Juvenile psammomatoid ossifying fibroma of the neurocranium

Report of four cases

JUVENILE PSAWMOMATOID OSSIFYING FIBROMA (JPOF) is a benign fibroosseous lesion predominantly arising within the paranasal sinuses in children and young adults. The lesion is characterized by a fibrous stroma with growth occurring in vague whorling patterns interspersed with calcified spheroid ossicles resembling psammoma bodies. Secondary extension of a sinonasal JPOF into the cranial cavity and three cases primarily affecting the neurocranial bones to increase clinical awareness of this uncommon tumor, which may be easily mistaken for meningioma. Moreover, the absence of activating missense mutations of the GNAS1 gene in two cases strongly argues against a relationship between JPOF and fibrous dysplasia.

KEY WORDS • juvenile psammomatoid ossifying fibroma • meningioma • fibrous dysplasia • children

Case 1
This 15-year-old boy harbored a large mass filling the ethmoid and sphenoid sinuses, which was accidentally discovered following a minor head injury. Results of a neurological examination were normal, his sense of smell remaining intact. On MR images, the mass appeared to be well-demarcated from surrounding bone and displayed moderate contrast enhancement. Extension into the anterior cranial fossa was apparent (Fig. 1). The tumor was accessed using a lateral rhinotomy and a bifrontal craniotomy. The advantage in this combined approach is clear exposure of the tumor and adjacent areas of tumor extension (orbit, cranial vault, and frontal and ethmoid sinuses). Intraoperatively, the tumor appeared to be encased by a bone shell. Complete removal could be achieved and the defect of the frontal craniobasis was covered by split calvarial bone and a periosteal flap. Eight months later, the patient continues to be free of neurological symptoms. A follow-up CT scan has not revealed recurrent tumor growth thus far. A follow-up visit will occur every 6 months.

Case 2
This 24-year-old man suffering from juvenile rheumatoid arthritis harbored a circumscribed osseous lesion in the frontoparietal skull, which had been accidentally discovered 5 years earlier. Results of a general physical and a neurological examination were normal. Because annually performed radiography (Fig. 2) revealed progression, the lesion was
The patient’s postoperative course was uneventful. Six months postsurgery, the patient continues to be free of symptoms and is followed up closely. Clinical examination has indicated no recurrent tumor growth so far. A follow-up visit will occur every 6 months.

Case 3
This 27-year-old woman harbored a lesion of the parietal skull, which was discovered in the course of a diagnostic work-up for vertigo. The results of the neurological examination were normal. A CT scan revealed an expansive intraosseus lesion with well-defined borders (Fig. 3). The tumor was excised and the postoperative course was uneventful. Eighteen months later, the patient continues to be free of tumor growth, and will continue to be followed up.

Case 4
This 23-year-old man demonstrated bulging in his left temple. Except for this finding, the results of a physical examination were normal. A CT scan (Fig. 4A) and an MR image (Fig. 4B) revealed an expanding mass with inhomogeneous contrast enhancement within the temporal bone. A craniotomy was performed and the tumor, infiltrating soft tissue and dura mater and displacing the temporal lobe, was removed completely. One year later, the patient continues to be free of symptoms. Neurological examination and results of CT scans have been unremarkable thus far, but follow-up will continue.

Histopathological Findings
In all cases, the tumor consisted of a cellular fibrous stroma with growth occurring in fascicles and vague whorling patterns interspersed with clusters of acellular rounded ossicles. These ossicles were calcified to some extent and thus resembled psammoma bodies (Fig. 5). The tumor cells displayed ovoid or elongated nuclei and spindle-shaped eosinophilic cytoplasms. Occasionally, multinucleated giant cells were noted. The Ki-67/MIB-1 proliferation index was low (< 3%) and epithelial membrane antigen immunoreactivity was absent.

Mutational Analyses
Nondecalcified paraffin-embedded surgical specimens obtained in the patients in Cases 1 and 3 were available for DNA extraction and analysis of the \( GNAS1 \) gene by using the LightCycler system (Roche Diagnostics Corporation, Mannheim, Germany). No activating missense mutations of the \( GNAS1 \) gene were detected.

Discussion
A multitude of synonyms have been used to denominate JPOF. After the initial phrase “osteoid fibroma with atypical calcifications,” the terms for this fibro-osseous lesion have included “psammo-osteoid fibroma,” “psammomatosus desmo-osteoblastoma,” and juvenile or aggressive “psammomatoid ossifying fibroma.” It has also been classified as a subtype of ossifying fibroma, a juvenile active ossifying fibroma, or an extravaginal variant of cemento-ossifying fibroma has been related to fibrous dysplasia.

As shown in Fig. 6, a JPOF in a neurocranial location has only rarely been reported: in addition to one definite case of parietal psammomatoid ossifying fibroma, three cases arising in the parietal bone—designated as “ossifying fibroma,” “desmo-osteoblastoma,” and “cemento-ossifying fibroma”—might have represented JPOF, whereas the...
Neurocranial psammomatoid ossifying fibroma

Histological characteristics and exact site of eight juvenile active ossifying fibromas in association with cranial sutures (< 8% of all cases in this large series) remain uncertain. Juvenile psammomatoid ossifying fibroma has a distinct histomorphology that includes the presence of rounded ossicles, which are calcified to a varying extent. Their concentric or laminated appearance is, in some respect, similar to psammoma bodies. Given this superficial similarity, JPOF might be easily mistaken for meningioma. Indeed, reports of sinonasal meningioma and intradiploic meningioma of the orbita may have actually represented JPOF. Importantly, in JPOF with a neurocranial location the likelihood of a misdiagnosis is certainly increased, because clinical and radiological findings might be strongly indicative of meningioma. If considered as a differential diagnosis, however, JPOF can be readily distinguished from meningioma not only morphologically, but also by the absence of distinct epithelial membrane antigen immunoreactivity.

Some authors relate JPOF to fibrous dysplasia, because calcifications may also occur in the latter. In contrast to fibrous dysplasia (as in Cases 1 to 3), however, JPOF is usually well-demarcated from surrounding bone, presenting as an expansive but circumscribed lesion on neuroimaging studies. Given that activating missense mutations of the GNAS1 gene have been detected in virtually all cases of fibrous dysplasia examined thus far, their absence in the present cases of JPOF provides additional evidence against a relationship with fibrous dysplasia.

The potential in JPOF toward locally aggressive behavior

Fig. 4. Case 4. A noncontrast CT scan (A) and a Gd-enhanced transverse T1-weighted MR image exhibiting an expanding mass with inhomogeneous contrast enhancement within the temporal bone.

Fig. 5. Case 2. Photomicrographs exhibiting histopathological findings. A: All tumors consisted of a cellular fibrous stroma interspersed with clusters of acellular calcified ossicles resembling psammoma bodies. B: At a higher magnification, the tumor cells containing ovoid or elongated nuclei, spindle-shaped cytoplasms, and growth in vague whorling patterns can be appreciated. Bar 100 μm. H & E.

Fig. 6. Schematic illustrating the localization of lesions in the presented cases (closed circles), compared with those of previously described cases of JPOF (open circles).
is highlighted by Case 4, in which the tumor infiltrated soft tissue and dura. Interestingly, the histological features as well as the Ki-67 proliferation index were comparable to those in other cases and did not predict aggressive tumor growth. Complete resection is the treatment of choice and generally curative. The tendency for locally invasive growth may occur.

Conclusions

In summary, JPOF in a neurocranial location may be easily mistaken for meningioma. This tumor can be clearly distinguished from fibrous dysplasia radiographically and by the absence of GNAS1 gene mutations. Despite its benign histological features, infiltrative growth may occur.

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References