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Original Research Paper

Radiodiagnosis

Pachydermoperiostosis- A rare radiologic case

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ABSTRACT *Pachydermoperiostosis (PDP) or primary hypertrophic osteoarthropathy is a rare syndrome characterized by digital clubbing, pachydermia and periostosis. Though on the basis of clinical and radiological features, a diagnosis of Pachydermoperiostosis (PDP) can be made, it is often missed due to variable presentations. It should be distinguished from the secondary form of HOA, which is much more frequent and mostly associated with severe pulmonary disease, bronchogenic carcinoma, lung emyema, bronchiectasis, congenital heart disease, thyroid and GI malignancy.*

KEYWORDS : Pachydermoperiostosis, primary hypertrophic osteoarthropathy

Introduction

A 60-year-old male presented to the medicine department with complaints of swelling of hands and feet since adolescence. Clinically, the patient had clubbing, deformities of the hands and feet; swelling without acute inflammatory signs at the wrist, ankle, and knee joints; and thickening and folding of the facial skin. The patient complained of excessive sweating and a feeling of heat and burning sensation in the palms and soles. He denied any history of trauma. Lingual enlargement was not present. There was no history of similar disease in the family. To exclude any systemic cause and acromegaly, the patient was referred to the radiology department for radiographs of both hands and feet and skull. Laboratory examination, including thyroid profile (S.Total T3: 0.66ng/ml; S.Total T4:66.7nmol/L; S.TSH: 0.34uIU/ml), growth hormone assay(ILGF-1 level 94.2 ng/ml), tests for syphilis and smears of skin for AFB were unremarkable. HbsAg and HIV were non reactive.Thehemoglobin was normal(12.6gm/dl). Cytology of synovial fluid from one of the knee joints showed features of chronic noninfectious inflammation.

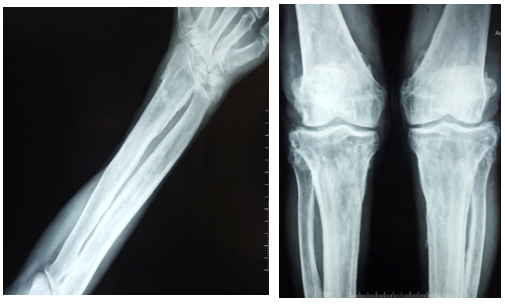

Figure: 1

Radiographs of both forearms and legs reveal symmetric, exuberant, shaggy subperiosteal bone formation; this is more prominent in the leg bones. Additionally, there is expansion of the distal ends of the radius and ulna and the proximal ends of the tibia and fibula, which is associated with a reduction in the radiocarpal and femorotibial joint spaces.

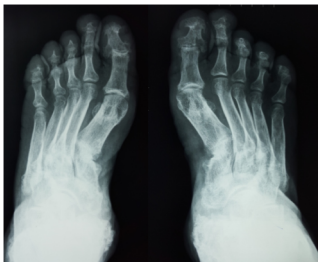

Figure 2

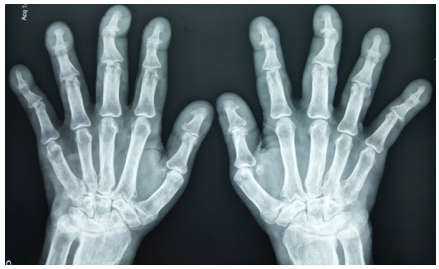

Figure 3

There is reduction in the joint spaces of the proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints. Periarticular osteopenia and resorption of the distal phalanges is noted with associated soft tissue swelling of the distal fingers and toes and contractures of the toes. There is evidence of widening of base of distal phalanx of all fingers of both hands. Enlargement and modeling deformities of the sesamoid bones in both hands and feet is noted; these changes were more severe in the feet.

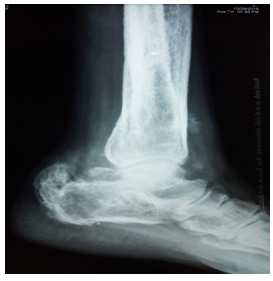

Figure 4

There is evidence of collapse of the calcaneum and calcification of tendoachilles tendon.

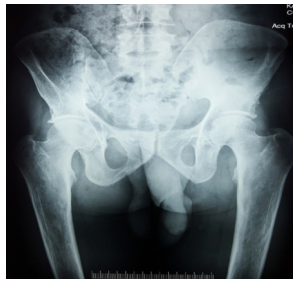

Figure 5

Radiograph of the pelvis, including both hip joints, shows symmetrical and shaggy periosteal reaction along lower lateral aspect of iliac bones. There is evidence of metaphyseal widening of bilateral femur. Cortical thickening with widening of the femoral shafts is noted bilaterally.

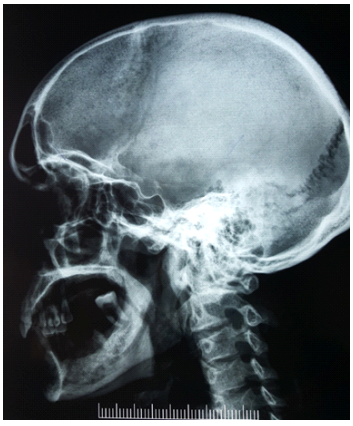

Figure 6

A lateral radiograph of the skull reveals mild hyperostosis of the skull bones in parietooccipital region. The sellaturcica appears normal.

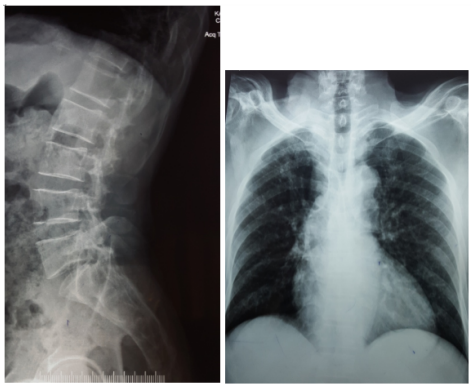

Figure 7

A radiograph of the chest and spine were unremarkable.

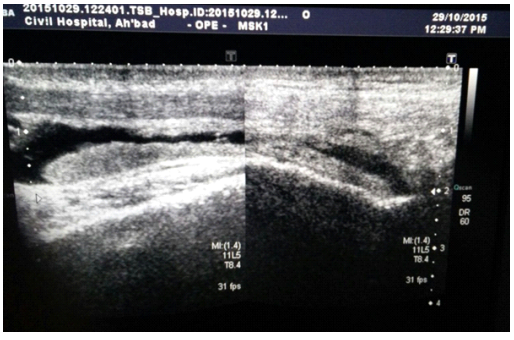

Figure 8

USG examination of the knee joints revealed mild effusion with thickened synovium bilaterally. The effusion was seen to extend into suprapatellar bursa on both sides.

Based on the clinical and radiological findings, a diagnosis of the classic or complete form of PDP or idiopathic hypertrophic osteoarthropathy was suggested.

Histopathological examination of the skin demonstrated basket weaving appearance of keratin suggestive of orthokeratosis with atrophic epidermis. The dermis showed increase in collagen bundles. Alcian blue did not show acid mucopolysaccharide in dermis.

Discussion

PDP or Touraine-Solente-Goleis a rare form of hypertrophic osteoarthropathy with no known cause and hence is often called idiopathic or primary hypertrophic osteoarthropathy to distinguish it from secondary or pulmonary hypertrophic osteoarthropathy. PDP is related to mutations of the gene encoding for 15-hydroxyprostaglandin dehydrogenase(15HPGD).[9]

PDP patients have high levels of PGE2 and decreased levels of PGE-M(the metabolite of PGE2). PGE2 can mimic the activity of osteoblasts and osteoclasts, which may be responsible for the acro-osteolysis and periosteal bone formation. PGE2 also has vasodilatory effects, which may be responsible for prolonged local vasodilation resulting in digital clubbing.[10] PDP accounts for 3–5% of cases of hypertrophic arthropathy[1,2] and affects males more often than females in a ratio of 7:1.

The secondary form results from cardiopulmonary diseases (e.g., bronchiectasis, cystic fibrosis, congenital heart diseases, and tuberculosis); hepatic diseases (e.g., portal and biliary cirrhosis); gastrointestinal diseases (e.g., inflammatory bowel disease and polyposis); and certain malignancies (e.g., Hodgkin's disease, carcinoma nasopharynx, and chronic myeloid leukemia).[2-5]

Touraine *et al*. described three forms of PDP, viz, *classic or complete form*, with skin and skeletal changes; *incomplete form*, with skeletal changes but no dermal findings; and *formefruste* with dermal changes but no skeletal findings.

Clinical manifestations of PDP are thought to relate to excessive collagen formation and dysregulation of matrix proteins owing to fibroblastic hyperactivation .The skin of face, forehead, and scalp become grossly thickened and are at times thrown into folds. A leonine facies is usually a late feature. Sometimes, the scalp takes on an undulating appearance and shows prominent grooves, the appearance being referred to as *cutis verticis gyrata* because of its resemblance to the sulci and gyri of brain. There can also be a so-called *bull-dog appearance*, a feature that was not seen in our case. Cutis verticis gyrata can also been seen in a variety of other conditions, including neurofibromatosis, diabetes mellitus, myxedema, cretinism, amyloidosis, acromegaly, etc., as well as in a variety of other syndromes including Turner's syndrome, Noonan's syndrome, tuberous sclerosis, etc., and hence it is not pathognomonic for PDP.

The eyelids are thickened in 30 to 40 percent of cases giving them an expression of weariness and despair and sometimes leading to difficulty in vision.[11] Seborrhea, as seen in our case, is present in more than 90 percent with sebaceous hyperplasia, oily skin, or acne . The skin of the extremities is thickened and clubbing of the fingers is often seen. Palmo-plantar hyperhidrosis is seen in nearly 44 to 67 percent patients.[11]

Skeletal findings include symmetric, shaggy subperiosteal bone formation in the long bones, especially of the forearm and leg bones, but also of the metacarpals, metatarsals, and phalanges. Involvement of the epiphyseal region distinguishes it from the secondary form, in which the epiphyses are usually spared.[2] There is widening of the ends of bones, especially at the wrist and knee joints. Widening is due to increased bone formation, which is concomitant with histological evidence of increased collagen formation and increased urinary excretion of hydroxyproline.[6] Factors that stimulate both osteoblasts and osteoclasts have been implicated, thus explaining both the periostosis as well as the osteoporosis / osteolysis seen in this condition.[7] A prominent feature is enlargement of the distal part of the digits with resorption of the distal phalanges or acroosteolysis and calcification of

ligaments and interosseous membranes. In later stages, cortical thickening with narrowing of the medullary cavity may be seen. Enlargement of sinuses may be seen uncommonly. Bone scintigraphy may reveal increased tracer uptake by the cortex in the diaphyseal and metaphyseal regions. Hyperostosis of the calvaria and skull base bones, as seen in our case, is common.

Joints affected in PDP show swelling due to joint effusion, with evidence of chronic nonsuppurative inflammation. There is reduction in joint spaces, with relative preservation of articular surfaces. Late-onset deformities, including contractures, may occur, especially in the digits. Periarticular erosions, as seen at the PIP joints in our case, are very rare.

Spinal manifestations are unusual but have been described. These include narrowing of the intervertebral disk spaces and foramina, dense striations in the vertebral bodies arranged in a horizontal or vertical fashion, and ligamentous ossification and laxity with secondary spondylolisthesis.[2, 3, 5] Spinal findings were not a prominent feature in our case.

Differential diagnoses include variants of PDP, secondary hypertrophic osteoarthropathy, thyroid acropachy, acromegaly, van Buchem's disease (in which there is absence of clubbing and skin changes), diaphyseal dysplasia (endosteal and periosteal proliferation), and syphilitic periostosis.

Variants of PDP include *Rosenfeld-Kloepfer syndrome* (characterized by enlargement of the jaws, especially mandible, and of the hands and feet, nose, lips, tongue, and forehead, along with cutis vertices gyrata and corneal leukoma); *Currarino idiopathic osteoarthropathy* (an incomplete form of PDP seen in children and adolescents and characterized by the presence of eczema and sutural diastases); and a *localized form* with only the radiographic features of PDP in the lower extremities.[8]

Conventional PDP drug treatments to decrease inflammation and pain include NSAIDs and corticosteroids .[12] Rheumatologic symptoms can be improved by treatment with bisphosphonates, such as pamidronate or risedronate.[12] In isolated cases, tamoxifen was effective in PDP treatment, especially for bone and joint pain.[12] Retinoids are used to improve skin manifestations. Isotretinoin improves cosmetic features by inducing apoptosis within human sebaceous glands. As a result, the increase of connective tissue and hyperplasia of sebaceous glands is inhibited. Retinoids also decrease procollagen mRNA in fibroblasts, improving pachyderma. [13,14] Colchicine can also improve skin manifestations.[12] The use of Botulinum toxin type A (BTX-A) may improve the leonine facies. Surgical methods, including facelifts and facial rhytidectomy, have also been used to improve facial appearance.

To summarize, our patient presents classic or complete form of PDP with the distinct clinicoradiologic features of clubbing and enlargement of digits, thick and coarse facial skin, subperiosteal bone formation in the long bones, and joint abnormalities, including effusion and deformities. He also had seborrhea, coarsening of facial features and hyperhidrosis. The absence of any chest complaints, normal chest radiograph and euthyroid state rule out the secondary pathologies. Normal X-ray of skull, absence of any frontal bossing or prognathism with normal growth hormone level rule out acromegaly.

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