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CASE REPORT

Chondromyxoid Fibroma of Sphenoid Sinus with Unusual Calcifications: Case Report with Literature Review

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Abstract Chondromyxoid fibroma (CMF) is a rare benign primary tumor which usually affects the metaphyses of the long bone of the lower extremities in childhood and young adults. Rarely, CMF occurs in the skull base and parasinuses, which may be difficult to distinguish from chondrosarcoma or chordoma and other tumors in the head. It is composed of chondroid, myxoid, and fibrous tissue growth in a lobular pattern, infrequently with calcifications. We report one case of CMF involving the sphenoid sinus mimicking a chondrosarcoma. The tumor mass showed calcifications on images and histology.

Keywords Chondromyxoid fibroma · Sphenoid sinus · Calcification

History

A 52-year-old woman presented with vertigo at the ENT clinic. The patient had no other obvious sinonasal signs or symptoms, and she had had no other medical or surgical history in the past. An endonasal examination was performed, and a well-circumscribed, firm, lobulated sphenoid mass was encountered.

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Radiographic Features

A computerized tomographic scan without contrast was performed, demonstrating a heterogeneous, partially calcified a 1.8 × 1.8 × 2 cm mass, located along the intrasinus septum and floor of the sphenoid sinuses. The mass was well-circumscribed, and partially eroded the floor of the sphenoid sinus; it bulged into the sphenoid cavity as well as protruding slightly into the left nasal cavity (Fig. 1). Since the lesion contained calcified matrix and was in the midline, the differential diagnosis included cartilaginous lesions such as enchondroma and chondrosarcoma as well as chordoma. The tumor was removed endoscopically. The curetted samples consisted of fragments of slightly lobulated, myxochondroid tissue with firm areas of calcification.

Histologic and Immunohistochemical Features

Fragmented tissue sample from the mass was fixed in neutral formalin and routinely processed for paraffin embedding and stained with hematoxylin and eosin. The histological morphology revealed a well-circumscribed, lobulated tumor consisting of myxochondroid matrix in which the tumor cells were dispersed either in loose and random aggregates with long cytoplasmic processes disappearing into the tumor matrix, or as spindle cells resembling fibroblasts. At low magnification, the tumor cells were organized into condensed areas of increased cellularity demarcating pseudolobules of looser areas of myxochondroid stroma of less cellularity; the tumor replaced the bone and extended almost into the sphenoid sinus. In addition, large and small aggregates of amorphous calcification in the myxoid stroma corresponded to the

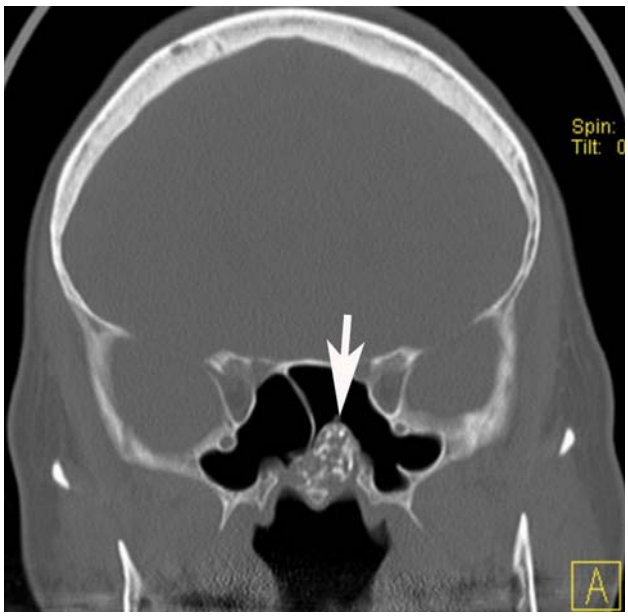

Fig. 1 A non-contrast CT scan of the paranasal sinuses showing a heterogeneous mass with fine calcifications, involving the left sphenoid sinus. The mass partially eroded the floor of the sphenoid sinus and protruded into the left nasal cavity (*arrow*)

radiodensities in the CT scans, but no actual tumor necrosis was seen (Fig. 2a–c). There was no hyaline cartilage differentiation anywhere in the tumor matrix. Immunohistochemical stains were positive for vimentin (Fig. 3a) and smooth muscle actin (Fig. 3b), and negative for S-100 protein, CD34, cytokeratin AE1/AE3 and EMA.

Discussion

Chondromyxoid fibroma (CMF), first described in 1948 by Jaffe and Lichtenstein [1] is an uncommon benign cartilage congener tumor, which is rare (<1% of primary bone tumors), which often occurs in children and young adults. It usually involves the metaphysis of long bones; the most common site is the proximal tibia [2]. Patients commonly complain either of pain or a non-tender mass; the duration of symptoms is highly variable [3, 4]. Only 1–2% of all cases of Chondromyxoid fibroma reported have occurred in the head and neck region [5]. It may affect facial bones, most commonly in mandible and less commonly in the nasal cavity and paranasal sinuses [6–9]. In the paranasal sinuses, it has been reported that CMF occurs in the ethmoid sinus [5, 10] frontal sinus [11, 12] and sphenoid sinus [7, 11, 13–15] (Table 1). Some authors have described a female predisposition for intracranial tumors [16, 17]. In the series of 33 cases reported by Karkuzhali et al. [18], the

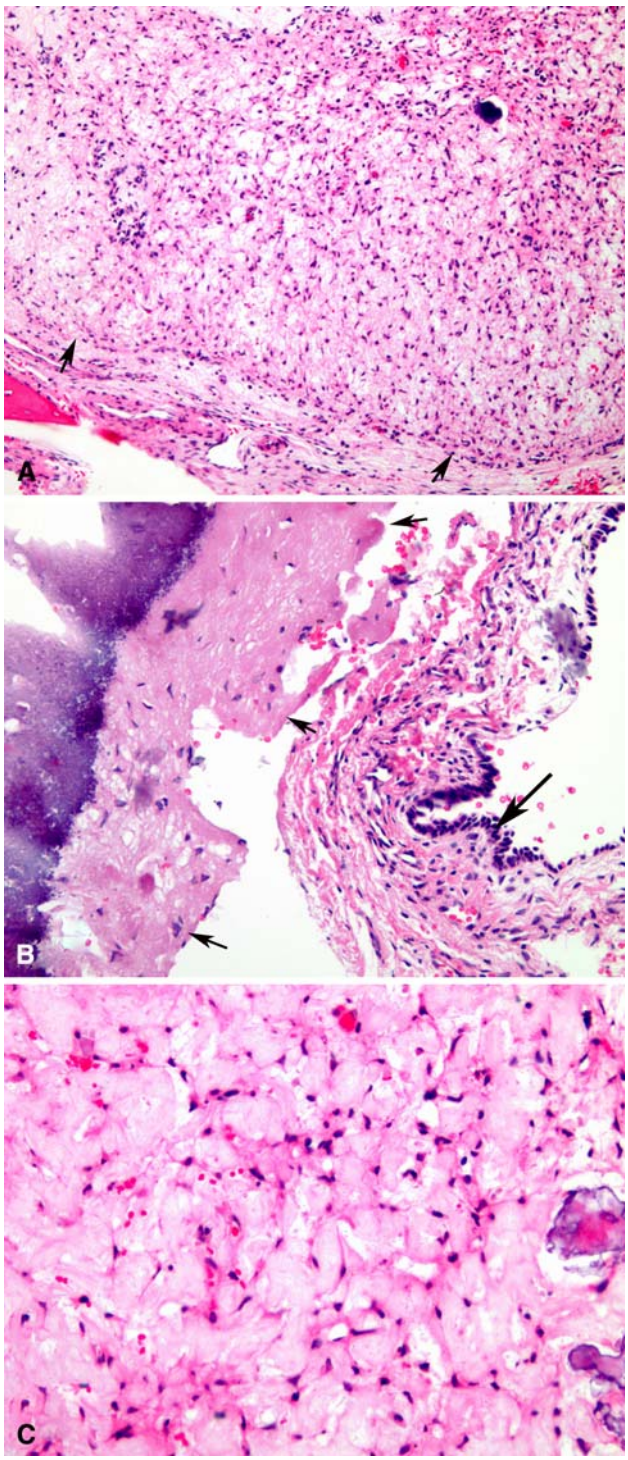

Fig. 2 Low magnification of tumor mass shows a well circumscribed cartilaginous neoplasm, with lobular border and peripheral hypercellularity (*arrowheads*) (**a**). Section shows the tumor (*arrowheads*) is adjacent to the sphenoid cavity lined by sinonasal mucosa (*arrow*), with calcification on the left side (**b**). High magnification shows tumor is composed of chondromyxoid matrix with stellate fibromyoblastic cells and calcifications (**c**)

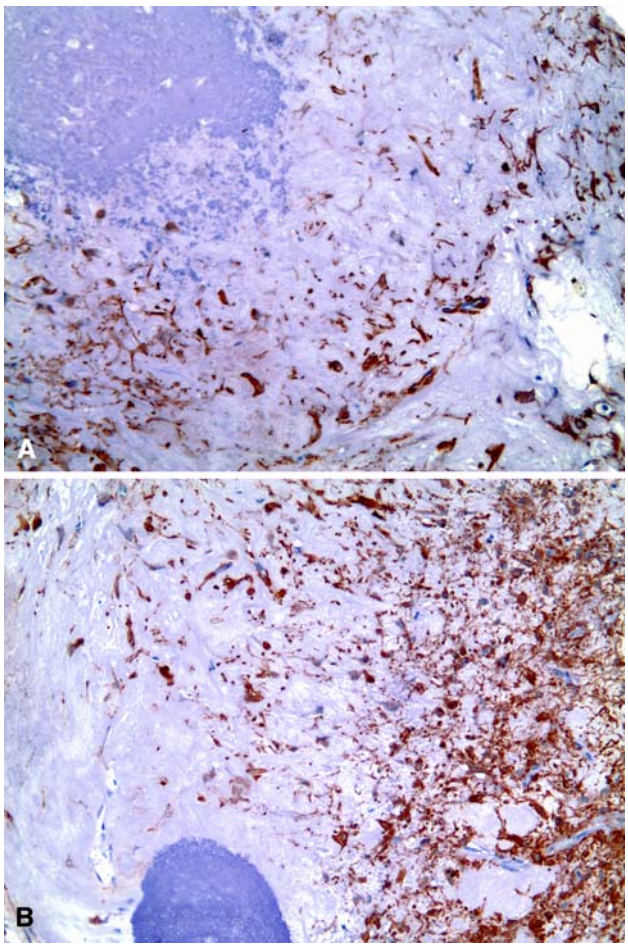

Fig. 3 Immunostains show tumor cells were positive for vimentin (**a**) and smooth muscle actin (**b**)

most common site was in the frontal bones, followed by the sphenoid bone, occipital bones, temporal bones and clivus. The patients were predominantly in their fifth decade of life.

Chondromyxoid fibromas grossly are well-circumscribed, solid, and glistening tan-gray masses showing a variety of histological features. The typical morphology of CMF is that of stellate and spindle-shaped cells arranged in a myxochondroid matrix, characteristically with denser cellularity at the periphery of loose matrix dividing them into pseudolobules (Fig. 2a). The neoplastic cells are spindle-shaped or stellate myofibroblasts, with occasional multinucleated giant cells seen in the cellular areas. Foci of calcification are usually not a prominent feature pathologically unless patients are older or the lesions are on or near the surface of bones (Fig. 2b, c) [19].

Immunohistochemical analysis usually highlights the immunoreactivity of tumor cells to vimentin (Fig. 3a), smooth muscle actin (Fig. 3b), Desmin, and sometimes for S100 protein and CD34. In general, they are negative for pancytokeratin, EMA and GFAP, and have a low proliferative rate with Ki-67. SOX9, a new marker, has been reported in the recognition of the chondroid nature of the CMF and may be useful as an adjunct the diagnosis of CMF [9].

Calcifications may be noted either radiographically—in 3–16% of cases [3, 20]—or microscopically—in 7–27% of cases [3, 18, 20, 21]. Yamaguchi and Dorfman [22] have reported that patients with calcifications tend to be older (mean age 46 years) than those without calcifications (21 years), and that calcifications are associated with a longer duration of symptoms (43.2 months) compared to tumors without calcification (6.4 months). Calcifications therefore appear to be related to the chronicity of the tumor (and to its location—see above).

Recent, a pericentric inversion of chromosome 6 [inv (6)(p25q13)] has been proposed as a specific genetic marker for CMF of long bone. [23] It has been suggested that several distinct breakpoints on chromosome 6 are nonrandomly involved in CMF. The other cytogenetic case report on a nasal cavity CMF has shown insertion between chromosome 6 and 19 in a nasal CMF [24].

Wu et al. [11] have evaluated the radiologic appearances of CMF in a large series. Of 191 cases, 87% had a purely lucent matrix, and 15% demonstrated some mineralization, most commonly in the form of calcifications. The

Table 1 Reported cases of chondromyxoid fibroma of the sphenoid sinus

Cases	Age/sex	Location	Treatment	Follow up	Authors
1	26/M	Petrous-sphenoid bone	Complete surgery removal	NA	Frank et al. [13]
2	66/F	Sphenoid sinus	Surgery	Local recurrence after 1 year; curetted, 6 months FOD	Nazeer et al. [6]
3	66/F	Sphenoid-occipital bone	Surgery and radiation	Local recurrence after 6 months; after radiation, 20 months FOD	Keel et al. [14]
4	65/F	Sphenoid-occipital bone	Surgery	26 months FOD	Keel et al. [4]
5	NA	Sphenoid sinus	NA	NA	Wu et al. [11]
6	44/M	Sphenoid sinus	Surgery	FOD	Vernon et al. [15]

NA not applicable, *FOD* free of disease

medullary margins were characteristically well defined: the majority had a scalloped, sclerotic rim. Cortical thinning or expansion, periosteal new bone formation, and poorly defined margins may also be present. The presence of calcifications on CT should raise the suspicion of a cartilaginous or a chondroid matrix-containing lesion. The typical MRI presentation is with low signal intensity on T1-weighted images and heterogeneous high signal intensity on T2-weighted images.

CMF is a benign tumor that may be locally aggressive. The recommended treatment is en bloc excision with a margin of normal bone. However, curettage is also an acceptable method in cases of difficult access, or in close apposition to vital structures. In cases treated with curettage, close surveillance is recommended due to the incidence of recurrence following incomplete resection. Radiation therapy is generally avoided due to reported cases of malignant transformation [18, 21].

Appropriate diagnosis of this benign entity is essential due to its potential misdiagnosis as chondrosarcoma, which carries a poorer prognosis and may require more radical surgery [7, 14]. This patient's CT scan was read as "suggestive of chondrosarcoma"—an important differential diagnosis, particularly in the location of basal skull. In the head and neck region, chondrosarcoma most commonly affects the skull base, with rare tumors occurring in other bones, such as maxilla, mandible and the laryngeal cartilages. Radiographically, chondrosarcomas are destructive lobulated masses that also show calcifications that tend to be stippled, arc-shaped, or ring-like rather than amorphous. Morphologically, they are composed of hyaline cartilage, often with myxoid changes. The chondrocytes are atypical with enlarged nuclei in which nuclear details are often visible. The immunophenotype of chondrosarcoma usually is positive for vimentin and S-100, but it does not express epithelial markers such as keratin or EMA. Chondrosarcomas are malignant tumors with 5-year disease-specific survival rates in the range of 40–80%. They often require radical resection to obtain negative margins, and other methods of tumor therapy have met with little success [25].

The other important differential diagnosis for a tumor presenting in this location is chordoma, especially the chondroid variant. Chordoma is a slow-growing malignant neoplasm arising from ectodermally derived notochordal remnants and accounts for less than 5% of primary bone tumors. Morphologically, chordoma is composed of cohesive cells with abundant, bubbly eosinophilic cytoplasm, known as physaliferous cells. Immunohistochmistry is useful to distinguish it from CMF. Unlike CMF, chordomas are positive for S-100 protein, cytokeratin, and EMA.

Chondromesenchymal harmatoma is the other differential from intranasal cartilaginous tumors. However, this tumor usually affects children in the first few weeks or months of life. Morphologically, these tumors present nodules of admixture of various mature cartilage and myxoid spindle fibrous stroma elements, collagen, and giant cell rich aneurysmal bone cyst-like features. The pathogenesis of this tumor is still not well understood.

After this biopsy, this patient's tumor was determined to be CMF, permitting total endoscopic resection with a rim of normal bone.

Although thorough curettage may be able to remove most of the tumor, a relatively high incidence of recurrence has been reported due to the inaccessibility the entire tumor volume to surgery in intracranial anatomical locations. Since the tumor cannot be completely excised technically, there is a potential to have local recurrence [21, 26].

In summary, we have presented CMF of the sphenoid sinus; a rare tumor in a very uncommon location. After surgery, the patient has remained free of disease for 2 years with no evidence of local recurrence. Because of some similarities between CMF and chondrosarcoma on imaging and morphology, it is important to recognize this rare entity when it occurs in an unexpected location, allowing the clinically optimal management and avoiding overtreatment.

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