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Clinical Study

Cerebellopontine angle paraganglioma – report of a case and review of literature

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Summary

Majority of the cerebellopontine angle (CPA) tumors are acoustic neuromas, while bulk of the non-acoustic tumors are formed by meningiomas and epidermoid cysts. Primary paraganglioma is a rare tumor in this location, with only two such cases having been reported in the literature, till date. Recently, a case has been described wherein a paraganglioma was apparently arising as a primary lesion in the cerebellar hemisphere. We report another case of an intracranial paraganglioma of the CPA in a 40-year-old female, which did not have any vascular attachment but had focal cerebellar extension.

Introduction

Paragangliomas are benign neuroendocrine tumors, derived from the extra-adrenal paraganglia. Although these tumors are known to arise in a wide variety of locations, central nervous system paragangliomas almost exclusively occur in the cauda equina region [1]. Rare cases of intracranial paraganglioma arising as a primary tumor have also been reported [2–11].

The cerebellopontine angle (CPA) harbors 6–10% of all intracranial tumors [4,12] of which 79–91% are acoustic neuromas [12]. The rest are an extremely heterogenous group, known as 'non-acoustic neuroma tumors', the commonest among which are meningiomas and epidermoid cysts [12]. Paraganglioma is a rare tumor in the CPA, and to the best of our knowledge, only two cases of primary CPA paragangliomas [4,5] have been reported in the English literature, till date.

We report another case paraganglioma of the CPA, in a 40-year-old female, which presented with atypical features both at radiology and at surgery, and on histopathology had focal cerebellar extension.

Case report

The patient was a 40-year-old lady who presented with complaints of progressively worsening bifrontal headache of 2 years duration. This was associated with hearing loss of 1½ year, and declining vision of 1 year duration. In addition, she had dysarthria, gait ataxia and episodic vomiting for the last 6 months. There were no comorbid conditions.

On examination, she had bilateral papilloedema, horizontal gaze evoked jerk nystagmus, which was more pronounced on right lateral gaze, and mildly impaired right corneal reflex.

There was normal tone, power and deep tendon reflexes in all her four limbs, while jaw jerk was absent. She also had lower motor neuron paresis (Grade III) of the right seventh cranial nerve, with right-sided sensorineural hearing loss. However, there was no sensory deficit.

Cerebellar signs were present in the form of dysarthric speech, dysmetria and dysdiadochokinesia on the right side, along with an ataxic gait with a tendency to lurch on the right side.

General examination, evaluation of other systems and routine laboratory investigations were within normal limits. Based on these findings, a clinical diagnosis of CPA mass lesion was considered.

Neuroimaging findings

MR imaging revealed an intraparenchymal lesion in the right cerebellar hemisphere with an exophytic component in the ipsilateral CP angle cistern. The mass was hypointense on T1WI (Figure 1A) and iso-intense to hyper-intense on T2WI (Figure 1B). Post-contrast MR examination showed variable enhancement in the solid component of the mass (Figure 1C, D). Predominant intraparenchymal location of the mass was further confirmed after obtaining the MRI in coronal plane (Figure 1E). In view of these features, the possibilities of a glioma and hemangioblastoma were considered radiologically, while metastasis to the cerebellum could not be completely ruled out.

Operative intervention and findings

A gross total excision of the tumor was done by the right retromastoid suboccipital approach. It appeared extracerebellar in location, and was grayish in color, firm in consistency and moderately vascular on the

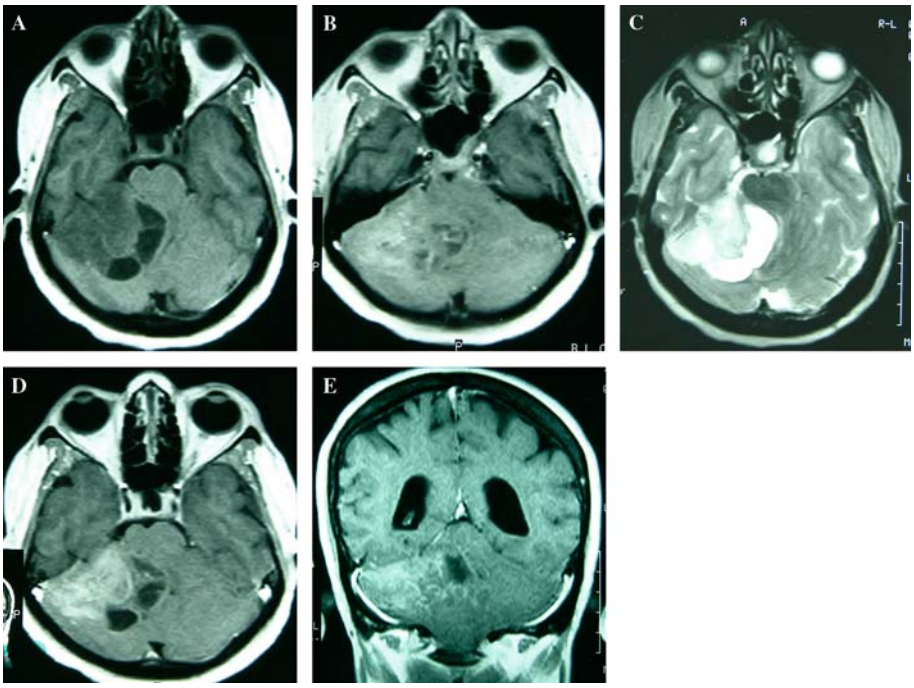

Figure 1. (A) Un-enhanced T1WI axial MR image shows right cerebellar intra-axial lesion with associated exophytic component in the ipsilateral CP angle cistern. The mass is hypo-intense compared to normal brain parenchyma. Posterior margin of the lesion is surrounded by CSF loculation. Mild rotation and displacement of the brainstem is also noted. (B) The solid component of the mass is iso-intense to hyper-intense on T2WI axial MR image along with CSF loculation that is homogeneously hyper-intense to normal parenchyma. Brainstem is displaced and distorted by the mass. (C) Post-contrast axial MR image. There is ill-defined and mild enhancement of the solid component of the mass. However, cystic component is not showing any enhancement. (D) Post-contrast MR image at higher level shows ill-defined mass with heterogeneous enhancement. Medial component of the lesion do not show clear demarcation of the interface between the tumor and brain parenchyma. (E) Coronal post-contrast MRI – the mass is predominantly intra parenchymal in location confined to right cerebellar hemisphere.

surface. However, in the deeper and medial aspects the tumor seemed to be arising from the cerebellar hemisphere, without any distinct cleavage plane. The tumor was away from the brain stem and cerebellar peduncles. Operative impression was of a cerebellar tumor, which could not be exactly characterized.

Histopathological examination

Resected tissue was fixed in 10% neutral buffered formalin, routinely processed and paraffin embedded. Five-micron thick sections were cut and stained by haematoxylin and eosin (H&E) stain. Serial sections were cut and immunohistochemical (IHC) staining was performed by the streptavidin-biotin immunoperoxidase technique (LSAB Kit) using monoclonal antibodies to synaptophysin (dil 1 : 25), chromogranin (CG; dil 1 : 200), neuron specific enolase (NSE; dil 1 : 200), neurofilament (NF; dil 1 : 200), glial fibrillary acidic protein (GFAP; dil 1 : 500), S-100 protein (dil 1 : 200), cytokeratin (CK; dil 1 : 200) and MIB-1 (dil 1 : 200). All antibodies were obtained from M/s Dakopatts, Denmark. Part of the tissue was fixed in 2.5% glutaraldehyde and processed for electron microscopy (EM).

Sections of tumor tissue examined showed a biphasic or biphenotypic pattern with cells arranged into compact nests or balls ('zellballen' pattern) separated by delicate fibrovascular stroma (Figure 2A and B). There was a predominance of 'chief cells', which were uniform in size, cuboidal to polyhedral in shape with a moderate amount of pale, eosinophilic granular cytoplasm and vesicular nuclei having finely stippled chromatin and inconspicuous nuclei (Figure 2C). There was no pleomorphism, mitosis or necrosis. The 'sustentacular' cells were peripherally located, and were spindle in shape with long cytoplasmic processes. Focal extension of the tumor into the adjacent cerebellum was also present (Figure 2D).

IHC showed positivity for synaptophysin (Figure 3A), CG (Figure 3B) and NSE in the chief cells, while the sustentacular cells showed positivity for S-100 protein (Figure 3C). The tumor was immunonegative for GFAP, NF and CK. MIB1 labeling index (MIB1-LI) was $<1\%$ (percentage of positive staining tumor cells out of 1000 tumor cells, evaluated by manually counting at least five representative microscopical fields at high power magnification – 400×).

EM showed numerous organelles in the cytoplasm of the 'chief cells', consisting of mitochondria and rough endoplasmic reticulum. Some of these cells also contained membrane-bound neurosecretory granules (Figure 4A and B).

Based on the neuroendocrine pattern on H&E, immunopositivity for synaptophysin, CG and NSE on IHC and electron-dense neurosecretory granules on EM, a diagnosis of paraganglioma of the CPA with cerebellar involvement was made.

Post-operative course

Post-operatively, the patient was not given any chemotherapy or radiotherapy. At the last follow-up 3 months

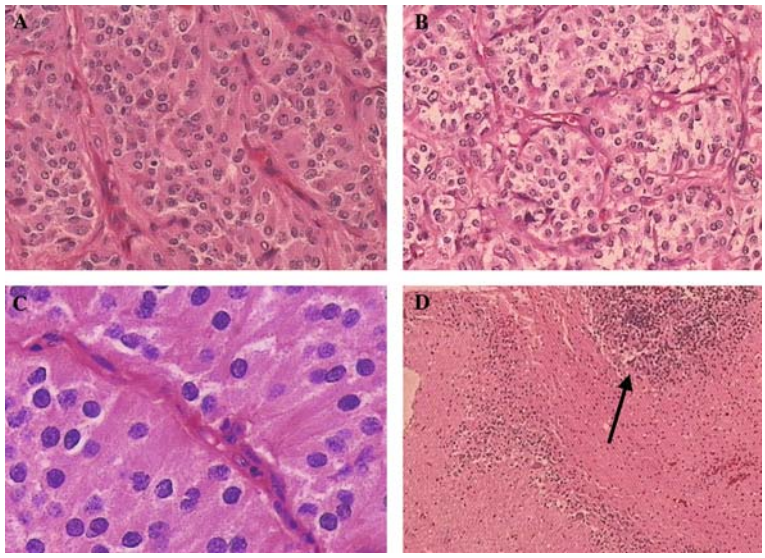

Figure 2. (A,B) Paraganglioma showing cells arranged into compact nested architectural pattern ('zellballen') separated by delicate fibrovascular stroma (H&E ×200). (C) The nests are composed of 'chief cells', which were uniform in size, cuboidal to polyhedral in shape with a moderate amount of pale, eosinophilic granular cytoplasm and vesicular nuclei having finely stippled chromatin and inconspicuous nuclei (H&E ×400). (D) Focal extension of the tumor (↑ arrow) into the adjacent cerebellum was also present (H&E ×100).

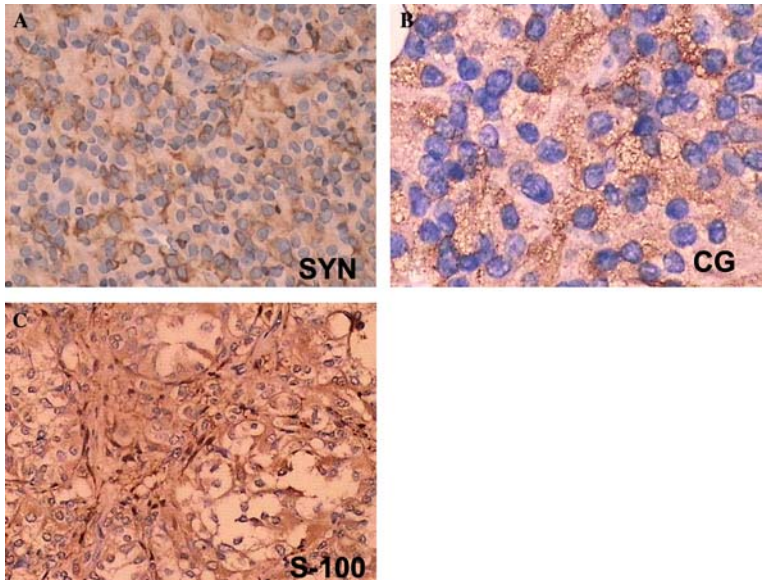

Figure 3. Immunohistochemistry showed positivity for (A) synaptophysin (SYN × 200) and (B) chromogranin (CG × 400) in the chief cells and (C) S-100 protein (S-100 × 200) in the sustentacular cells.

back, she was symptomatically better with reduction in the frequency and intensity of headaches.

Discussion

Paragangliomas account for 0.01–0.6% of all tumors in the head and neck region, of which about 80% are located either in the carotid body or in the glomus jugulare [13]. Although, normally there are no paraganglia in the central nervous system, both primary intracranial [2–11] and intraspinal [14,15] paragangliomas have been reported. Primary intraspinal paragangliomas are more common, with cauda equina being the most preferred location [1]. Rarely, paragangliomas affecting the thoracic [16] and cervical cord [15] have also been reported. Occasionally, extension from the mediastinal or retroperitoneal paragangliomas into the spine has also been documented [17].

Intracranial paragangliomas are largely a result of direct extension from the glomus jugulare or glomus tympanicum [18,19], with some cases being metastatic from other sites [15,20,21]. Few cases of primary intracranial paraganglioma have been reported [2–11], majority of which were in the sellar region or the pituitary gland [6–10]. A rare case of pineal gland paraganglioma has also been documented [11].

Paragangliomas in the CPA are also commonly extensions from the glomus jugulare or glomus tympanicum, constituting 1.7% of all CPA tumors and

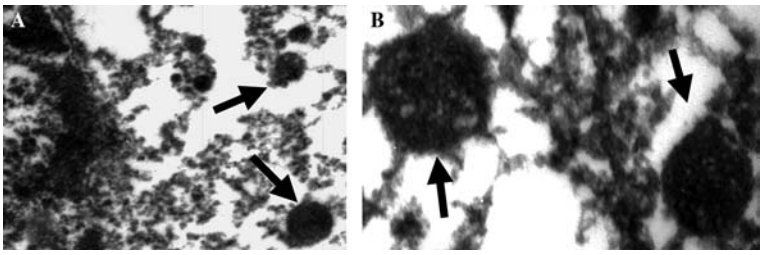

Figure 4. (A,B) EM showed membrane-bound neurosecretory granules (↑ arrow) in the cytoplasm of few of the 'chief cells'.

8.6% of all unusual CPA tumors [12]. They are locally aggressive and invade the CPA, thus destroying the temporal bone and mimicking acoustic neuroma [4]. Only two cases of primary paraganglioma in the CPA have been reported till date [4,5]. Jamjoom et al. [5] reported the first case of primary CPA paraganglioma in a 28-year-old male, where the tumor grew from the internal auditory meatus into the CPA, and was clinically, radiologically and intra-operatively indistinguishable from an acoustic neuroma. Guevera et al. [4] reported another similar case of paraganglioma in a 64-year-old male, arising from the anterior inferior cerebellar artery, with clinical and radiological features mimicking acoustic neuroma. However, intra-operatively the tumor resembled a meningioma. Recently, Prayson et al. [3] have documented a case of paraganglioma in an 11-year-old girl, apparently arising as a primary lesion in the left cerebellar hemisphere.

Unlike these three [3–5] cases, our patient had a moderately vascular tumor in the CPA without any vascular attachment or involvement of the internal auditory meatus, but having focal extension into the adjacent cerebellum, i.e. it had both an intraparenchymal as well as an extraparenchymal component. In view of these features, the possibility of a metastatic paraganglioma from an undiagnozed primary was considered in our case. However, since a thorough investigation did not reveal any apparent primary, this case was labeled as primary CPA paraganglioma.

The various theories existing for the occurrence of primary paragangliomas in the paraganglia-free cerebral tissue are: (i) *Anomaly of migration* [2,4]: inhibition of fetal migration from the neural crest, between the skull base and chest, when some paraganglia cells are found to lie in the CPA; (ii) *Anomaly of involution* [4]: incomplete regression of fetal paraganglia, with persistence of vestigial tissue till adult life.

Most paragangliomas display a benign behavior akin to WHO grade I tumors [1]. Features like intracranial extension, as seen in 14.6–20% [13,22] of all skull base paragangliomas, or local recurrences after surgery, which is generally attributed to inadequate excision, do not qualify as an expression of malignant behavior [1]. Only about 2–13% of all paragangliomas show malignant behavior manifesting as metastasis to the regional lymph nodes or to distant sites [13,23]. Malignancy rate is site-dependant with incidence being high for retroperitoneal tumors (28–42%) [1], as compared to carotid body tumors (2–9%) [1,21]. About 98% of all malignant paragangliomas are located in the abdomen [24]. Unlike other tumors, there are no reliable histological criteria to distinguish between benign and malignant paragangliomas [1,13]. Evidence of metastasis is the only definite criteria for malignancy [13,23]. Presence of mitosis, giant cell formation, necrosis and invasion of capsule and/or vascular spaces are merely features that suggest an aggressive behavior in a paraganglioma. Absence of or decreased number of sustentacular cells generally correlate with higher tumor grade and imply worse prognosis [13]. However, none of these features were present in our case, and this correlated well with signs of clinical improvement in the patient, as seen during the post-operative follow-up period.

In conclusion, we report a rare case of primary CPA paraganglioma with cerebellar extension. It is important to be aware of occurrence of a rare tumor in an unusual location, as highlighted in this case report. Further, it is essential to exclude the possibility of a metastasis, before labeling such rare lesions as primary [21]. Though the clinical, radiological and operative appearances at times may resemble neuroma or meningioma, but histopathological and EM diagnosis is imperative for final confirmation.

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