



Primary Hypertrophic Osteoarthropathy: A Case Report

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ABSTRACT

The primary hypertrophic osteoarthropathy (PHOA or pachydermoperiostosis) is a rare (5% of total HOA) hereditary disease. One study described that the prevalence of PHOA is 0.16%. PHOA characterized by skin thickening (pachydermia), finger clubbing, and proliferation of periosteum (periostitis) with subperiosteal new bone formation and enlarged extremities secondary to periarticular and bone proliferation. Clinical manifestations are variable; the term complete syndrome is used for the patient with pachydermia, coarsening of the face skin and scalp, periostitis, and cutis verticis gyrata; the incomplete form is used when there is no sparing of the scalp; and the frusted form is used for pachydermia with minimal or absent periostitis. We describe a 29-year-old white man with PHOA, and clinical and radiological characteristics of this syndrome, as well as therapeutic approach of PHOA.

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Introduction

Pachydermoperiostosis or primary hypertrophic osteoarthropathy (PHOA), described for the first time by Friedreich in 1868, is a hereditary disease and a rheumatologic condition in which the patient presents with digital finger clubbing of hands and feet, enlarged extremities

secondary to bone and periarticular tissue proliferation, joint pain and edema, bilateral eyelid ptosis, periostosis, leonine face, and skin thickening (pachydermia), coexisting with a variety of clinical manifestations including hyperhidrosis, arthritis, cutis verticis gyrata, joint pain, edema, and hypertrophic gastritis (1-9).

The ratio of the disease in men to women is 8:1. It has genetic aggregation in 25% to 38% of cases, being mainly autosomic dominant in nature (10, 11). It is classified as either primary (pachydermoperiostosis) or secondary. The primary, or idiopathic, form is considered rare, appearing in 3-5% of all cases. Here, we describe the clinical and radiological manifestations of a patient with the primary form of hypertrophic osteoarthropathy, focusing on the therapeutic challenge of refractory joint pain.

Case Report

A 29-year-old white man was admitted to the hospital 5 years ago with leonine facial features (Figure 1a), hyperhidrosis, swelling, and pain in the knees and ankles, with worsening during exercise and without morning stiffness. Fever or other associated symptoms were denied. The patient had taken non-steroidal anti-inflammatory drugs (NSAIDs) without sensing any improvement. He denied any rheumatologic disease or similar condition in his family. The osteoarticular examination showed digital clubbing with watch-glass nails (Figure 1b), and swelling of the knees (Figure 1c).



Figure 1. The symptoms of primary hypertrophic osteoarthropathy in a 29-year-old man with leonine facial features (a), digital clubbing with watch-glass nails (b), swelling of the knees (c), gross irregularities and intense periosteal proliferation in the epiphyses, metaphysis, and diaphysis in the tibia and fibula X-rays (d and e)

Tibia and fibula X-rays (Figures 1d and 1e) showed gross irregularities and intense periosteal proliferation in the epiphyses, metaphysis, and diaphysis. Laboratory analysis showed an erythrocyte sedimentation rate (ESR) of 10 mm/hour in the first hour, C-reactive protein (CRP), non-reactive rheumatoid factor, antinuclear factor (ANF), and anti-DNA antibodies were normal. Insuline-like growth factor 1 (IGF1), thyroid functional tests (TFT), calcium, and uric acid were normal. Purified protein derivative (PPD) was negative.

In arthrocentesis, about 500 ml of synovial fluid of the right knee and 400 ml of the left knee was obtained, found to have white blood cells (WBC) as 320 cell/mm³, predominantly lymphocytes (90%), and normal glucose concentrations. No crystals were seen using polarized light microscopy. Imaging and cardiac echocardiography and laboratory tests were performed, which excluded secondary causes of osteoarthropathy. Knee massive effusion, nodularity, and thickening with maximum thickening in suprapatellar pouch (approximately 9 mm), and moderate effusion with nodularity and maximum thickening of about 4 mm in right knee were seen in the magnetic resonance imaging (MRI) pictures (Figure 2).



Figure 2. The magnetic resonance imaging (MRI) picture with knee massive effusion, and sinovium nodularity and thickening with maximum thickening in suprapatellar pouch (approximately 9 mm), and moderate effusion with nodularity and maximum thickening (about 4 mm) in right knee

During his follow up, upper gastrointestinal (GI) endoscopy diagnosed nothing.

Indomethacin, pamidronate, and short-term low-dose prednisolone were prescribed; but the patient was not treated successfully. Finally, because of the thickness (more than 3-4 mm) and multidisciplinary consultations between orthopedist, rheumatologist, and radiologist, we decided to do surgery and synovectomy.

Discussion

Autosomal dominant with variable expression inheritance and incomplete penetration is the main method of transmission of pachydermoperiostosis; however, in some patients, heredity has been autosomal recessive or even X-linked (7, 12, 13).

In the histological evaluation, hyperplasia of the subcutaneous conjunctive tissue was observed (1, 13). The exact etiopathogenesis of PHOA is unknown; but, a pathogenic role for vascular endothelial growth factor is well known (2, 14).

A brief study of patients agreed abnormal peripheral blood supply. Biopsies of skin and bone marrow showed an exacerbated proliferation of fibroblasts, associated with diffuse epidermal hyperplasia, partial occlusion of vascular lumen, and lymphohistiocytic infiltration with collagen deposition (3). Frequent studies indicated capillary endothelial hypertrophy in skin. But, an isolated study showed just a decrease in total protein rate and collagen synthesis, with significant increase of proteoglycans and sulfated glycosaminoglycans (7).

Some studies showed an increase of plasmatic substances including osteocalcin, endothelin-1, β -thromboglobulin, platelet-derived growth factor (1), von Willebrand factor, and vascular endothelial growth factor (15). Increased nuclear steroid receptor concentrations in these patients suggest an increase in tissue sensitivity to circulating sex hormones (1).

The idiopathic form (pachydermoperiostosis, primary hypertrophic osteoarthropathy, or

touraine-Soulente-Golé syndrome) is a rare disease with unknown etiology, and represents 3% to 5% of all cases of hypertrophic osteoarthropathy (1, 8, 16).

The presence of digital clubbing, radiographic periostosis and leonine facial features are the main diagnosis criteria symptoms of PHOA usually appear during puberty, and are more frequent and intense in men (2, 3, 17). Sebaceous hypersecretion associates with acne, hyperhidrosis, skin fold thickening, or pachydermia, originating deep facial skin folds around the nose, mouth, and on the forehead, as well as lower limb edema (2, 3, 6, 7, 15, 18).

A mutation linked to the X chromosome, in association with hormonal alterations (testosterone-dependent proliferation), may be involved in the distribution of disease by the gender (1, 19). One third of patients with PHOA show swelling, pain, and functional impairment of a sufficient intensity to interfere with activities of daily living (1, 3, 15, 18).

Along with PHOA, co-morbidity, the association of pachydermoperiostosis with ankylosing spondylitis, rheumatoid arthritis, and palindromic rheumatism, is possible (10, 16, 17).

The coexistence of psoriatic arthritis, especially its onco-pachydermoperiostosis variant, also has been reported (17, 20).

In PHOA, in contrast to secondary hypertrophic hyperostosis, it is rare to see symmetric arthritis with an intense inflammatory component or villionodular synovial proliferation (1, 13, 17). Pachydermia with minimal bone disease can be seen with prominent bone and joint manifestations without pachydermia (3, 17, 21).

Simple X-rays permit the evaluation of hyperostosis of the ribs, cranium, and pelvis; but it is useful especially for long bones analysis of the diaphysis, metaphysis, and epiphysis, and acroosteolysis of the distal phalanges (1, 17). Bone scans with Tc99 methylenediphosphonate shows increased uptake (7, 17). More than 20% of patients

with PHOA present hypertrophic gastritis or gastric ulcer (6, 17, 22-25).

The diagnosis is done based on clinical and radiological data. It is necessary to exclude secondary forms of hypertrophic osteoarthropathy. The recommended treatment for pachydermoperiostosis is the use of analgesics, NSAIDs, colchicine, or courses of oral corticoids, although all of them may be ineffective (17).

Tamoxifen citrate (22), biphosphonates (1, 17) colchicine, and retinoids improve skin manifestations, while tamoxifen and biphosphonates significantly alleviate musculoskeletal symptoms, especially joint and bone pain (26).

Genetic counseling for patients is a guide for treatment, regarding to the difficult diagnosis (1).

Conflict of Interests

Authors have no conflict of interests.

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