

CASE REPORT

Pachydermoperiostosis (Touraine-Solente-Golé syndrome). Case report

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Abstract. Pachydermoperiostosis or primary hypertrophic osteoarthropathy, also known as Touraine-Solente-Golé syndrome, is a rare process, frequently inherited. In its complete form it is characterized by pachydermia (thickening of the skin), skeletal changes (periostosis) and acropachia (digital clubbing). We report a patient that consulted for skeletal symptoms, as the acropachia and cutaneous manifestations (thickening of the skin of the face, scalp, hands and feet) went unnoticed due to their slow and progressive development. We review the characteristic features of this syndrome. We highlight the importance of ruling out secondary forms of hypertrophic osteoarthropathy and of a close follow-up of these patients because of complications that might develop on the long-term.

Key words: pachydermoperiostosis, primary hypertrophic osteoarthropathy, Touraine-Solente-Golé syndrome.

PAQUIDERMOPERIOSTOSIS (SÍNDROME DE TOURAINE-SOLENTE-GOLÉ). DESCRIPCIÓN DE UN CASO

Resumen. La paquidermoperiostosis u osteoartropatía hipertrófica primaria, también conocida por síndrome de Touraine-Solente-Golé, es un proceso infrecuente, a menudo hereditario. Se caracteriza en su forma completa por paquidermia (engrosamiento cutáneo), alteraciones óseas (periostosis) y acropaquia (dedos en palillo de tambor). Se presenta un caso, cuyo motivo de consulta fueron los síntomas óseos, habiendo pasado desapercibidas, por su desarrollo lento y progresivo, la acropaquia y las manifestaciones cutáneas (engrosamiento en la piel de la cara, cuero cabelludo, manos y pies). Revisamos los rasgos fundamentales de este síndrome. Destacamos la importancia de descartar las formas secundarias de osteoartropatía hipertrófica y hacer un seguimiento de estos pacientes por las complicaciones que, a largo plazo, pueden desarrollar.

Palabras clave: paquidermoperiostosis, osteoartropatía hipertrófica primaria, síndrome de Touraine-Solente-Golé.

Introduction

Hypertrophic osteoarthropathy (HOA) is a syndrome characterized by acropachy (clubbing), periostosis, and arthritis. A distinction is made between 2 varieties of HOA. Primary or idiopathic HOA is more commonly known as pachydermoperiostosis (PDP) or Touraine-Solente-Golé syndrome.¹ A secondary—and more common—form of HOA develops fundamentally as a consequence of underlying lung or heart disease (which may occasionally be neoplastic).^{2,3} PDP is defined by major and minor criteria. The 3 major criteria are pachydermia, periostosis, and digital

clubbing, and the minor criteria include seborrhea with sebaceous hyperplasia, folliculitis, acne, hyperhidrosis, and cutis verticis gyrata. The primary form is considered to be hereditary, even though a family history of the disease can, in fact, only be traced in around 25% to 38% of cases. Approximately 95% of cases are secondary HOA and 5% are primary HOA. Expression tends to be variable, and so complete versions of the syndrome are infrequent. Skin manifestations when present may go unnoticed by the patient and his or her family and friends.

Below we report the case of a patient with the complete form of primary HOA (ie, PDP), who was referred to us by the rheumatology department.

Case Description

The male patient, aged 54 years and with no children, was a construction worker. Of note in his medical history was

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Figure 1. Hyperostosis and periostitis in the metacarpal bones and proximal phalanges. and tumefaction of the soft tissues.

the third-degree consanguinity of his parents. He had a healthy brother. His personal history included a fracture of the left tibia and fibula in 1990, and diagnosis of Paget disease in 1992. He was a regular drinker of 1 L of wine daily.

The patient was referred to the rheumatology department because of pain in his fingers, toes, and knees, which worsened on climbing up and down stairs. He also had nighttime pain in the lower limbs that responded to treatment with nonsteroidal anti-inflammatory drugs.

A radiographic study of the skull, long bones, spine, pelvis, hands, and feet revealed hyperostosis of the forearm bones, the femur, and the tibia, with marked periostitis and healed fractures in the left tibia and fibula. X-rays of the hands revealed soft tissue tumefaction, particularly in the distal phalanges, and periostitis and hyperostosis of the metacarpal bones and proximal phalanges (Figure 1); x-rays of the feet showed hyperostosis of the metatarsal bones, osteophytes, and sclerosis in the right foot.

Given that the development of the patient's skin lesions was insidious, they had gone unnoticed by the patient and his family. The patient had very pronounced folds in the area of the forehead, between the eyes, and in the nasolabial grooves (Figure 2). Several very noticeable folds (cutis verticis gyrata) were also evident in the occipital region (Figure 3). Thickened eyelid edges were also evident (Figure 4), and the patient's general facial expression was sad. The skin of the hands was rough to the touch. The patient's fingers were enlarged and showed evidence of clubbing (Figure 5), and likewise the toes, which—in addition—had thickened nails. The ankles had an edematous appearance.

Routine tests (complete blood count, erythrocyte sedimentation rate, serum electrolytes, blood sugar, blood urea nitrogen, creatinine, uric acid, calcium, phosphorus, liver and thyroid function, lipid profile, proteinogram,



Figure 2. Highly marked skin folds on the face.



Figure 3. Occipital folds indicating incipient cutis verticis gyrata.

immunoglobulins, rheumatoid factor, and urine analysis) revealed no abnormalities. Chest x-ray, electrocardiogram, and bone scintigraphy results were normal.

A skin biopsy of the back of the hand showed a normal epidermis and a thickening of the dermis due to collagen fibers (Figure 6).



Figure 4. Thickened upper and lower eyelid edges.



Figure 5. Hands with clubbed fingers.

Discussion

Primary HOA—also referred to as PDP—is a rare entity. Some of the abnormalities caused by this syndrome were described by Hippocrates in 450 BCE and were also observed in skeletons found in Central America around the same time.⁵

Primary HOA was first described by Friedrich in 1868 as “hyperostosis of the entire skeleton.”^{2,3} In 1890 Pierre Marie defined it as pneumonic hypertrophic osteopathy.^{2,3} Touraine, Solente and Golé—who gave the syndrome one of its names—characterized PDP as a primary form of hypertrophic osteopathy in 1935.¹ These authors recognized the disease as inherited with 3 possible presentations: a complete form that co-occurs with pachydermia and periostosis; an incomplete form without pachydermia; and a *forme fruste* or minimal form with pachydermia and minimal bone modifications.

PDP predominates in males, occurring in around 9 men for every woman. The disease, often hereditary, is transmitted in autosomal dominant form with incomplete

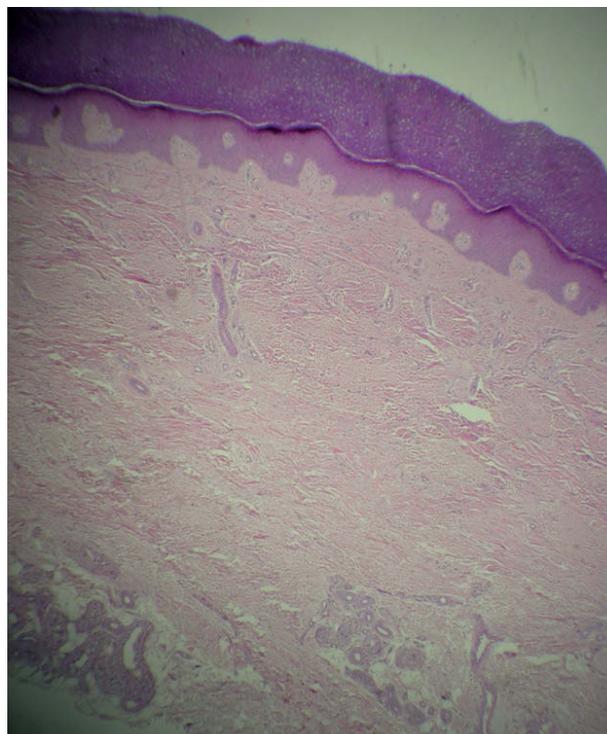


Figure 6. Diffuse thickening of the dermis due to collagen bundles (hematoxylin-eosin magnified $\times 60$)

penetrance. However, cases have also been described that are transmitted in autosomal recessive form, and also cases with a history of consanguinity (as was the case with our patient, whose parents were consanguineous). Chromosomal abnormalities and a greater incidence of the HLA-B12 antigen have also been detected in these patients. The disease typically appears in infancy and adolescence, progresses for a number of years, and then stabilizes. Pachydermia—which affects the face and limbs—is the most frequent skin symptom. Patients may also present with seborrhea, acne, folliculitis, dilated pores, hyperhidrosis of the palms and soles, large skin folds, and reduced facial and pubic hair.^{4,6} A differential diagnosis is required given the clinical similarity to acromegaly, which is also accompanied by skin abnormalities, including *cutis verticis gyrata*. In the case of acromegaly, however, bones in general are larger in the face, jaw (prognathism), skull, and limbs, and this is very evident in a radiographic study in the absence of signs of periostosis.⁴

Rheumatology symptoms—from which our patient suffered—are a typical presenting complaint (bone pain, accumulated joint fluid, and asymmetric arthritis).³ A radiographic study of our patient revealed irregular periosteal ossification affecting, above all, the long bones, the metacarpal and metatarsal bones, the phalanges, and the epiphysis. Soft-tissue thickening, rotator cuff calcifications, and more rarely, eroded joints may also be observed.⁷ A

differential diagnosis with psoriatic arthritis and rheumatoid arthritis is required.⁸

Other possible nonskin and nonbone symptoms include gynecomastia, mental retardation, and periodontal anomalies.⁴

A range of processes (some malignant) have been reported in association with PDP. These include facial epidermoid carcinoma,⁹ hypertrophic gastritis, peptic ulcer, gastric adenocarcinoma,¹⁰ Crohn disease, and myelofibrosis.¹¹ As a consequence of increased soft tissue bulk and hyperostosis, complications may arise such as ptosis,⁵ compression of the nerve endings, hearing problems, kyphosis, arthrosis, osteonecrosis of the femoral head, and carpal tunnel syndrome.⁴

The clinical picture is of interest because of the importance of distinguishing between the primary (PDP) and secondary form of the disease. Secondary HOA is typically preceded by lung disorders (tumors, abscesses, emphysema, bronchiectasias, cystic fibrosis), cardiac disorders (congenital diseases, endocarditis), hepatic processes (cirrhosis, neoplasms), intestinal processes (neoplasms, inflammatory bowel disease, polyposis), and/or thyroid diseases (Graves disease). Bone lesions in this secondary form are more painful and progress more rapidly, whereas skin changes range from slight to moderate. The prognosis ultimately depends on the underlying disease.^{6,12-14}

Both PDP and secondary HOA share the same poorly understood pathogenesis. A neurological basis is posited, and stimulation of the vagal neural crest has been suggested as an etiological factor, given that the syndrome in some patients reverses after a vagotomy.¹⁵ More recently, abnormalities in fibroblast functionality have been implicated, along with an increase in the synthesis of collagen fibers.⁸ Platelets, with their potent growth factors, have also been suspected.^{8,10} Alcohol intake aggravates the process in some cases.⁴ A degree of chromosomal instability is considered possible, as genetic disorders such as xeroderma pigmentosum, ataxia-telangiectasia, and Fanconi anemia, among other diseases, have been described in association with PDP.⁹ Finally, greater cellular hypersensitivity to external stimuli (physical and chemical agents) may explain the predisposition of these patients to develop certain kinds of cancer.¹⁰

Many of these patients do not undergo biopsy. Pathology findings are usually the same as those encountered in our patient: normal or acanthotic epidermis, diffuse thickening of the dermis due to collagen bundles, and increased acid mucopolysaccharides. In more advanced phases, capillary thickening, an increase in pericapillary collagen, and hypertrophy of the sebaceous and eccrine glands may be observed.⁴

Treatment, which is symptomatic and aimed at attenuating the bone pain, is based on nonsteroidal anti-inflammatory drugs, pamidronate, or colchicines. Oral

isotretinoin has also been used to treat skin problems such as seborrhea or acne. Surgery may be necessary for ptosis.⁵

Our patient had the complete form of PDP, since he had hyperostosis, finger clubbing, and pachydermia. Although his parents are consanguineous, there is no evidence that they suffer from the disease. Joint problems were the presenting complaint. The clubbing in the hands and feet had developed gradually and was not considered important by the patient, who likewise was unconcerned about the facial manifestations. Given the complementary tests performed, and bearing in mind the slow development of the process, once the possibility of a systemic disease was ruled out, we were left with the diagnosis of a secondary form of osteoarthropathy.

We conclude that a diagnosis of PDP or primary HOA (Touraine-Solente-Golé syndrome) requires a high degree of clinical suspicion, given that many patients are erroneously diagnosed for years as having Paget disease or acromegaly. These patients are typically initially assessed by orthopedic surgeons or rheumatologists. A family history exists in about a third of the cases and so it is important to consider close relatives. Skin lesions, if not very evident, easily go unnoticed. Given that there may be no family history or complete clinical or radiological expression, in order to arrive at a diagnosis, skin symptoms (pachydermia, acropachy) and radiological evidence (periostosis) need to be assessed in conjunction. Furthermore, any cardiac or pulmonary disorders that might explain the development of secondary forms of the disease must be ruled out. Finally, it needs to be underlined that patients with primary HOA require regular monitoring as, in the long term, they may develop malignancies and complications due to excessive growth in the soft tissues and bone tissues.

Conflicts of Interest

The authors declare no conflicts of interest.

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