The case:

An 18-year-old man was referred to the authors’ institution’s thoracic cancer specialists for further consultation after abnormal findings were seen on chest radiograph.

Your diagnosis?

For answer see page 780
Diagnosis: Polyostotic Fibrous Dysplasia

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Answer to Radiologic Case Study
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This is a case report of polyostotic fibrous dysplasia (FD) in an 18-year-old Hispanic man referred to the authors’ institution for further evaluation of abnormal findings on chest radiograph. Fibrous dysplasia was first described by Lichtenstein in 1938, and is a relatively rare benign skeletal disorder caused by defective osteoblast differentiation, abnormal fibroblast proliferation, and replacement of normal bone structures with fibrous connective tissue. Fibrous dysplasia does not display gender predominance, and the overall disease incidence is approximately 1 in 30,000. Fibrous dysplasia accounts for approximately 5% to 7% of benign bone tumors and has a predilection for the ribs, femoral neck, pelvis, and craniofacial bones. The disease may be monostotic (involving 1 bone) or polyostotic (involving several bones), with the ratio of occurrence of monostotic to polyostotic FD being approximately 7:3. The monostotic form is most prevalent in the second and third decades of life. In contrast, polyostotic FD typically affects children younger than 10 years, and most commonly affects craniofacial bones, ribs, and metaphysis or diaphysis of long bones.

Approximately 3% of patients with polyostotic FD will have endocrine disturbances. McCune-Albright syndrome is a rare disorder that combines polyostotic FD, skin pigmentation, and one of several endocrinopathies (especially precocious puberty in girls). Fibrous dysplasia has also been associated with hyperthyroidism, hyperparathyroidism, acromegaly, Cushing syndrome, diabetes mellitus, and Mazabraud’s syndrome (polyostotic FD and soft tissue myxomas).

CLINICAL FINDINGS

Individuals with monostotic FD may be asymptomatic, having a bony deformity identified incidentally on radiographic studies. Signs and symptoms of FD include bone pain, pathological fractures, and bone deformities. However, individuals with the polyostotic variant are more likely to present with leg pain, limp, or pathologic fractures. On physical examination of the patient in this case, a painless asymmetry of the skull on the left vertex and left proptosis were noted. On further questioning, the patient’s mother stated that the abnormalities had been present for many years. In fact, the patient had undergone surgery for the expansile cranial abnormality, which the mother reported was a “benign disease process” (pathology report not available for review), 6 years earlier. A review of the patient’s medical records indicated a history of hypertension diagnosed 3 years earlier, prompting work-up for an endocrinopathy.

LABORATORY EVALUATION

A laboratory evaluation was undertaken, and the re-
sults of a serum protein electrophoresis and immunofixation workup were found to be normal. Additionally, complete blood cell count, comprehensive metabolic panel, and quantitative immunoglobulin levels were all within normal ranges. Tumor markers (alpha-fetoprotein, beta human chorionic gonadotropin), urine metanephrines, thyroglobulins, thyroid stimulating hormone, and calcitonin levels were also found to be normal.

IMAGING

Radiographic findings in FD are nonspecific and diverse, depending on the proportion of mineralized bone to fibrous tissue in the lesion. Generally, lesions have a characteristic lytic or “ground-glass” density, and are metaphysial or diaphyseal when located in long bones. Additionally, lesions may be surrounded by a thick rind of sclerotic bone, and may demonstrate expansion and sharp margination. Several rib lesions with expansile remodeling were discovered on the patient’s chest radiograph (Figure 1) and computed tomographic angiogram (CTA) of the chest (Figure 2), the largest measuring 9.8 cm in the right fifth rib. Of note, the CTA was performed in the Emergency Department due to the patient’s new onset complaint of dyspnea and anxiety. Although no evidence of pulmonary embolism was found, the multiple expansile rib lesions were better delineated and areas of ground-glass density were identified in several additional ribs (Figure 2).

Magnetic resonance imaging was performed to evaluate the calvarial lesions and left proptosis. Imaging demonstrated 3 separate calvarial lesions located in the greater wing of the left sphenoid bone, left parietal calvarium, and occipital calvarium. The largest lesion, in the left parietal calvarium, demonstrated expansile remodeling, without mass effect on the underlying cerebrum. Lesions were slightly heterogeneous and fairly isointense to gray matter on T1-weighted image, diffusely hypointense to adjacent calvarial marrow on T2-weighted image, and moderately enhancing (Figure 3).

In this young adult, although these lesions had the classic appearance of FD on imaging, the differential diagnosis of multiple lesions includes Langerhans cell histiocytosis, enchondromas, and osteochondromas in this age group. However, Langerhans cell histiocytosis usually will...
not have circumferentially sclerotic margins, and there was no mineralized chondroid matrix to suggest enchondromas or exophytic lesions with medullary continuity to suggest osteochondromas.\(^2\) Metastases are rare in this age group. Of note, an ultrasound scan of the scrotum performed to exclude a primary testicular malignancy was significant only for microlithiasis in the left testis. Myeloma, renal cell, and thyroid carcinoma metastases may exhibit expansile lytic lesions somewhat similar to the dominant rib lesion in this case; however, they typically show more aggressive destruction on imaging and are usually detected in adults older than 40 years.

**PATHOLOGY**

Although characteristic imaging findings usually lead to the diagnosis of FD, bone biopsy may be required to reach a definitive diagnosis, such as in the current case.\(^5,6\) This young man underwent a computed tomography-guided needle biopsy of a right lateral fifth rib skeletal lesion (Figure 4). Gross pathology of a FD lesion should reveal a yellowish-white tissue with a distinctive gritty feel, imparted by the small trabeculae of bone scattered throughout the lesion.\(^6,7\) These lesions can often easily be pulled apart from the encircling shell of reactive bone surrounding them. Key histologic features of FD include delicate trabeculae of immature bone, with no osteoblastic rimming, enmeshed within a bland fibrous stroma of dysplastic spindle-shaped cells with no cellular features of malignancy.\(^6,7\) Overall, FD has a variable number of immature, disconnected dysplastic trabeculae floating in a sea of mesenchymal cells that have little to no collagen about them, a pattern that has been likened to “alphabet soup.”\(^3\)

**TREATMENT**

There is no cure for FD, and treatment varies greatly depending on the degree of bony involvement and patient symptomatology. Asymptomatic lesions may simply be monitored every 6 months with radiographs to verify a lack of disease progression.\(^3\) Surgery is indicated for confirmatory biopsy, correction of deformities, failure of medical therapy, prevention of pathologic changes, and eradication of symptomatic lesions.\(^7\) When polyostotic disease is initially discovered, referral to an endocrinologist for pertinent testing is warranted so that endocrine abnormalities can be identified and treated early in the course of disease.\(^3\) Additionally, when surgery is not an option, which is often the case with the polyostotic form, bisphosphonate therapy can result in positive effects on bone density and an overall reduction of pain.\(^7\)

**PROGNOSIS**

Although FD may be an asymptomatic disease, some individuals may display marked disease progression and can be severely debilitated by this condition. The more extensive and aggressive lesions are typically encountered in polyostotic FD, which can involve from 2 bones to up to 75% of the skeleton.\(^2\) Malignant transformation has been reported in 0.5% of patients with monostotic FD and in approximately 4% of those with McCune-Albright syndrome. Lesions most commonly transform into osteosarcomas, but fibrosarcomas, chondrosarcomas, and malignant fibrous histiocytoma have also been noted.\(^1\)

**REFERENCES**