Posttraumatic Reactive Fibrous Bone Neoformation of the Anterior Skull Base Mimicking Osteosarcoma

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ABSTRACT

Objectives: Malignant bone tumors and fibro-osseous bone lesions of the skull base are uncommon, although fibrous dysplasia in this anatomic location is not a rare condition. In general, fibro-osseous lesions of the skull are often difficult to classify on either clinical presentation, radiological findings, or histological presentation alone. The objective of this article is to present a probably important differential in the management of bony neoformations of the skull and to highlight the diagnostic difficulties when dealing with osseous and fibro-osseous conditions affecting the craniofacial bones. **Design:** We present here a novel case of posttraumatic reactive fibrous bone neoformation of the anterior skull base mimicking osteosarcoma in a 16-year-old boy. **Results:** Diagnostic steps, clinical, histological, and radiological presentation, as well as surgical treatment are described in detail. The international medical literature concerning reactive fibrous bone neoformations is reviewed, and the problem of adjusting the correct differential diagnosis when dealing with fibro-osseous bone lesions of the skull base is discussed. **Conclusions:** The highlights of this case are an uncommon location of a rare pathological entity, which might constitute an important differential of fibro-osseous conditions affecting the craniofacial bones.

KEYWORDS: Skull base, bone neoplasm, fibrous dysplasia of bone, bone diseases, osteosarcoma

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Tumors of the anterior skull base may clinically become apparent with exophthalmos, disorders of globe motility and diplopic images, compression syndromes, as well as frontal cephalgia and sinusitis due to drain obstruction of the paranasal sinuses. The most common osseous and fibro-osseous conditions affecting the craniofacial bones are osteoma and fibrous dysplasia. Furthermore, ossifying fibroma and benign osteoblastoma are reported to appear in this location.¹ Malignant bone tumors of the head and neck region in general and the skull base in particular are rare.¹ Nevertheless, ~6% of all osteosarcomas and from 1 to 6% of all Ewing's sarcomas affect the skull, and these typically arise in a child or adolescent in the first three decades.^{2,3} Osseous and fibro-osseous conditions affecting the craniofacial bones are often difficult to classify on either radiological imaging, clinical symptoms, or histology alone and need clinicoradiopathologic correlation for definitive diagnosis.^{1,4} Posttraumatic reactive fibrous bone neoformation is a rare pathological entity and was almost exclusively found in ribs up to now. It has been described as a discrete bone tumor entity and previously also been documented as fibro-osseous reparative lesion (FORL) or fibro-osseous reparative pseudo-tumor (FORP).⁴⁻⁶

CASE REPORT

A 16-year-old male patient presented to our department with a tumor of the left medial orbital roof and the nasion. The tumor had been increasing in size for about 1 year and the boy showed exophthalmos, diplopic images, and disorders of globe motility. Computed tomography and magnetic resonance imaging of the skull was performed and showed a calcified neoformation of the anterior skull base, 3 to 4 cm in diameter, between the anterior ethmoid cells, the left orbit, and the left frontal sinus (Fig. 1). The tumor showed an unsharp demarcation, accumulated contrast medium, and seemed to infiltrate the dura and to extend into

the anterior cranial fossa. Furthermore, the tumor-adjointing bone showed signs of reactive transformation and destruction. Skeletal scintigraphy revealed increased metabolism in the tumor region. Because of these radiological findings and the age of the patient, the predominant tentative diagnosis at this point was primarily a malignant bone tumor of the skull base, especially osteosarcoma. As the neoformation affected the skull in a young patient, fibrous dysplasia was another clinical differential.

A biopsy of the tumor was taken via Killian's approach. During surgery, it was noticed that the corticalis of the bony base of the left frontal sinus was partly destroyed by the tumor. The neoformation was also adherent to the dura and showed intracranial extension. These findings underlined the tentative diagnosis of a malignant bone tumor. Nevertheless, histology showed a fibrous stroma with distinct signs of reorganization and strong vascularization but without any signs of malignancy (Fig. 2). Material was also sent to the reference center for bone tumors in Basel (Switzerland), where a primary bone tumor as well as fibrous dysplasia could be excluded by histological investigations. Histologically, the lesion displayed metaplastic woven bone trabeculae arranged in an arcuated fashion within a highly vascularized fibrous stroma without atypias or mitoses. Infiltrations of lymphocytes could sparingly be found. Some areas of anastomosing bone trabeculae showed rims of attached osteoblasts and transformation of the metaplastic woven bone to lamellar bone. Between this newly formed bone trabeculae, signs of hemorrhage with evidence of brown pigment resembling hemosiderin and fresh extravasates of erythrocytes were seen. Also, distinct signs of reorganization with notably enlarged osteoclasts could partly be found. Characteristic features of fibrous dysplasia, such as irregularly shaped woven bone trabeculae, which are arranged in a peculiar fashion resembling Chinese letters but lacking the anastomotic arrangement and osteoblastic rimming, as well as the complete maturation arrest of woven bone, not being transformed to lamellar bone, were absent.

The question regarding a preceding trauma was raised by the pathologist, as histology showed characteristic features of a fibro-osseous reparative lesion. We therefore explored the patient's history for preceding trauma, and the boy reported that a traumatic laceration after a bike accident had occurred in the tumor region 4 years earlier. On

clinical examination, we found a small, inconspicuous scar close to the left eyebrow.

Taking all findings into consideration, the diagnosis of a "posttraumatic reactive fibrous bone neoformation" was made in an interdisciplinary conference with pathologists and radiologists. Tumor resection was performed by a navigated

Figure 1 Computed tomography and magnetic resonance imaging of the anterior skull base. (A) A calcified neoformation, 3 to 4 cm in diameter, between the anterior ethmoid cells, the left orbit, and the left frontal sinus. (B) The tumor accumulated contrast medium, showed an unsharp demarcation, and seemed to infiltrate the dura and to extend into the frontal cranial fossa. (C) The tumor-adjointing bone showed signs of reactive transformation and destruction.

Figure 2 A biopsy of the tumor in hematoxylin-eosin staining. Histological examination showed a fibrous stroma with distinct signs of reorganization, strong vascularization, and signs of hemorrhage with hemosiderin pigment but without any signs of malignancy (original magnification A: 40 $\times$, B: 100 $\times$).

osteoplastic transfrontal sinus approach with duraplasty (Fig. 3). Navigation support was used to control the tumor resection accurately, as the loss of anatomic landmarks and the need to resect tumor along the dura of the anterior skull base makes computer-assisted surgery a helpful instrument.⁷ Exophthalmos, diplopic images, and disorder of globe motility greatly improved after surgery. The patient is currently 26 months from diagnosis with no evidence of disease. Clinical and radiological control investigations have been normal without signs of residual or recurrent tumor, supporting the benign diagnosis of the lesion.

Figure 3 Intraoperative aspect after bitemporal coronal incision. Tumor resection was performed by a navigated osteoplastic transfrontal sinus approach with duraplasty.

DISCUSSION

Osteosarcoma is a highly malignant bone neoplasm that accounts for approximately 20% of all malignant bone tumors and has a marked propensity for dissemination and metastatic spread. It typically arises in a child or adolescent in the first and especially in the second decade with a slight preference of the male gender. The sites of affection are primarily the metaphyses of long tubular bones, particularly the region of the knee, with the leading clinical symptoms of local pain and local swelling. With the treatment of choice, a combination of initial chemotherapy, followed by radical surgery and adjuvant chemotherapy, long-term survival rates of more than 50% can be achieved. Despite a series of typical histological and radiological features that characterize osteosarcoma, the morphologic pattern and radiological behavior is to a great extent variable and may cause major diagnostic difficulties. Despite the fact that malignant bone tumors of the craniofacial bones in general and the skull base in particular are rare, ~6% of all osteosarcomas arise within the skull.^{1-3,7-9}

Malignant bone neoplasms and benign space-occupying osseous lesions of the skull most commonly become apparent with local pain and local swelling like they do in extracranial location. Furthermore, bony neoformations of the anterior skull base may clinically become apparent with exophthalmos, disorders of globe motility, and

diplopic images resulting from the proximity to the orbital cavity and the affection and dysfunction of orbital structures. Compression syndromes can result from the interference of cranial nerves. Frontal cephalgia and sinusitis is often due to drain obstruction from the paranasal sinuses.^{1,10}

As malignant neoplastic bone tumors are fortunately uncommon in the craniofacial bones, mention especially must be made of benign osseous and fibro-osseous conditions affecting the head and neck region and the anterior skull base. According to Harrison, the most frequent benign bone lesions of the craniofacial bones are osteoma and fibrous dysplasia, followed by ossifying fibroma and benign osteoblastoma.¹ Fibrous dysplasia constitutes a relatively common aberration of the osteoblastic bone-forming mesenchyme, in which the bone marrow is replaced by fibrous marrow, and fibrous bone trabeculae persist in the absence of the transformation into lamellar bone. Seventy percent of the cases become apparent in the first three decades, most of them at the age of 5 to 15 years. The bone lesions do appear monostotic in 80% and polyostotic in 20% of the cases and can be associated with endocrine dysfunction and café au lait spots (McCune-Albright syndrome). The monostotic type primarily affects the skull and the jaw; according to Adler, skull lesions of fibrous dysplasia can be found in 14% of the cases.¹¹ Radiological appearance of fibrous dysplasia is variable, depending on the amount and distribution of osteoid matrix in the lesion.¹²

As radiological appearance of fibrous dysplasia is variable, in the presented case radiological investigations in fact could not exclude a monostotic lesion of fibrous dysplasia. On the other hand, clinical findings and intraoperative presentation were suspicious for skull base involvement of a malignant bone tumor, but malignancy could easily be excluded by histological investigations. On grounds of the characteristic histological features of the lesion and the history of preceding trauma in the tumor region, the diagnosis of a "posttraumatic reactive fibrous bone neoformation" was made.

We surveyed the international medical literature for the topic of posttraumatic fibro-osseous bone lesions. Of course, it is easy to associate any medical condition with a past history of minor trauma. However, due to the characteristic histological appearance, some bone lesions were classified as a separate, trauma-induced entity of fibro-osseous bone neoformations and have been found almost exclusively in ribs up to now.^{4,5,13-17} Apart from rib involvement, we found two reports in which scapular lesions are described, but there is no report of skull involvement as yet.^{4,6} Most of the authors postulated that the lesions may represent an aberrant healing response to clinical or subclinical trauma and showed evidence that trauma is an etiologic agent in the development of the lesion and that the lesion represents a pseudo-reparative neoplastic phenomenon.⁴⁻⁶ The lesion resembles an entity that has been previously reported in the literature as the "fibro-osseous lesion of rib," "symmetrical fibro-osseous dysplasia of rib," or "focal Erdheimer-Chester disease" and was also designated as FORL or FORP.⁴⁻⁶ Most of the lesions were asymptomatic and therefore incidental findings or discovery was made following investigations for metastatic disease.

Only a few cases were found as a consequence of pain related to the lesion. A history of trauma was evident in most but not in all of the cases, which can easily be explained by the fact that the overwhelming majority of the cases under discussion have been discovered as asymptomatic lesions in the ribs, an area of the body frequently subject to minor or inconsequential episodes of trauma.⁴⁻⁶ In those cases in which a concrete episode of trauma could be found, the interval between trauma and diagnosis ranged from 1 to more than 40 years.⁴⁻⁶ According to Kessler et al, the histological differential diagnosis of this entity, which he designated as "fibro-osseous reparative pseudotumor" (FORP), includes other osteoid- and bone-producing lesions with a fibrous dysplasia or osteoid osteoma type of histological appearance and encompasses osteoid osteoma/osteoblastoma, fibrous dysplasia, osteofibrous dysplasia, adamantinoma, and intramedullary low-grade

osteosarcoma.⁶ Microscopic features in particular resemble those of fibrous dysplasia and osteoid osteoma, due to the combination of metaplastic woven bone and fibrous stroma, which could easily be interpreted as fibrous dysplasia and due to the pattern of trabecular anastomoses and sclerotic rim, which could especially be suggestive of osteoid osteoma.⁴⁻⁶ Kessler et al, as most of the authors, postulated that the lesion represents a reactive response to trauma rather than a neoplasm as it demonstrates features of a reactive rather than a neoplastic process.⁶

McDermott et al in 1999 reported 11 cases of an unusual, benign, fibro-osseous lesion of the rib in adults, which were asymptomatic and discovered by bone scans done to rule out metastatic disease and previously reported under a variety of designations.⁵ There was a history of preceding trauma in most of the cases. Although having a considerable clinicopathologic overlap with other conditions, most notably fibrous dysplasia and osteoid osteoma, the histological features of the lesion were thought to be distinctive. Thus McDermott et al designated the lesion as "fibro-osseous reparative lesion" (FORL). The authors also emphasize that fibrous dysplasia besides osteoid osteoma is one of the conditions most likely to be confused with FORL, histologically as well as radiologically.⁶ Although there was a lack of trauma history in several reported cases, McDermott et al believe, as do others, that FORL represents a reparative response to prior trauma, as the information of preceding trauma is often absent from the patient history.⁶ According to McDermott et al, all of the lesions occurred in flat bones, like in our presented case in which the lesion arose in the anterior skull base, which may imply that such factors as a lack of weight bearing or stress from muscular pull on these bones makes them more likely to develop a less than complete, or an abortive, form of healing. The authors also underline that, like in our case, the significance of FORL resides in its clinical distinction from a malignant process.⁶

In the following discussion, mention must also be made on the difficulty of classifying and of

distinguishing fibro-osseous lesions in general and osseous and fibro-osseous conditions affecting the craniofacial bones in particular. Blanco et al reported in 2001 a case of posttraumatic fibro-osseous lesion of ribs and scapula and gave a review of the pathological and radiological features of this entity along with the summary of the differential diagnoses.⁴ According to the authors, fibrous lesions of bone are rare and difficult to classify. On the one hand, radiologically and histologically, the differential diagnosis of posttraumatic fibro-osseous lesion includes other benign lesions of bone; on the other hand, this entity must be entertained in the differential diagnosis of malignant and metastatic tumor. Blanco et al, as well as Harrison in his study on osseous and fibro-osseous conditions affecting in particular the craniofacial bones, concluded that fibrous tumors of bone consist of several entities that need clinicoradiopathologic correlation for definitive diagnosis.^{1,4}

In many patients, separation into individual categories is possible on clinical grounds alone, but osseous and fibro-osseous conditions affecting the craniofacial bones are often difficult to classify on either radiological imaging, clinical symptoms, or histology alone. The differentiation between the various fibro-osseous lesions affecting the bones of the skull is only possible by correlating clinical features with radiological and histopathologic findings, as clinical, radiological, and histological appearance varies and may cause confusion in diagnosis.¹ Histologically, it is the varying degrees of woven or lamellar bone, stroma, osteoid, giant cells, and osteoblasts that form the basis of most histological classifications. Because these may vary with site of biopsy and stage of disease, it is obvious that such findings must be correlated with the clinical history and radiological findings.¹ In most of the cases, malignancy can easily be excluded on histological grounds alone, although even the morphological pattern of histological examination might be variable to a great extent and cause major diagnostic difficulties.¹⁻⁴ For all benign fibro-osseous bone lesions of the craniofacial region, the common denominator is

replacement of normal bone by benign cellular fibrous tissue containing varying amounts of mineralized material.¹

According to Harrison, the pathologist's role is to exclude malignancy and to establish the fibro-osseous nature of the lesion. Tumor extension and radiological appearance have to be judged by the radiologist. The author emphasizes that the clinician, with the aid of the patient's history and clinical examination, has to take all findings into consideration and is in the unique position to collate this information and to produce a final diagnosis.¹ Nevertheless, it remains an interdisciplinary challenge and needs clinicoradiopathologic correlation to establish a final diagnosis on different osseous and fibro-osseous lesions of the craniofacial bones, which may largely differ in management and prognosis.^{1,4}

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