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Case Report

Calcifying pseudoneoplasms of the neuraxis (CAPNON): The great tumor mimicker☆

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ABSTRACT

Calcifying pseudoneoplasms of the neuraxis (CAPNON) are very rare intracranial lesions with less than 50 cases reported in literature. These are non-neoplastic in etiology and despite having unique imaging characteristics, are often misdiagnosed as a neoplastic condition like meningioma, chordoma and gliomas. These do not have any predilection for any age, gender or intracranial location and can be seen in a wide range of age groups. Despite having an imaging overlap with neoplastic conditions, CAPNONs have classic histopathologic findings including chondromyxoid matrix, palisading spindle cells and calcific or ossific metaplasia. As more cases are being described in literature the imaging features are also being better defined. We discuss the clinical, imaging and histopathological findings of 2 cases of CAPNON mimicking posterior fossa meningioma and glial neoplasm.

Introduction

Calcifying pseudoneoplasms of the neuraxis (CAPNON) are very rare non-neoplastic lesion of the central nervous system (CNS) presumed to be sequelae of remote trauma, infection and non-infective inflammatory conditions. These are also known as fibro-osseous lesion of the CNS and are slow-growing, solitary lesions, most frequently seen in the supratentorial compartment. These are more frequently extra-axial but can be intra-axial as well with characteristic histopathological finings [1,2]. As this is a relatively newly described entity, it is presumed that many of these conditions were historically misdiagnosed. The clinical presentation of these lesions is variable and depends upon the size and location of the lesions and range from headaches to seizures and motor deficits. Occasionally these might be asymptomatic and seen incidentally on imaging. The most common differential for extra-axial CAPNONs include meningioma and intra-axial-lesions tend to mimic cavernous malformation and glial neoplasm with calcification. The radiological findings are now better described and includes heavily calcific meningeal (extra-axial) or parenchymal (intra-axial) pseudo-masses with low signal on T1 and T2 weighted images and drop-out on

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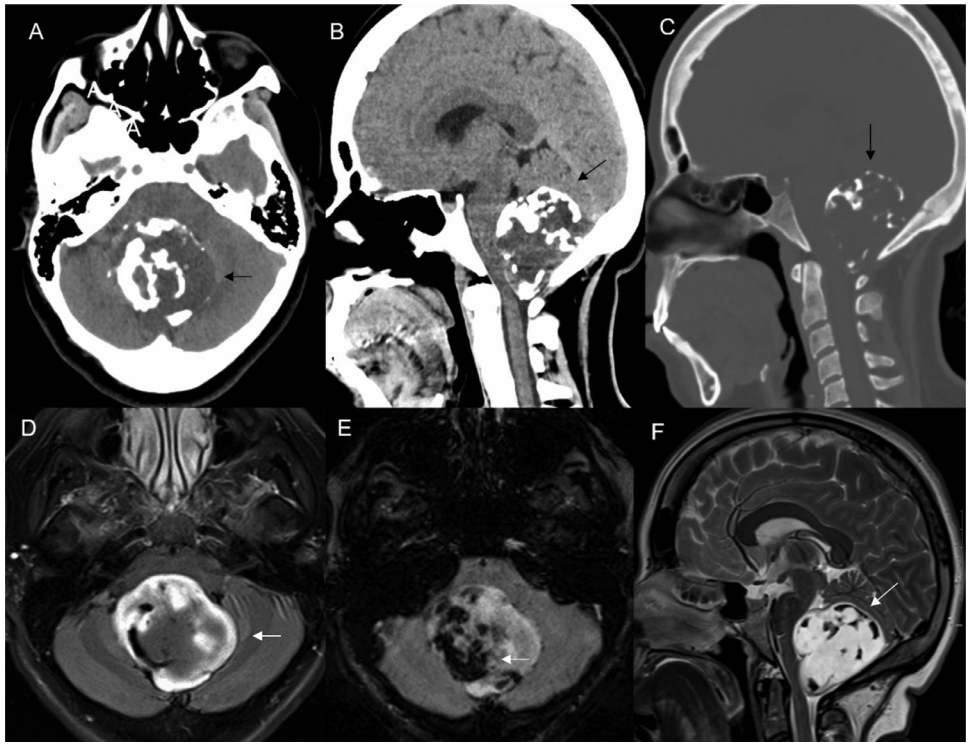

Fig. 1 – Case 1-Multiple CT images (A,B,C) reveal a large partially calcified lesion in posterior fossa in the region of cerebellar vermis (*black arrows*). MRI images (D,E,F) better characterizes the midline posterior fossa lesion centered along the cerebellar vermis (*white arrows*) with heterogenous T2 bright contents (F). Multiple areas of SWI dropout (*white arrow*) were noted within the lesion (E) corresponding to the calcification seen on prior CT.

gradient sequences (T2* and susceptibility weighted SWI). Lesions have bulky amorphous chunks of calcification as compared to fine stippled calcification seen in some tumors like chondrosarcoma. Surgical resection is curative for symptomatic lesions with rare recurrence and no malignant potential [2–4].

Case report

Case 1: CAPNON mimicking ependymoma

A 33-year-old female was referred to neurosurgery brain "tumor" found incidentally on head computed tomography (CT) after presenting to the emergency room following a motor vehicle accident. Head CT demonstrated a large partially calcified mass in posterior fossa in the region of cerebellar vermis with differentials including ependymoma and subependymoma (Fig. 1A,B,C). Mild mass effect and ventricular effacement was noted with no hydrocephalus. This was followed up by neurosurgery through imaging with no need felt for immediate intervention. However, she presented to the emergency room after few months with acute worsening of headaches and new facial paresthesias. Patient denied having any vision changes, loss of balance, with no coordination or speech issues. Given the large size of her lesion on prior CT, neurosurgery decided to admit the patient with plan to expedite imaging and possible surgical intervention. Magnetic resonance imaging (MRI) scan revealed a large "mass" in the midline posterior fossa centered along the cerebellar vermis with heterogenous T2 bright contents and poor enhancement (Fig. 1D-F). Multiple areas of SWI dropout were noted within the lesion (Fig. 1E) corresponding to the calcification seen on prior CT. There was severe mass effect and complete effacement of the fourth ventricle with flattening of the pons, no hydrocephalus. Imaging differentials included ependymoma and CAPNON. Subependymoma was felt to be less likely given the large size and bulky calcification. Neurosurgical excision was planned given the large size and worsening symptoms. This was approached through sub-occipital craniotomy with C1 posterior arch laminectomy. After durotomy, a large, calcified mass was seen in the midline which was very dense and fibrous. Sonopet was used to aspirate yellowish soft contents and then Spetzler tip on the Sonopet was utilized to drill through the calcification. Only a small portion of the mass was adherent to the cerebellar tonsils which was carefully dissected free with the microscissors and the mass was removed. The specimen obtained was an aggregate of calcified, yellow-pink tissue and was submitted to pathology for frozen and permanent sections following decalcification. Pathology revealed collagen-rich fibrous tissue and chondromyxoid, par-

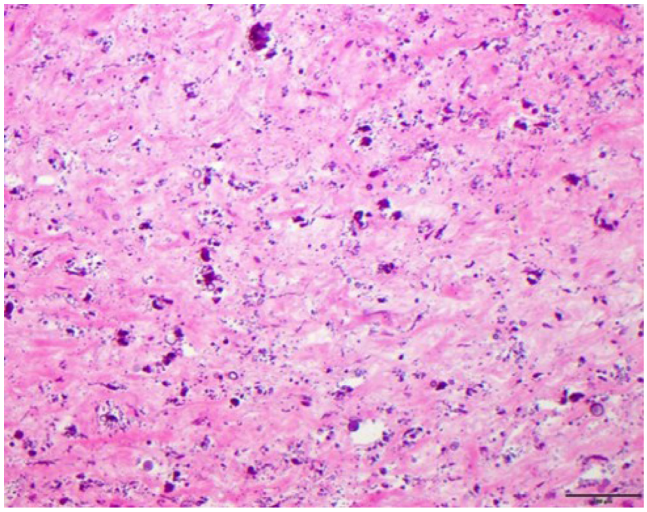

Fig. 2 – Hematoxylin and eosin staining (100X) reveals collagen-rich fibrous tissue and chondromyxoid, partially ossified matrix, with very hypocellular loose texture fibrous matrix, consistent with CAPNON.

tially ossified matrix, with very hypocellular loose texture fibrous matrix (Fig. 2). These findings were consistent with CAPNON.

Case 2: CAPNON mimicking cavernous malformation and meningioma

A 56-year-old man with a known history of "mass" in his posterior fossa, that was referred to as a scar, presented with significant headaches worsening over time. In addition, the patient developed new vestibular symptoms over the last few months. Review of his CT scans (Fig. 2A,B) showed a large partially calcified lesion abutting the tentorium on the right with adjacent parenchymal edema and mass effect. This lesion had slowly grown over the course of last few years. Subsequent MRI revealed a circumscribed lesion with bright T1 central contents, low T1 and T2 signal margins with signal-drop out on SWI (Fig. 2C-F). There was moderate adjacent cerebellar edema and mass effect including partial effacement of fourth ventricle. Imaging differentials included cavernous malformation, tentorial meningioma and CAPNON. Although, malignancy was felt to be unlikely, it was decided to proceed with surgical excision given the worsening symptoms. Suboccipital craniotomy was performed, and the lesion was approached using MRI-guided stereotactic localization. Under microscopic guidance, the top of the cerebellum was approached, and the mass was found to be adherent to the undersurface of the tentorium and quite firm. Notably, the tumor itself had a solid chalky consistency and had to be removed in a piecemeal fashion. At the completion of the surgery, there was no gross tumor visible. The tissue was fresh labeled "right cerebellar mass" and was a 4.5 × 3.0 × 1.3 cm aggregate of calcified, yellow-pink tissue, submitted to pathology for frozen and permanent sections following decalcification. The final pathology revealed CAPNON (Figure 3).

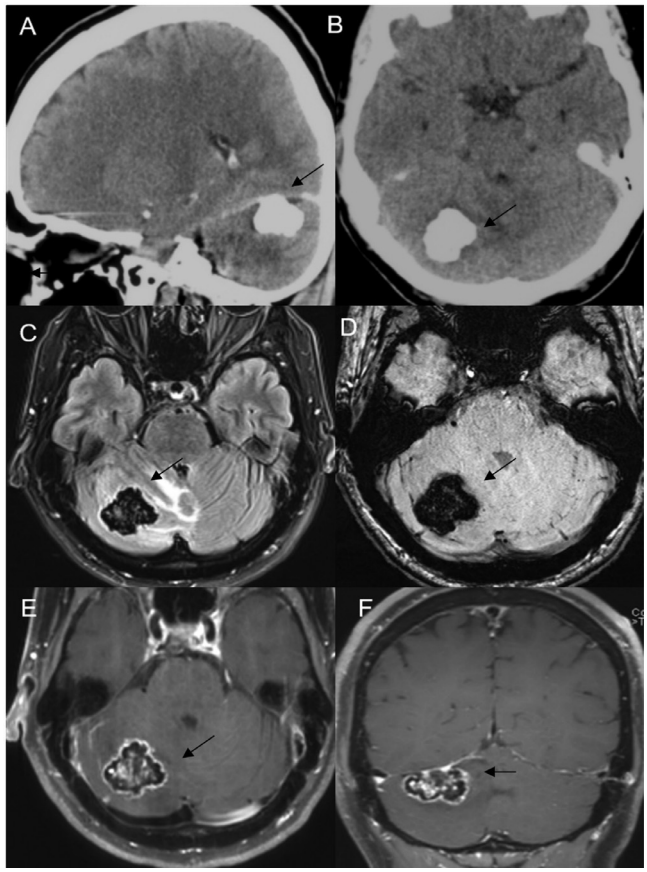

Fig. 3 – Case 2- Multiple CT images (A,B) reveals a partially calcified lesion in posterior fossa abutting the right tentorium (*black arrows*). MRI images (C,D,E,F) better characterizes the lesion which shows dark signal on FLAIR (C) with signal-drop out on SWI(D), heterogenous T1 bright signal with no enhancement (*arrows*) (E,F).Dark signal margins are noted on all sequences including T1 images.

Discussion

CAPNONs are rare lesions of the CNS affecting both children and adults with a modest male predominance [1]. They are slow-growing benign lesions presumably attributable to a reactive proliferative process induced by various trigger factors, such as infection, inflammation and injury, and may be possibly associated with inflammatory, degenerative, vascular and neoplastic diseases [2–4]. However, its underlying etiology is still non completely defined and other explanations have been proposed too, including neoplastic process [5], immune-mediated process [6], tissue calcinosis [7], and less likely, metaplastic transformation [8]. Total surgical resection is considered the gold standard of treatment and no additional chemotherapy or radiotherapy is needed [9], even if some cases of recurrence or local progression after surgery have been described in literature [10–12]. CAPNONs prognosis depends principally on both their anatomical location and dimension, in fact clinical symptoms are determined by the mass effect of the lesion instead of its pathological nature

[13]. Intracranial CAPNONs are most frequently intra-axial and supra-tentorial [4,14,15]. The main associated clinical symptoms are headache, seizures and focal neurological deficits [16], and may also be asymptomatic, as shown by the fact that some cases described in literature were incidentally identified at autopsy or during the course of radiological investigation for some other condition [17]. When CAPNONs are located in the skull base, neuropsychological alterations and cranial nerve deficits (particularly CN XI) may also be present, as a result of cerebellum and neurovascular structures involvement, respectively [18–23]. Moreover, in these cases, gross total resection may also be associated with a major rate of surgical complications, especially with greater lesion dimensions [13].

Here we reported 2 cases of CAPNONs, both located within the posterior fossa that were operated in our department. In the first case the tumor was intra-axial centered along the cerebellar vermis and the presenting symptoms were worsening headaches and paresthesias. In the second case, the tumor was extra-axial along the right tentorial leaf presenting with headaches and vestibular symptoms. The neuroradiological features of intracranial CAPNONs are consistent with a calcified mass resembling a fibro-osseous lesion [1]. Specifically, on CT CAPNONs appear as outlined solid lesions that are peripherally calcified, whereas on MRI they show some extent of hypointensity in both T1- and T2- sequences, with absent or minimal peripheral gadolinium enhancement, and are not associated to surrounding vasogenic edema [24]. Even though these features can be considered as CAPNONs key distinctive imaging findings, the radiological diagnosis of CAPNONs is not always easy since they can share some radiological elements with other numerous and more frequent calcified lesions. When CAPNONs are located in the skull base, as in our cases, they may imitate some intra-axial calcified lesions such as low-grade glial neoplasms (eg, oligodendroglioma, ependymoma), mixed neuronal-glial tumors (eg, ganglioglioma), vascular malformations (eg, cavernous malformation) and granulomatous/infectious processes (eg, tuberculosis) [2,4,15,18,25]. On the other hand, they can also mimic some extra-axial lesions, such as calcified meningiomas above all, particularly the psammomatous and metaplastic subtypes, followed by chordoma, chondrosarcoma and vestibular schwannomas [16,18,22,24]. In our first case, CAPNON mimicked a glial neoplasm (ependymoma). On imaging, ependymomas are common posterior fossa heterogenous density/signal neoplasm with varying degree of calcification. However, presence of prominent enhancing components, cystic areas and prelesional edema seen in ependymomas are useful demarcating features [24,26]. In our second case, CAPNON showed some radiological features in common with both cavernous malformation and meningioma Compared with CAPNONs, cavernous malformations show greater contrast enhancement and demonstrate on T2- scans a characteristic hyperintensity with a “popcorn” or "berry" pattern and a hemosiderin ring [26]. Meningiomas typically present some radiological findings rarely present in CAPNONs, including avid and homogeneous contrast enhance and adjacent dural enhancement appearing as a “dural tail” [15,24]. Furthermore, psammomatous meningiomas are commonly isointense on T1-scans and have mixed hypo- and hyperintensity on T2-scans, while metaplastic meningiomas show iso- or hypointensity on T1-scans and mixed or hypointensity on T2-scans [15]. Calcified meningiomas are associated with a perilesional vasogenic edema more often than CAPNONs [27]. Our lesions did not show any enhancement or perilesional vasogenic edema. Finally, regarding the aforementioned differentials: chordoma, chondrosarcoma and vestibular schwannoma typically show very high signal on T2-weighted images with variable enhancing component [24].

Our 2 cases attest and highlight the remarkable ability of CAPNONS to imitate other lesions by sharing with them some clinical and radiological elements. For this reason, CAPNON can be considered a “great tumor mimicker”, also considering the rarity of this entity in comparison to other conditions. The histopathological and immunohistochemical examination is necessary for the final diagnosis [24]. Intraoperatively, CAPNONs appear as well-demarcated, firm, and calcified irregularly shaped lesions [13] as also noted in both of our cases. The histopathological examination of CAPNONs displays nodular patterns of chondromyxoid matrix containing variable amount of granular/fibrillary materials, calcification and ossifications, peripherally surrounded by palisading spindle/epithelioid cells. Areas of osseous metaplasia, psammoma bodies and foreign body granulomas may be also identified [2,4,28]. Since these elements may be individually present with high variability, some CAPNONs may not have this classic histopathologic characterization. [2] In these cases, differential diagnosis may include infectious granulomatous diseases, foreign body reaction and neoplasms such as chordomas, chondro-blastomas, chondrosarcomas and metaplastic meningioma [4,24]. As regards immunohistochemistry, the peripherical palisading cells are positive for epithelial membranous antigen (EMA) and vimentin and are negative for glial fibrillary acidic protein, smooth muscle actin, and S-100 protein, even if the latter has been shown to be positive in some cases [6,24]. Among these, EMA may represent an immunohistochemical marker helpful to distinguish CAPNONs from calcified psammomatous and metaplastic meningiomas. In fact, CAPNONs usually display an inconstant EMA expression, typically confined linearly at the periphery of the chondromyxoid matrix, differently from meningiomas that instead express a widely EMA positivity[28]. This consideration also led Yang et al. to suggest that CAPNON express EMA only when meningeal involvement is present because its positivity is limited to the arachnoid meningothelial cells entrapped in CAPNON lesions [15]. Complete surgical resection is the treatment of choice with no reported case of recurrence or malignant transformation [15,24].

Conclusion

CAPNONs are rare lesions of the CNS with a slow-growing and benign behavior. Prognosis depends principally on both their anatomical location and dimension: skull base and large CAPNONs are associated with more numerous and worse clinical symptoms, along with a major rate of surgical complications. Even if CAPNONs show some distinctive imaging features, they often share similar radiological findings with other more common lesions, including low-grade glial neo-

plasms, cavernous malformations and meningiomas. For this reason, CAPNON can be considered a “great tumor mimicker”. The histopathological and immunohistochemical characterization is necessary for the final diagnosis, even though the etiopathogenesis is not yet completely understood.

IRB and patient consent

We acknowledge that our institution does not require IRB approval for case reports or image submissions. Written patient consent has been obtained as per Institutional policy. All the images included are non-identifiable images consistent with Elsevier policies.

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