Abstract. Fibrous dysplasia can be monostotic or, less commonly, polyostotic. The imaging features of polyostotic fibrous dysplasia may closely mimic those of metastatic bone disease, Paget disease, or enchondromatosis (Ollier disease). We present a unique case of polyostotic fibrous dysplasia in a 57-year-old female with a medical history of enchondromas involving the proximal phalanges of the left hand. The skeletal radiographs showed unilateral multiple bone lesions suggestive of polyostotic fibrous dysplasia. On magnetic resonance imaging, the lesions exhibited low-to-intermediate signal intensity on T1-weighted images and heterogeneous high signal intensity on T2-weighted images. Contrast-enhanced fat-suppressed T1-weighted images demonstrated moderate heterogeneous enhancement. Integrated positron-emission tomography (PET)/computed tomography scan demonstrated increased 18F-fluorodeoxyglucose (FDG) uptake within several bones, including the humerus, ilium, femur, and fibula, all on the left side. The maximal standardized uptake value of these lesions ranged from 2.18 to 3.78. We performed an open biopsy of the left humerus and histological examination confirmed the diagnosis of fibrous dysplasia. To the best of our knowledge, this is the first case of biopsy-proven FDG PET-positive polyostotic fibrous dysplasia with enchondromas of the hand.

Case Report

A 57-year-old female was referred to Fukuoka University Hospital with dull pain in the left hip while standing or walking. There was no pain at rest, swelling, or tenderness in the lower left limb. The patient had no history of endocrine dysfunction, and no skin pigmentation was found. Laboratory data did not show any elevation of serum alkaline phosphatase (ALP). When the past medical history of the patient was reviewed in detail, Ollier disease had been diagnosed 13 years earlier. The patient had undergone curettage and packing of the bony defect with synthetic bone substitutes for a painful enchondroma involving the proximal phalanx of the left middle finger.

At our Institution, plain radiographs of the left hand revealed lytic lesions with faint calcifications in the proximal phalanges of the middle and ring fingers (Figure 1). Moreover, plain radiographs of the left limb showed multiple radiolucent lesions with sclerotic contours in the humerus (Figure 2A), ilium, femur (Figure 2B), and fibula (Figure 2C). On magnetic resonance imaging (MRI), the lesions exhibited low to
intermediate signal intensity on T1-weighted sequences (Figure 3A) and heterogeneous high signal intensity on T2-weighted sequences (Figure 3B). Contrast-enhanced fat-suppressed T1-weighted sequences demonstrated moderate heterogeneous enhancement (Figure 3C). Positron-emission tomography (PET) images demonstrated increased $^{18}$F-fluorodeoxyglucose (FDG) uptake in the left humerus, left ilium, left femur, and left fibula. The accompanying computed tomography (CT) showed cortical thickening and increased density within the medullary cavity in the affected bones (Figure 4). The maximal standardized uptake value ($SUV_{max}$) of these lesions ranged from 2.18 to 3.78. The differential diagnosis at this point included polyostotic fibrous dysplasia and Ollier disease.

An open biopsy of the left humerus was performed. Microscopically, the tumor consisted of fibroblastic spindle cells admixed with irregular woven bone trabeculae lacking osteoblastic rimming (Figure 5). The spindle-shaped cells exhibited neither nuclear atypia nor mitotic activity. The histological diagnosis was fibrous dysplasia.

These findings were interpreted in favor of polyostotic fibrous dysplasia. The patient is currently being followed-up clinically and radiographically every three months and shows no evidence of disease progression.

Discussion

Polyostotic fibrous dysplasia is often unilateral in its distribution, as in our case. It tends to involve larger segments of bone and is frequently associated with pathological fractures and severe deformities. Some patients with polyostotic forms have endocrinopathies and skin pigmentation abnormalities (McCune-Albright syndrome) or intramuscular myxomas (Mazabraud syndrome) (1). To the best of our knowledge, this is the first case of biopsy-proven polyostotic fibrous dysplasia associated with enchondromas of the hand.

The imaging findings of fibrous dysplasia are characteristic, although not specific, and depend on the underlying histology of a given lesion (4). Lesions are located within the medullary cavity of the metaphysis or diaphysis. Radiographically, the lesions show varying degrees of hazy density with a ground-glass quality (4). The lesions may be bound by a distinct rim or shell of reactive bone. Endosteal scalloping of the adjacent cortex may be present, but the periosteal surface is smooth and non-reactive (5). CT is the best technique for demonstrating the typical radiographic descriptions of fibrous dysplasia. In the current case, thorough interpretation of the CT information from PET/CT study was helpful in making an accurate diagnosis. MRI is useful for evaluating the entire extent of the lesion. Signal intensity on T1- and T2-weighted images and the degree of contrast enhancement on T1-weighted images depend on the amount and degree of fibrous tissue, bony trabeculae, cellularity, and cystic and myxoid changes (1). Typically, the lesions exhibit intermediate-to-low signal intensity on T1-weighted images, intermediate-to-high signal intensity on T2-weighted images, and heterogeneous enhancement after intravenous administration of gadolinium, as in our case. Radionuclide bone scintigraphy is useful to identify the extent of the skeletal involvement, particularly in the polyostotic form. A bar-shaped pattern, whole bone involvement, and a close match between the size of the lesion on plain radiographs and bone scans are helpful to differentiate fibrous dysplasia from metastatic bone disease (6).

FDG-PET is being increasingly used for the evaluation and management of bone tumors. In the current case, mild-to-moderate FDG uptake was observed in the skeletal lesions. There have been a few reports describing FDG PET/CT findings for fibrous dysplasia (7-11). Our case and others suggest that fibrous dysplasia may have a wide skeletal distribution, with variability of FDG uptake. Moreover, several authors have reported that significantly increased FDG uptake can mimic bone metastasis in cancer patients with fibrous dysplasia (11-17). Co-registered CT may help resolve equivocal PET findings, as in our case. On the other hand, Berrebi et al. (18) reported that FDG-PET might be useful for the early detection of malignant transformation.
The differential diagnosis of polyostotic fibrous dysplasia includes metastatic bone disease, Paget disease, and Ollier disease, especially in adult patients.

Paget disease is a chronic disorder characterized by focal areas of increased and disorganized bone remodeling affecting one or more bones throughout the skeleton. Unlike fibrous dysplasia, Paget disease is rare before the age of 55 years (19). Although any bone may be affected, the innominate bone is the most common site. Almost invariably, serum ALP levels are increased. Sequestosome 1 (SQSTM1) mutations have been implicated in the pathogenesis of Paget disease (20). Radiographically, the lesion shows a sharply demarcated radiolucency associated with thickened cortex and medullary bone. In the long bones, the process almost always extends to the end of the bone. The use of CT or MRI is not routinely indicated, although it does have a role in selected

Figure 2. Plain radiographs showing radiolucent lesions with sclerotic contours in the left distal humerus (A), the left proximal femur (B), and the diaphysis of the left fibula (C).

Figure 3. Coronal magnetic resonance images of an extensive lesion in the left proximal femur. The lesion exhibits low-to-intermediate signal intensity on T1-weighted sequence (A) and heterogeneous high signal intensity on T2-weighted sequence (B). Contrast-enhanced fat-suppressed T1-weighted sequence shows moderate heterogeneous enhancement of the lesion (C).
patients in whom complications such as fractures, spinal stenosis, or secondary neoplasms are suspected (19). The extent of disease is best determined on radionuclide bone scintigraphy. FDG-PET shows no abnormal accumulation in the majority of patients (21). In the current case, we were able to eliminate the possibility of Paget disease on the basis of imaging features.

Ollier disease is a non-hereditary disorder characterized by the presence of multiple benign cartilaginous masses involving the entire skeleton. When soft tissue hemangiomas are also present, the disorder is referred to Maffucci syndrome. Seventy-five percent of patients are diagnosed with this disease before the age of 20 years (22). Unlike fibrous dysplasia, Ollier disease often involves the small tubular bones in the hands and feet.
Somatic mosaic isocitrate dehydrogenase 1 (IDH1) and isocitrate dehydrogenase 2 (IDH2) mutations are implicated in Ollier disease (23). The prevalence of malignant transformation is variable and estimated to occur in 5-50% of the cases (22). Radiographs are usually diagnostic when the patient is young. The radiolucent skeletal lesions are well demarcated and show expansible remodeling of the affected bone with predominant thinning of the cortex and endosteal scalloping. Matrix mineralization frequently occurs in the osseous lesions, resulting in the typical arc-and-ring appearance of chondroid lesions. CT and MRI do not show specific features in enchondromas. However, CT may show calcification not appreciated on plain radiographs. Moreover, these modalities may help to better define the extension of the lesion and to confirm the lack of cortical involvement. Radionuclide bone scintigraphy may be used to assess lesions depicted on plain radiographs (24-26). Recent PET analyses indicate that enchondroma has mild FDG uptake (SUV: 0.7-1.8) (27, 28). In the current case report, we confirmed the diagnosis of polyostotic fibrous dysplasia with enchondromas of the hand. Our case report indicates that FDG-PET/CT can provide more diagnostic information than PET alone in fibrous dysplasia.

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References


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