CASE REPORT

Apport de l'imagerie hybride dans l'ostéopetrose bénigne: A propos d'un cas et revue de la littérature

Contribution of hybrid imaging in benign osteopetrosis: A case report and litterature review

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Abstract

Introduction: Benign osteopetrosis is a rare metabolic bone disorder characterized by a generalized and symmetrical increase in bone density. While the radiographic features of osteopetrosis are well-known, scintigraphic aspects, particularly in hybrid imaging (single-photon emission computed tomography coupled with computed tomography (SPECT/CT), have been rarely described in the literature.

Observation: A 16-year-old adolescent boy presented with chronic diffuse osteoarticular pain. Radiological exploration revealed osteosclerosis in the femoral heads, distal ends of the femurs, and upper ends of the tibiae, suggesting the diagnosis of osteopetrosis. Planar bone scintigraphy supplemented by SPECT/CT confirmed the diagnosis, mapped the various bone locations, and ruled out fractures.

Conclusion: Although rare, benign osteopetrosis should be recognized because it causes bone integrity impairment, leading to various bone complications, including spontaneous fractures. SPECT/CT plays an important role in assessing the extent of bone lesions and identifying complications. As highlighted, this case underscores the utility of combining functional and anatomical imaging modalities in one examination, which decreases the time to diagnosis and offers a comprehensive assessment of benign osteopetrosis.

Key words: Albers Schönberg disease –Case Report - Hyperostosis - Osteosclerosis

Résumé

Introduction: L'ostéopétrose bénigne est l'une des rares maladies métaboliques osseuses qui se caractérise par une augmentation généralisée et symétrique de la densité osseuse. Les caractéristiques radiographiques de cette maladie sont bien connues ; cependant, les aspects scintigraphiques, notamment en imagerie hybride (tomographie par émission monophotonique/tomodensitométrie (TEMP/TDM)), ont été rarement décrites dans la littérature.

Observation: Un adolescent âgé de 16 ans a consulté pour des douleurs ostéoarticulaires diffuses chroniques. L'exploration radiologique a révélé des ostéocondensations au niveau des têtes fémorales et des extrémités distales des fémurs ainsi que des extrémités proximales des tibias, évoquant le diagnostic d'une ostéopétrose. La scintigraphie osseuse complétée par TEMP/TDM a permis de confirmer le diagnostic, de cartographier les différentes localisations osseuses, et surtout d'éliminer un foyer de fracture.

Conclusion: Bien que rare, l'ostéopetrose bénigne devrait être connue en raison de son effet fragilisant sur l'os, pouvant entraîner plusieurs complications osseuses, notamment des fractures spontanées. La TEMP/TDM joue un rôle important dans l'évaluation de l'extension des lésions osseuses et la recherche de complications. Comme le souligne ce cas, l'avantage de combiner dans un seul examen les modalités d'imagerie fonctionnelle et anatomique est de réduire le délai de diagnostic et de fournir une vue d'ensemble complète de l'ostéopétrose bénigne.

Mots clés: Hyperostose-Maladie d'Albers Schönberg-Ostéosclérose – Rapport de Cas

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Introduction

Osteopetrosis, also known as marble bone disease, is one of the rare genetic osteosclerosing disorders [1]. It was first described by Albers-Schonberg in 1904 and presents in two main forms: a benign dominant form and a malignant recessive form [2]. This rare disease should be particularly recognized in its benign dominant form because it weakens bones, leading to several bone complications, including spontaneous fractures [2].
Single-photon emission computed tomography coupled with computed tomography (SPECT/CT) is a sensitive morpho-functional imaging technique [3] .This technique allows for mapping the different bone locations affected by the disease, especially in the early phase of its management [4].
In this context, we reported a new case of benign osteopetrosis. This case provides an opportunity to review the typical morphological and functional imaging aspects of this condition.

Observation

The patient was a 16-year-old adolescent boy without significant medical history or consanguinity. He was presented to rheumatology with diffuse osteoarticular pain, more pronounced in the knees, evolving over three months. Clinical examination yielded unremarkable findings. Laboratory tests did not indicate inflammatory syndrome with a C-reactive protein level of 2 mg/L (normal range: 0-5 mg/L). Pelvic radiography revealed condensation of the femoral heads and necks (Figure 1a).

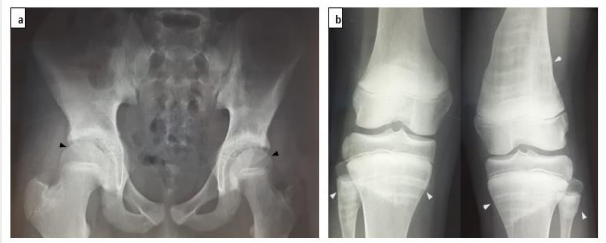

Figure 1. (**a**) Frontal pelvic conventional radiography showing coronal condensation of the femoral heads (black arrowheads). (**b**) Frontal conventional radiography of the knees showing osteosclerosis of the distal metaphyses of the femora and proximal metaphyses of the tibiae and fibulae (white arrowheads).

Knee radiographs showed osteosclerosis characterized by alternating radiolucent and radio-opaque bands at the distal metaphyses of the femora and proximal metaphyses of the tibiae and fibulae, accompanied by left metaphyseal widening (Figure 1b).
Based on these radiological findings, a diagnosis of benign osteopetrosis was considered. However, other potential diagnoses needed to be ruled out, mainly conditions in which secondary bone sclerosis can occur including metastatic bone disease, myeloproliferative disease and Paget's disease. On the other hand, it was important to detect complications like osteomyelitis and fractures.
The patient was referred for bone scintigraphy to map the bone lesions. The isotopic examination included static images scanning the entire body three hours after injection of 555 MBq of technetium-99m hydroxymethylene diphosphonate, followed by SPECT/CT acquisitions centered on the dorsolumbar spine, pelvis, and knees.
The scan revealed heterogeneous peri-articular high uptake at the humeral and femoral heads, distal metaphyses of both femora with greater intensity on the left side, as well as proximal metaphyses of the tibiae and fibulae. A focal intense uptake was particularly present at the distal metaphysis of the right tibia (Figure 2).

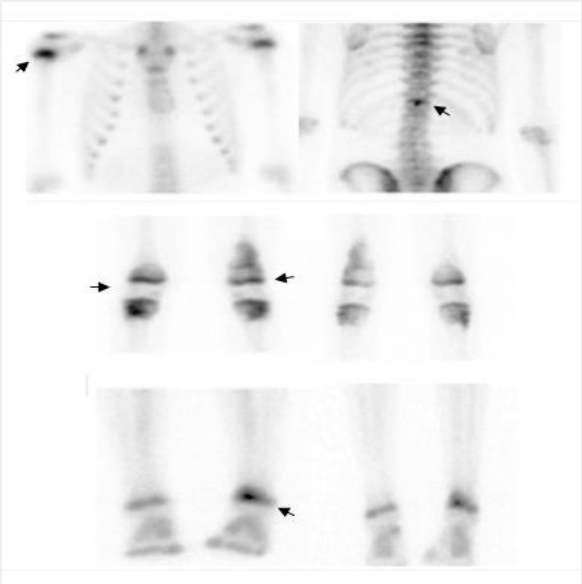

Figure 2. Planar static images centered on the thorax, knees, and ankles in anterior and posterior views showing high uptake foci at the metaphyses of long bones and in L1 vertebra (Black arrows).

On SPECT/CT slices, the detected uptake abnormalities corresponded to diffuse metaphyseal sclerosis of the knees and femoral heads, creating a "bone within a bone" appearance (Figure 3).

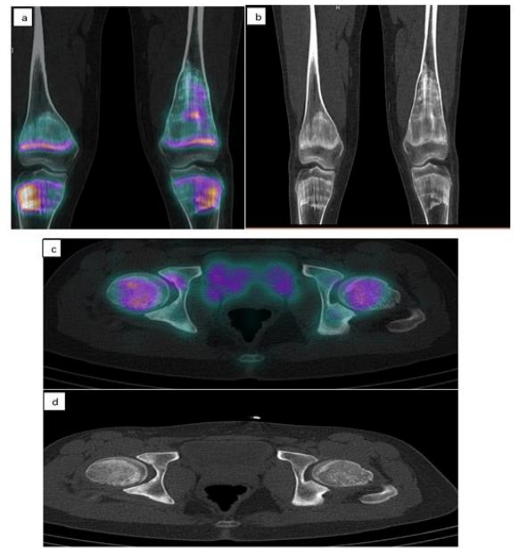

Figure 3. Single-photon emission computed tomography coupled with computed tomography (SPECT/CT) centered on the knees and femoral heads. (**a**) SPECT/CT fusion image showing high metaphyseal uptake of the knees (**b**) Computed tomography (CT) component of the SPECT/CT showing diffuse sclerosis corresponding to the uptake in the metaphyseal area. (**c**) SPECT/CT fusion image showing high uptake in the femoral heads (**d**) CT component of the SPECT/CT showing sclerosis in the femoral heads giving a "bone-in-bone" appearance.

In the spine, high uptake was noted at L1 vertebra, which corresponded to endplate sclerosis on the SPECT/CT slices, creating a sandwich appearance (Figure 4).

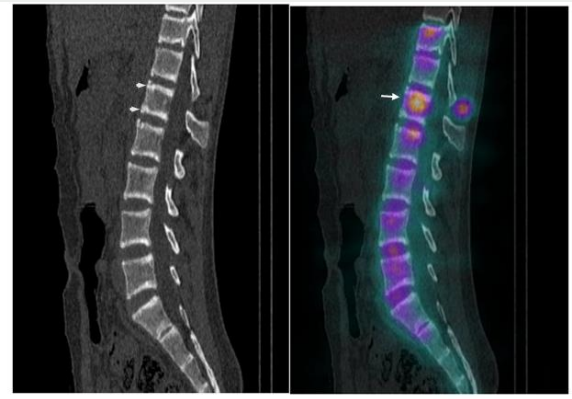

Figure 4. Single-photon emission computed tomography coupled with computed tomography (SPECT/CT) centered on the dorsolumbar spine demonstrating high uptake along the vertebral endplates (Arrow) with well-defined regions of increased bone density (arrowheads), giving the appearance of the "sandwich vertebra."

These results were consistent with the diagnosis of benign osteopetrosis. No fracture foci or any other abnormalities of complications were noted.

The management of the patient included avoidance of high impact and intense physical activities to prevent any onset of complications. A 12-month follow-up showed no new events and a partial improvement in symptoms under corticosteroids.

After confirming the diagnosis in our patient, a follow up on his family history revealed the presence of osteopetrosis in the 30-year old patient's maternal cousin upon a bone examination. She presented similar osteoarticular pain without any accompanying symptoms, and after receiving symptomatic therapy, she was put under surveillance.

Discussion

This case highlights the value of hybrid imaging (SPECT/CT) in diagnosing and managing osteopetrosis by distinguishing it from other potential diagnoses as well as eliminating any complications associated. Osteopetrosis is a rare bone metabolic disease linked to a functional abnormality of osteoclasts [5]. Table 1 summarizes the main scintigraphic manifestations of osteopetrosis as presented in the literature.

Table 1. Review of literature concerning osteopetrosis with bone scan findings

1st author [reference]	Age at diagnosis (years)	Patterns of presentations	SPECT/CT or planar mode
Junquera et al. [6]	76	Increased uptake in cranial base, skullcap, left mandibular ramus, and vertebrae	Planar
Kapoor et al.[9]	23	Intense tracer uptake in the entire skeleton, notably in the proximal and distal shafts of bilateral femora, pelvic bones, lumbar vertebrae and proximal shafts of bilateral humeri.	SPECT/CT
		Fused SPECT/CT images demonstrated extensive sclerosis in areas of intense tracer uptake.	
Barral et al. [11]	35	Abnormal uptake in proximal epiphysis of appendicular skeleton and the knees, and focal in the ribs suggesting old fractures. Bone “superscan” associated.	Planar
Sit et al. [7]	59	Increased tracer uptake at the proximal ends of humeri and tibiae along with proximal and distal ends of femora. Linear uptake at the proximal femora and several lower ribs bilaterally is suggestive of fracture at these sites.	SPECT/CT
Zheng et al. [10]	56	Intense diffuse tracer uptake throughout the axial skeleton, resembling a «superscan,» with accentuated uptake in the metaphyseal regions.	Planar
Matrane et al. [4]	02	Double fracture of the right coracoid process and the 10th right rib.	SPECT/CT
Present study	16	High uptake corresponding to characteristic bone sclerosis in the metaphyses and epiphyses of appendicular skeleton as well as the spine.	SPECT/CT

SPECT/CT: Single-photon emission computed tomography/Computed tomography.

It is characterized by a deficiency in lysosomal enzymes responsible for osteoclast differentiation abnormalities, leading to dysregulation of bone tissue resorption and resulting in bone accumulation within the medullary space [2,5]. It encompasses two main forms:

- Benign autosomal dominant osteopetrosis (ADO), including type I predominant in the skull and type II or Albers-Schönberg osteopetrosis predominant in the spine and long bones [1, 6].
- Malignant autosomal recessive juvenile osteopetrosis (ARO) is very rare, and typically fatal in early childhood without treatment [1].

Benign osteopetrosis often remains asymptomatic for a long period [5]. Its diagnosis is primarily radiological, guided by clinical suspicion [2]. Pathological fractures are the most frequent revealing manifestation of benign osteopetrosis [7]. Bone pain is another significant symptom, found in 25% of cases [7]. Cranial nerve involvement and osteomyelitis, particularly affecting the mandible, are specific complications of this disease [2].

In conventional radiology, osteopetrosis is characterized mainly by generalized and symmetric increase in bone density affecting both cortical and cancellous bone [8]. Its extent varies according to the clinical form considered [4]. In advanced forms, the metaphyses of long bones are widened due to impaired bone remodeling, taking on a club-shaped appearance ("Erlenmeyer flask deformity") [4]. In some patients, there may also be an endosteal thickening ("bone within a bone") affecting mainly the tarsus, vertebral bodies, phalanges of the hands and feet, and iliac wings [4]. Vertebrae have a typical appearance on lateral radiographs: endosteal thickening with thickened endplates creating a "rugger jersey spine" appearance [4].

Osteopetrosis assessment can be done with different nuclear medicine examinations.

The most effective method for displaying the disease's bone marrow distribution is 99mTc-sulfur colloid scintigraphy [7]. Bone scintigraphy is also useful for osteopetrosis diagnosis, and for detecting associated complications such as osteomyelitis or fractures [7]. It allows exploration of the entire skeleton and has the advantage of early positivity [7]. Additional use of SPECT/CT increases the sensitivity and specificity of the isotopic examination [7,9].

While the radiographic characteristics of osteopetrosis are well known, scintigraphic aspects, particularly in hybrid imaging, have been rarely described in the literature [4]. Reported features include intense radiotracer uptake in the proximal and distal metaphyseal regions of long bones, as seen in our patient [4,9]. A focal pattern of intense uptake at the base of the skull, cranial vault, and spine have also been described [4,7]. Osteopetrosis may also present as diffuse radiotracer uptake throughout the axial skeleton, resembling a "superscan," with accentuated uptake in the metaphyseal regions, distinguishing it from other causes of "superscan" [10,11].

Supplemental SPECT/CT allows for better localization and extent of bone lesions, as well as their relationship with other structures, particularly joint surfaces [4,9]. Moreover, SPECT/CT is useful in confirming occult fractures that may be obscured by significant bone sclerosis on conventional radiology and intense uptake on planar images [7,9].

In our case, SPECT/CT confirmed the diagnosis of benign osteopetrosis by providing precise lesion mapping throughout the skeleton. Specifically, it ruled out the presence of fracture foci, particularly at the knees, as the cause of symptoms observed in our patient.

Numerous genetic variants can cause osteopetrosis, resulting in a wide range of clinical symptoms, age onset, and prognosis (from mild to severe). Imaging patterns help guide the specific inheritance type and the disease severity in the absence of genetic confirmation. ADO type I is characterized by a pronounced and symmetrical osteosclerosis of the skull and an enlarged thickness of the cranial vault [6]. The “bone in bone” aspect is shared by both dominant and recessive forms, the sandwich vertebrae aspect is typical to ADO type 2 osteopetrosis. The metaphyseal enlargement especially in the femoral bones is more frequent in ADO type 2 [12]. Genetic testing was not available in the clinical setting and our patient’s lesion mapping suggests that the ADO type 2 is the most likely corresponding inheritance type in his case.

Aside from the osseous involvement, neurological involvement may also arise which are more frequent in patients with ARO type. In this case, MRI has a leading role in the detection, evaluation and follow-up of neuronal damage [12]. Patients with ARO type can also exhibit a reduction in bone marrow space visible on MRI, which results in pancytopenia and extramedullary haematopoiesis [12].

The treatment is primarily supportive and symptomatic, particularly through the management of certain complications like osteomyelitis, arthritis and non-union of fractures. Red blood cell and platelet transfusions are used to treat bone marrow failure and calcium and vitamin D deficiency in hypocalcaemic seizures [13]. Treatment response and prognosis depend on the different subtypes of osteopetrosis. That’s why the characteristics of imaging features should be recognized in order to evaluate the progression and severity of disease on follow-up controls.

Certain limitations should be outlined within this case report. The single-case nature may limit the generalizability of findings. Additionally, long-term follow-up data are lacking, precluding a comprehensive assessment of disease progression and treatment outcomes. Further studies with larger cohorts are warranted to validate these observations. They will be valuable for correlating clinical and imaging features with genetic variants, as well as for providing new information on the molecular pathways of the disease.

Conclusion

Osteopetroses are characterized by significant clinical and genetic heterogeneity. Their diagnosis heavily relies on radiological appearance. Prognosis is largely determined by the risk of complications. SPECT/CT confirms the diagnosis and explores bone complications, thus providing a more tailored management.

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