Calcifying pseudoneoplasms of the neuroaxis

Calcifying pseudoneoplasms of the neuraxis (CAPNON) are rare tumors of unknown origin that can occur anywhere within the neuraxis. They are benign lesions that mimic ossified vascular lesions clinically and radiologically [1].

Calcifying pseudoneoplasms of the neuroaxis was first described by Rhodes and Davis in 1978 as an unusual intracranial fibro-osseous lesion component [2]

Pathology

Soukup et al. explored phenotypic spectrum of the entity with respect to possible histogenesis. They collected 5 cases of CAPNONs, performed a detailed morphological assessment, and performed an extensive immunohistochemical analysis (EMA, progesterone receptors, MUC4, SSTR2A, cytokeratin AE1/3, cytokeratin 18, GFAP, neurofilaments, desmin, nestin, synaptophysin, S100 protein, SOX10, CD56, Podoplanin, SATB2, ERG, CD45, and CD163) to elucidate the histogenesis. Furthermore, we performed NGS analysis of one case. The clinical course was benign in all cases. All lesions showed extensively calcified matrix in multilobular arrangement, with a palisade of osteoblast-like cells. Characteristic fibrohyaline matrix was notable in 4/5 cases, while one case was myxoid with rod-like calcifications. Metaplastic lamellar bone was present in 4/5 cases and psammoma bodies were present in 2/5 cases. In 4/5 cases, areas of entrapped glial tissue were present. Expression of EMA was focally present in 3/5 cases, SSTR2A and nestin in 2/5 cases, and progesterone receptor in 2/5 cases in rare cells. We did not observe concomitant expression of EMA, SSTR2A, and progesterone receptor in the same cellular subsets. In one case, NGS showed multiple chromosomal alterations and missense mutation in PIK3CA, attributable to the admixed meningothelial population compatible with meningioma. In another case, biphasic proliferation with myoepithelial phenotype was present. The lesions showed no lineage-specific immunoprofile. Additional pathology was identified in two cases, furthermore suggestive of a possible reactive origin of the lesion. [3].

Clinical features

The clinical presentation of patients with CAPNON is heterogeneous and generally depends on the location and size of the lesion. Symptoms are related to local compression or irritation of the adjacent tissue. In spinal affections, the predominant presentation is local or back pain. In contrast, intracranial CAPNON may present with not only headache but also seizures, cranial neuropathy, or motor deficits. In few cases, it was an incidental finding [4].

Diagnosis

The MR and CT imaging features in 4 patients with a pathologic diagnosis of “calcifying pseudoneoplasms of the neuraxis” were retrospectively reviewed. A neuropathologist also analyzed

the histopathologic features for typical and atypical patterns.

Imaging features were strikingly similar for all 4 patients. All lesions appeared T1 and T2 hypointense without vasogenic edema. All tumors had dense calcification, and 3 tumors showed minimal linear internal or rim enhancement on MR imaging.

CAPNON may mimic more common vascular malformations or neoplasms and are often not considered in the differential diagnosis of calcified lesions. CAPNON should be included in the differential diagnosis of a calcified mass with marked T1 and T2 Hypointensity and limited to no enhancement. Careful CT and MR imaging evaluation can suggest this entity, and this preoperative recognition may help subsequent management decisions [5].

Differential diagnosis

CAPNON should be considered in the imaging differential diagnosis of a heavily calcified lesion in neuroaxis and the differential will depend on the location. It is worth considering this entity to avoid aggressive surgical intervention in a lesion that is difficult to resect, as the natural history of CAPNON is generally indolent.

cavernous malformation

oligodendroglioma [6].

meningioma

choroid plexus papilloma [7].

Treatment

If resection is required then it is usually curative.

Outcome

Morbidity relates to operative complications and damage to structures adjacent to the mass

Case reports

A 56-year-old woman who presented with a history of recurrent headache for the previous six years. Magnetic resonance imaging (MRI) revealed a 2.3-cm-sized solid mass in the right frontal lobe that was surrounded by marked edematous areas. The lesion demonstrated dense calcification and avid enhancement. The lesion was initially diagnosed as oligodendroglioma, and then found to be CAPNON based on histopathology of a surgically resected tissue. Genetic analysis revealed a nonsense mutation in the CUL4B gene. The patient's condition appeared to reflect a reactive, rather than

neoplastic, process. Clinicians should be prepared to detect such pseudotumors histopathologically in order to avoid unnecessary differential tests of neoplastic or infectious diseases, as well as potentially harmful therapies [8].

A case report and review of the literature [9].

Thakur et al reported a CAPNON in the posterior fossa and its associated neuropsychological sequelae to provide further evidence for the role of cerebellum in cognitive function. They reported the clinical details, imaging, pre-operative neuropsychological assessment, histological features and management of a patient with such a tumour in the posterior fossa location. Detailed pre-operative neuropsychological assessment identified a number of cognitive deficits that had the hallmarks of dysexecutive syndrome. Post-surgery, there was considerable improvement, most notably on processing speed tasks and selected executive tests. This rare case provides further evidence for the role of cerebellum in cognitive function. [10].

An asymptomatic patient with an incidentally discovered right anterior cranial fossa mass with extension through the posterior and anterior table of the right frontal sinus and right superior orbital roof. Open biopsy was performed via a transblepharoplasty incision with pathological diagnosis of CAPNON. The biopsy approach was well hidden and resulted in minimal to no postoperative scarring and little postoperative pain. We present the first documented case of CAPNON involving the frontal sinus via the anterior cranial base. Given our experience, in a patient with a mass involving the frontal sinus and superior orbital rim, the transblepharoplasty approach provides excellent exposure and access for pathological diagnosis. Further, they recommended that CAPNON remain on the differential for aggressive appearing calcified masses of the anterior cranial fossa. [11].

Brasiliense et al. were the first to illustrate the development of multiple intraaxial CAPNONs and shed more light on the origin of these lesions. We discuss the case of a 67-year-old woman who presented with a six-year history of recurrent seizures. Magnetic resonance imaging revealed two similar heterogeneous intracranial masses in the ventral midbrain and left frontal white matter with indications of more aggressive behavior in the supratentorial tumor. The lesion was resected, and histopathological analysis showed tissue containing nodules of chondromyxoid material with a coarsely fibrillar matrix and focal alveolar pattern. Palisading cells were noted around the edges as well as dystrophic calcifications and osseous metaplasia, consistent with CAPNON. Interestingly, the patient had a previous history of multiple brain abscesses and a mycotic aneurysm. At her four-month follow-up visit, the patient remained seizure-free and there were no indications of residual tumor or recurrence. In contrast to previous reports, intracranial CAPNONs may manifest as multiple lesions and clinicians should include these tumors in the differential diagnosis of intra-axial calcified masses. The previous history of brain abscesses raises the suspicion of an abnormal proliferative process following an insult to the brain tissue as the underlying origin of these lesions [12].

An 18-year-old part-time teacher presented with headache and diplopia. Physical examination showed

partial left oculomotor palsy. Neurology examination was otherwise unremarkable. Cross-sectional imaging was arranged for investigation of third nerve palsy. On CT scan, the lesion was calcified, and on MRI, hypointense on T 1 and T 2 weightedimages with thin rim enhancement, resembling an atypical meningioma. CT angiogram showed no vascular connection. Following worsening diplopia and a slight increase in lesion size on follow-up MRI, the patient was re-reviewed in our regional skull base multidisciplinary team meeting, where a decision for excision was made. Pre-operatively, the absence of a vascular connection was confirmed on catheter angiogram. Histopathological examination demonstrated features typical of calcified pseudoneoplasm of the neuraxis, with extensive metaplastic calcification with stroma containing variable fibrovascular tissue and focal inflammatory cell infiltrates, spindle and epithelioid cells, and psammoma bodies at the rim of the lesion. Following surgery, the patient had persisting diplopia. He remains under clinical review. As surgical resection is considered curative, no further imaging follow-up is planned [13].

A case of a patient with an incidentally found calcifying pseudoneoplasm involving the cervicomedullary junction with further involvement of the vertebral artery and the hypoglossal nerve [14].

A 48 year old male with complex partial seizures who had a right temporobasal calcified lesion that clinically and radiologically mimicked an oligodendroglioma. Histopathology revealed a large necrotic lobulated mass with admixture of chondromyxoid zones, nodular fibrovascular stroma, metaplastic calcification and ossification in varying proportions [15].

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