meningothelial subtype resembled the arachnoid cap cells of the outer layers. These benign yet locally agressive tumours arise from cap cells gathered in tips around arachnoid villi [22] .

CPA ependymomas are uncommon variants of ependymomas of posterior fossa originating from ependymal cell rests which are present in the foramen of Luschka and appear to arise from the lateral surface of brain stem. They may surround the lower cranial nerves and adjacent blood vessels .In general adults with ependymomas are having better prognosis after treatment than the children age group, due to higher grading and posterior fossa location in children.

Astrocytomas in the cerebellum is extremely rare,[23] and such tumor presenting as CPA mass is not common.[24],[25]. They develop secondary to diffuse or anaplastic astrocytomas. In our cases both the lesions presented with diffuse headache and vomiting, and gait ataxia. Both cases were secondary to diffuse variant.

Glioblastomas which are grade iv astrocytomas can be seen in all age groups; however, patients are generally over 50 years of age. When compared to children, localization in the posterior fossa in adults is rare [26].

Only three cases of epidermal inclusion cyst were reported and all were benign. They commonly occur in the cerebellopontine angle, although the petrous apex and suprasellar region are also the other common sites. They tend to be slow growing masses and presentation is dependent on the site of the lesion. Malignant transformation to a squamous cell carcinoma is an exceptionally rare event and this should be considered in case off of rapid progression of a patient's clinical symptoms.[27,28]. Only single case of arachnoid cyst and choroid plexus papilloma were seen. Etiology of arachnoid cyst may be due to trauma, subarachnoid haemorhage or adjacent mass.[29] No such etiology was present in our case.

Choroid plexus papillomas (CPP) are benign slow growing tumors of neuroectodermal origin. Their incidence among all intracranial neoplasm, at all ages, varies between 0.4% to 1%. Incidence amongst children is greater (1.5% to 4%), with a peak in first two years of life [30]. They are less frequent in adults, comprising 0.3% to 0.89% of intracranial tumors [31]. Areas generally involved are lateral ventricles in children and fourth ventricle in adults in the cerebellar locations. [32,[33]. The patients generally complain of increasing headache and visual disturbances. Some may present with gait ataxia and unilateral hearing loss. Microscopic examination generally show papillary structures with delicate fibrovascular core lined by columnar cells with vesicular nuclei, which is typical of choroid plexus papilloma. Postsurgery, headache and other compications generally resolve, cerebellar signs also improve with time. Differential diagnosis of lesions at CPA includes certain common extra axial lesions like acoustic neuromas, meningiomas, vascular ectasia and aneurysms.

Less common lesions are epidermoid cysts and other schwannomas as well as metastases, paragangliomas, and arachnoidal cysts. Intra-axial tumors in the area of the cerebellopontine angle include the medulloblastoma, astrocytoma, and the ependymoma [34]. Total excision offers the patient maximal chances of prolonged overall survival.

**Conclusions:-**

A large variety of unusual lesions can be encountered in the CPA and should be differentiated from acoustic neuromas or meningiomas. Histopathology plays a key role in differentiating different CPA lesions and is primarily based on the site of origin of the masses and their variable clinical presentation. Age of the patient and medical condition, specific tumor growth rate, and pathologic behavior are taken into account when recommending a proper mode of treatment.

**Table 1 Distribution of Cases according to Sex**

| Sex | Vestibular schwannoma | Meningioma | Ependymoma | Epidermoid | Astrosytoma | Araachnoid cyst | CPP* | Total No. of Patients | (%) |
|---|---|---|---|---|---|---|---|---|---|
| Female | 21 | 9 | 2 | 1 | | | 1 | 34 | 56% |
| Male | O8 | 7 | 1 | 2 | 2 | 1 | | 21 | 42% |

**Table 2: Distribution of tumors according to age(*=choroid plexus papilloma)**

| Age | Vestibular schwannoma | Meningioma | Ependymona | Epidermoid cyst | Astrosytoma | Araachnoid cyst | CPP* | Total No. of Patients |
|---|---|---|---|---|---|---|---|---|
| 0 – 20 | 4 | 1 | | 0 | | | | 3 (6%) |
| 21 – 30 | 3 | 3 | 1 | 0 | | 1 | 1 | 8 (16%) |
| 31 – 40 | 11 | 5 | 2 | 1 | | | | 19 (38%) |
| 41 – 50 | 5 | 6 | | 1 | 1 | 1 | | 9 (18%) |
| 51 – 60 | 4 | 1 | | 1 | 1 | | | 8 (16%) |
| 61 – 70 | 2 | 0 | | 0 | | | | 2 (4%) |

**Table 3**

| Clinical features of patients presenting with cp angle tumour | No of patients | Percentage |
|---|---|---|
| Hearing loss | 44 | 80 |
| Headache | 36 | 65 |
| Tinnitus | 19 | 35 |
| vertigo | 18 | 32 |
| Nerve dysfunction | 08 | 15 |
| Diplopia | 06 | 10 |

**Table 4**

| Incidences | Percentage | Histopathological typing of CP angle tumour |
|---|---|---|
| 29 | 53 | Schwannoma |
| 16 | 29 | Meningioma |
| 03 | 5 | Ependymoma |
| 03 | 5 | Epidermoid cyst |
| 02 | 4 | Astrocytoma |
| 01 | 2 | Arachnoid cyst |

Fig -1 Histopathological section of **Ependymoma (40X)**

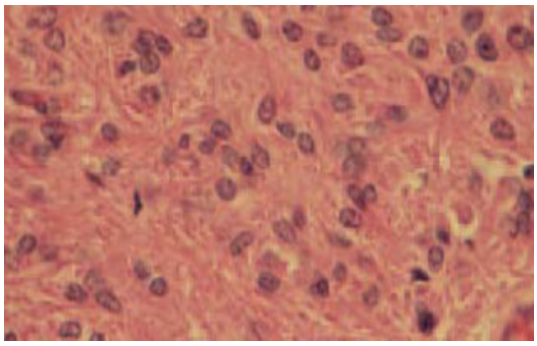


Fig -2 Histopathological section of **Schwannoma(10X)**

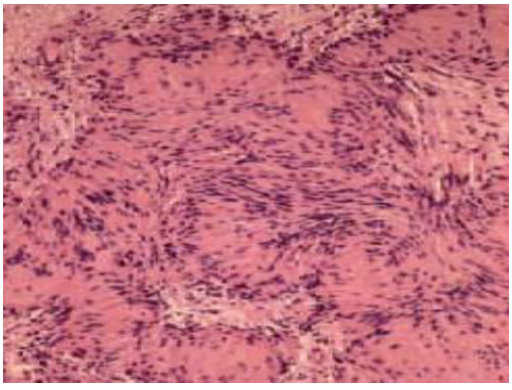


Fig - 3Histopathological section of **Meningioma(10X) ( Fibrous variant)**

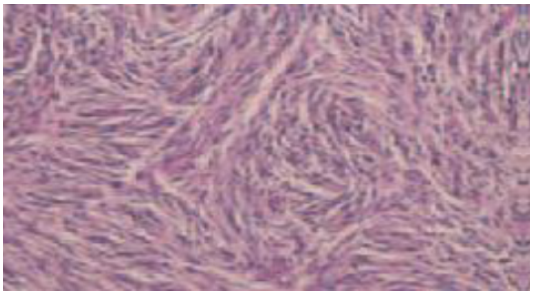
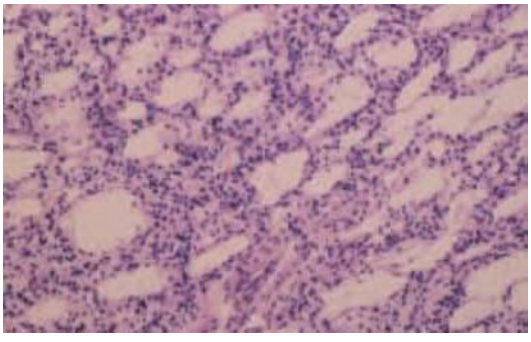


Fig - 4Histopathological section of **Astrocytoma(40X) ( Diffuse variant)**



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