Osteopoikilosis: case series from Portuguese Rheumatology centers

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ABSTRACT

Osteopoikilosis (OPK) is a rare, hereditary, usually asymptomatic disease characterized by the presence of multiple, well-defined sclerotic lesions distributed in peri-articular locations, frequently diagnosed as an incidental finding. Differential diagnosis with osteoblastic metastases is fundamental. This article reports six cases of OPK diagnosed in Portuguese Rheumatology Centers.

Keywords: Case series; Osteopoikilosis.

INTRODUCTION

Osteopoikilosis (OPK), *osteopathy condensans disseminate* or "spotted bone disease" is an uncommon osteosclerotic dysplasia[1]. It is a benign and usually asymptomatic disease of unknown cause. Inheritance is autosomal dominant; although cases with no family history have been reported. Radiologically it is characterized by the presence of multiple, well-defined, oval or rounded sclerotic lesions distributed in peri-articular locations, epiphysis and metaphysis of long bones. It is not uncommon for its diagnosis to be obtained during the investigation carried out after a conventional radiography requested in the context of another concomitant clinical situation, such as a trauma[1–3]. Herein we report 6 cases of OPK, identified in Portuguese Rheumatology Centers, describing clinical and radiographic features.

CASE SERIES

Portuguese Rheumatology trainees, from 11 Rheumatology Centers, were invited by e-mail in November 2017 to collaborate in a multicentric project which main objective was to identify and characterize OPK's cases ever diagnosed in these Centers. Cases were identified by asking the physicians of each Center if they had ever diagnosed this condition in any patient. Six cases were reported, from 3 Rheumatology Centers, the earliest diagnosed 19 years ago. Data were collected through retrospective analysis of clinical processes. Four of the six OPK patients (66.7%) were men, with a median age at diagnosis of 29 years (IQR 9.5, minimum 22, maximum 42). Table I summarizes all these case reports.

CASE 1

A previously healthy 42-year-old Caucasian woman developed complaints of mechanical knee pain and bilateral gluteal pain. She performed a pelvic conventional radiography which revealed multiple dense rounded lesions scattered in the iliac bones and ischiopubic branches. A computed tomography (CT) scan was requested to exclude a tumor, and it confirmed the presence of irregularly contoured osteocondensing focal lesions, some of them showing a spiculate appearance strongly suspicious of a secondary lesion. Blood tests, including phospho-calcium metabolism, did not show relevant changes and serum tumor markers were negative. Mammography and thoraco-abdominopelvic CT scan were also normal. Technetium-99m (99mTc) whole body bone scintigraphy did not show any fixation zone thus supporting the diagnosis of OPK.

CASE 2

A 22-year-old Caucasian male, soldier, smoker (20 cigarettes a day for 4 years), with no known personal or family history, suffered trauma to the left wrist. He performed radiographs (Figure 1) which excluded fracture and revealed the presence of small, multiple symmetrically distributed, oval and rounded lesions of increased and well-defined density located at the distal radii and

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TABLE I. OSTEOPOIKILOSIS CASES DIAGNOSED IN PORTUGUESE RHEUMATOLOGY CENTERS

Case	Gender	Comorbidities	Age at diagnosis (years old)	Known family history of OPK	Reason for the first X-ray	Articular symptoms	Relevant clinical examination findings	Known bone involvement	Dermato-logical involvement	Laboratory changes	Imaging exams performed
1	Female	None	42	No	Bilateral gluteal pain	Bilateral gluteal pain	No	PB	No	No, including serum tumor markers	CR, CT of PB, mammography, TAP CT, Whole body bone scintigraphy
2	Male	Smoking	22	No	Left wrist trauma	Very sporadic arthralgia of feet and wrists	No	H, R, U, CB, MC, Pges of hands and feet, PAR, PB, Fem., Fibul., T, MT, Tarsal bones	No	No	CR, CT of hands, Whole body bone scintigraphy
3	Male	None	26	No	Minor trauma of left forearm	No	No	H, R, U, CB, MC Pges of hands and feet, PB, Fem., Fibul., T, MT, Tarsal bones	No	No	CR
4	Male	None	29	Yes (sibling of case 3)	Family history of OPK	No	No	Hands (MC, Pges), PB, K, Feet	No	No	CR
5	Female	JIA, total bilateral hip replacement, type 2 DM, AHT, CRF	32	No	Inflam. polyarthralgia and prolonged MS in the context of JIA	Inflam. polyarth-ralgia	None other than those assigned to JIA	Sh, Hips, K	No	None other than those assigned to JIA	CR, Whole body bone scintigraphy
6	Male	Renal lithiasis	29	NA (LTF)	NS arthralgia of Sh, hips, K	NS arthral-gia of Sh, hips, K	None	Sh, Hips, K	No	NA (LTF)	CR

OPK: osteopoikilosis; JIA: juvenile idiopathic arthritis; CT: computed tomography; H: humeri, U: ulnae, CB: carpal bones; PAR: peri-acetabular region; PB: pelvic bones; Sh: shoulders; Pges: phalanges; NA: not applicable; CR: conventional radiography; DM: diabetes mellitus; TAP: thoraco-abdominopelvic; CRF: chronic renal failure; LTF: lost to follow-up; MS: morning stiffness; AHT: arterial hypertension; Inflam.: Inflammatory; R: radii; MC: metacarpals; MT: metatarsals; T: tibiae; Fem: femur; K: knee; NS: non-specific.

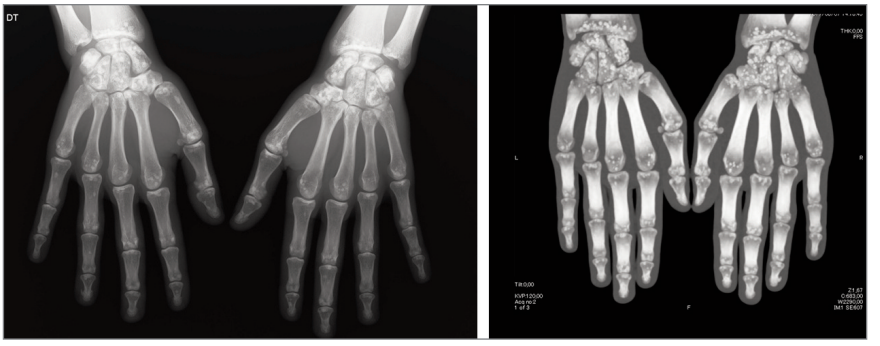

FIGURE 1. Hands AP radiography and computed tomography (case 2)

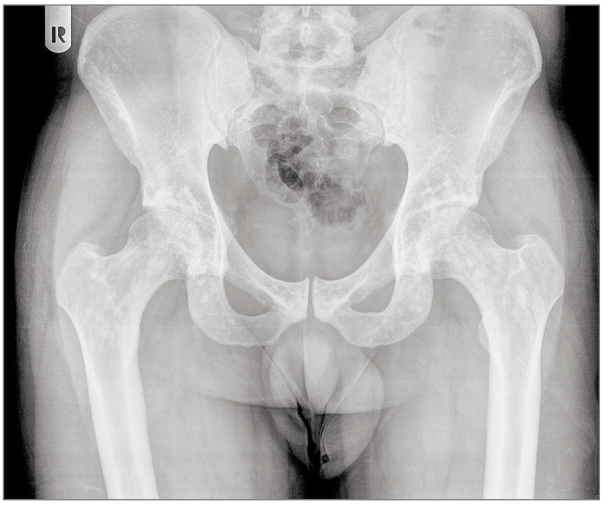

FIGURE 2. Pelvis AP radiography (case 3)

ulnae, carpal bones and peri-articular regions of the metacarpals and phallanges. The patient was referred to a Rheumatology appointment in the following month, in which he reported episodes of very sporadic feet and wrists pain in the past. Clinical examination and laboratory tests were unremarkable. Additional conventional radiographs were requested and similar lesions were found in peri-acetabular region, ischium and iliopubic branches, proximal epiphysis of humeri and femura, distal epiphysis of fibulae and tibiae, tarsal bones, peri-articular areas of the metatarsal bones and interphalangeal regions of the feet, bilaterally; no changes were found in skull and chest conventional radiographs. 99mTc whole body bone scintigraphy excluded the existence of focal osteoblastic lesions or suspicious alterations of metabolic bone disease. CT scans of the hands (Figure 1) demonstrated micronodular images of increased density, dispersed by all the bone structures, compatible with OPK.

CASE 3

A 26-year-old Caucasian male, with no relevant personal or family history, was observed at the emergency department due to a minor trauma of his left forearm. At that time, he performed a conventional radiography of the left forearm and hand which revealed several sclerotic oval and rounded lesions of approximately 2 to 4 mm in diameter in the periarticular areas of the carpal bones, metacarpophalangeal and interphalangeal regions, distal radii and ulnae. He was then referred for a rheumatologic evaluation, where he did not present any symptom or relevant finding on clinical examination. To confirm the diagnosis, additional conventional radiographs were requested, which showed similar lesions, symmetrically distributed in the pelvic bones (Figure 2), metaphysis and epiphysis of femura, fibulae, tibiae, carpal and tarsal bones, metatarsals and phalanges of feet, humeri, radii and ulnae. Blood tests requested were also normal, excluding other etiologies and supporting the diagnosis of OPK.

CASE 4

A 29-year-old previously healthy Caucasian male without any relevant finding at clinical evaluation, performed multiple conventional radiographs after his brother was diagnosed with OPK (case 3). They revealed similar lesions on hands, pelvic bones, knees and feet (Figure 3). These findings were not present on their mother's conventional radiographs. Their father refused the investigation. Also, it was not possible to establish if anyone else in the family had this condition.

CASE 5

A 32-year-old Caucasian female, diagnosed with rheumatoid factor negative polyarticular juvenile idiopathic arthritis (JIA) since she was 8 years old, with a

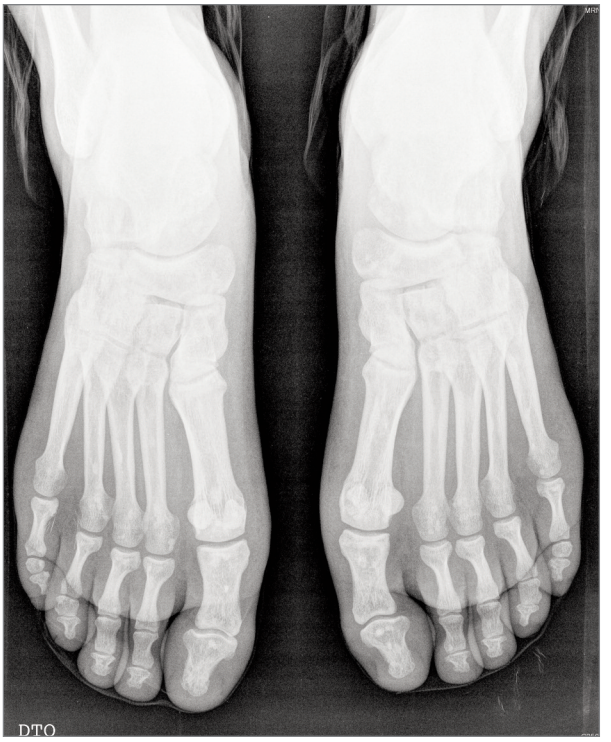

FIGURE 3. Feet AP radiography (case 4)

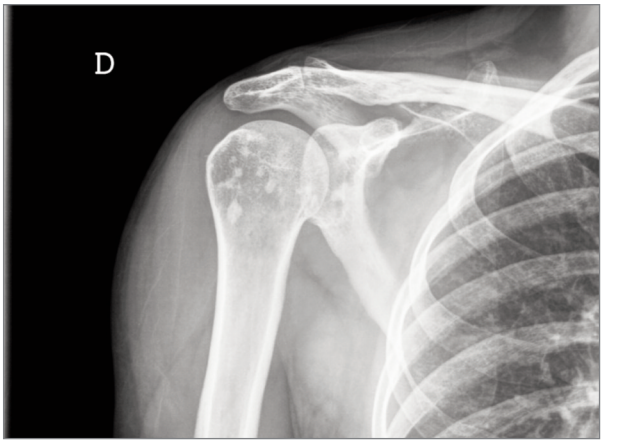

FIGURE 4. Right shoulder AP radiography (case 5)

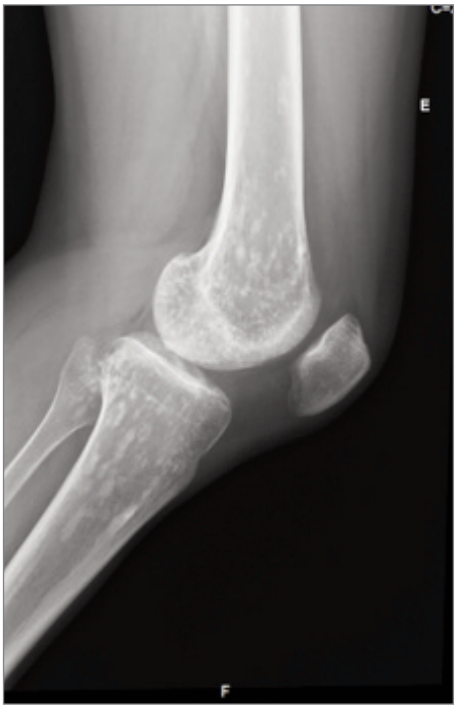

FIGURE 5. Left knee AP radiography (case 6)

past history of bilateral total hip replacement, arterial hypertension, type 2 diabetes mellitus and chronic renal failure, referred complaints of inflammatory polyarthralgia and prolonged morning stiffness at a Rheumatology follow-up visit. Multiple conventional radiographs were requested which revealed accidental findings of OPK lesions on shoulders (Figure 4), hips and knees. 99mTc whole-body bone scintigraphy did not reveal any image suggestive of metastases and showed mild hyperfixation in these locations. Blood tests of phospho-calcium metabolism were normal. She denied a family history of rheumatic diseases.

CASE 6

A 29-year-old Caucasian male attended his assistant physician because of non-specific arthralgia of shoulders, hips and knees, without any associated symptoms. He reported a history of renal lithiasis and denied any relevant family history. Clinical examination was normal, without arthritis or limited range of motion. Conventional radiographs showed multiple small, well defined, circular or ovoid sclerotic areas on the shoulders, hips and knees (Figure 5). Unfortunately, the patient missed the following appointments and did not perform the requested blood tests with phospho-calcium metabolism.

DISCUSSION

The first description of OPK dates from 1915, by Albers-Schönberg[1]. It is a rare bone dysplasia, with an estimated incidence of 1 in 50 000[4]. It is inherited in an autosomal dominant pattern, with variable pene-

trance, and characterized by an abnormality in the endochondral bone maturation process that develops during childhood and persists throughout life, causing focal deposits of compact lamellar bone within cancellous bone. Sporadic cases have also been reported[2,5].

According to the published literature, men and women are equally affected[6]. However, in our national case series, male sex was twice as frequent, although it is important to notice that we are only describing six patients. Diagnosis was established at a relatively young age and regarding personal history, there was no common previous pathology in these patients. As very often described[1–4,7], we too found that in half of the cases, diagnosis was an incidental finding, either because the patient had some trauma (case 2 and 3) or because of probably unrelated pain (case 5). Two patients referred joint pain (case 1 and 6).

According to the published literature, clinical manifestations, if present, are usually mild. Mild articular pain with or without joint effusion have been reported in 15 to 20% of the cases[7]. In our series, only two patients were totally asymptomatic. As for the others, it is difficult to clinically demonstrate that the symptoms could be directly attributed to the OPK lesions, since they were very unspecific and each one had multiple lesions in multiple places but not all were symptomatic. Physical abnormalities were only found in the patient with JIA, given her concomitant rheumatic disease. The coexistence of other rheumatic diseases such as rheumatoid arthritis, systemic lupus erythematosus, spondyloarthritis (including psoriatic arthritis), systemic sclerosis, family Mediterranean fever or fibromyalgia were previously described in published report cases[2,6].

Interestingly, none of these patients had dermatologic disorders. However, it has been reported that in 25% of the cases, OPK can be associated with several dermatologic manifestations, such as dermatofibrosis lenticularis disseminata (Buschke-Ollendorff syndrome), characterized by multiple papular fibromas on the back, arms, and thighs, or a predisposition to keloid formation, scleroderma-like lesions or discoid lupus erythematosus[6,7]. According to some authors, OPK has been associated with other conditions such as dacryocystitis, heart or renal malformations and endocrine disorders[2]. As comorbidities, we highlight the history of renal lithiasis in case 6 and type 2 diabetes mellitus and chronic kidney failure in case 5.

Radiologically, OPK lesions appear as sclerotic, numerous, well defined, homogenous, circular or ovoid, varying in size from a few millimeters to several centimeters[6]. They are symmetrically distributed in periarticular locations, more frequently in the epiphysis and metaphysis of long tubular bones, carpal and tarsal bones, metacarpals, metatarsals, phalanges of hands and feet and pelvic bones[7,8]. The involvement of the skull, ribs and clavicles is rare[8]. Our case series is consistent with the published literature, since the most involved bones were carpal bones (3/6), metacarpals (3/6), humeri (3/6), femura (3/6), knees (3/6), ischiopubic branches (3/6), radii (2/6), ulnae (2/6), metatarsals (2/6), tarsals (2/6), phalanges of hands and feet (2/6) and iliac bones (2/6).

Despite being a benign entity, differential diagnosis with other bone pathologies is essential, especially with osteoblastic metastases, mastocytosis, melorheostosis and tuberous sclerosis[3,7]**.** Unlike OPK lesions, osteoblastic metastases are usually asymmetric, highly variable in size, associated with bone destruction and located in vertebral bodies, ribs and diaphysis of long bones[2,9]. In mastocytosis and tuberous sclerosis, sclerotic lesions are more often asymmetric, less defined and have less preference for peri-articular localization[2,7]. 99mTc bone scintigraphy with radiotracer uptake is suggestive of metastases or systemic diseases such as mastocytosis and tuberous sclerosis, while a negative bone scan hints at benign bone disease. Bone scintigraphy can also be useful to exclude the differential diagnosis of melorheostosis, a rare sclerosing bone dysplasia, characterized by cortical and medullary hyperostosis with typical "dripping candle wax" appearance, usually involving the long bones[7,11]. Although bone scintigraphy is usually normal in OPK, it must be borne in mind that cases with mild hyperfixation had been previously reported in the published literature, as described in case 5, reflecting active osseous remodelling similar to what had been observed in bone islands[10]. If doubts remain in the differential diagnosis, a bone biopsy may be considered to exclude other processes.

In half of the cases described the diagnosis was established by the presence of typical radiographic findings together with the absence of laboratory abnormalities, and for one of these patients, also supported by the family history. For the remaining three patients, 99mTc whole body scintigraphy was requested and one exclude metastases but showed mild hyperfixation at the sites where radiographic lesions were identified, probably due to active osseous remodeling. CT scans were also requested in two of these patients to

confirm conventional radiographs findings. For one case only (case 1) some of the lesions had a spiculate appearance that raised the suspicion of a secondary lesion. Complementary evaluation with mammography and thoraco-abdominopelvic CT excluded a primary malignancy. For this particular case, a normal scintigraphy confirmed the diagnosis.

The majority of patients are asymptomatic and do not require treatment. For symptomatic patients, treatment relies essentially on pain relief by using non-steroidal anti-inflammatory drugs, acetaminophen and/or weak opioids. Previously published case reports have reported occasional complications or coexisting pathological conditions such as premyelopathic syndrome due to spinal canal stenosis, hip fracture and tumors (osteosarcoma, chondrosarcoma and giant cell tumor) in OPK patients, suggesting that a regular clinical follow-up of these patients is needed[4]. Nevertheless, the association with these diseases has not yet been confirmed[3], and none of these conditions was seen in our patients.

In conclusion, after exclusion of common differential diagnosis, particularly osteoblastic metastases, diagnosis of OPK should be considered in the presence of the typical, well-defined radiographic findings, in an asymptomatic patient or with mild joint symptoms and without laboratory tests abnormalities.

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