





Complete pachydermoperiostosis: A case report

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ABSTRACT

Pachydermoperiostosis (PDP), also known as Touraine-Solente-Gole syndrome or primary hypertrophic osteoarthropathy, is a very rare disease mainly characterized by pachyderma, finger clubbing, hyperhidrosis, and periostosis. We reported a case of a patient who suffered from gradual pain and enlargement of both hands and feet for 25 years despite receiving treatment from multiple clinics. He also experienced gradual abnormal changes in his face and scalp. Radiographic images of the lower limbs revealed the presence of subperiosteal bone growth and periosteal hypertrophy. The diagnosis of complete PDP was made late due to its rarity and the unfamiliarity of medical practitioners with the diagnosis. This case highlighted the need for medical practitioners to be aware of rare diseases so that patients may be diagnosed and treated earlier and thereby relieving their anxiety and improve their quality of life.

Keywords: cutis verticis gyrata, osteoarthropathy, pachydermoperiostosis, Touraine-Solente-Gole syndrome

INTRODUCTION

Pachydermoperiostosis (PDP) is a very rare genetically determined condition characterized by skin thickening (pachyderma), finger clubbing, hyperhidrosis, and extremity enlargement secondary to overproduction of bone tissue (periostosis) [1]. This condition is postulated to be associated with mutations in two genes: the hydroxyprostaglandin dehydrogenase (HGPD) gene [2] and the solute carrier organic anion transporter family member 2A1 (SLCO2A1) gene [3, 4]. Mutations in SLCO2A1 gene that affect prostaglandin transportation were previously reported in patients of African, Asian, and Caucasian descends [3-8]. Due to the limited number of cases, many health practitioners are not familiar with the diagnosis. This case is intended to shed light on the importance of increasing awareness about rare diseases. By doing so, we can better understand the challenges faced by those affected and work towards improved diagnosis, treatments, support, and inclusion for individuals living with rare conditions

CASE REPORT

We reported a case of a 41-year-old man who presented with bilateral hands and feet pain that started insidiously and was throbbing in nature. He also noted that his hands and feet had increased in size gradually and that he had experienced excessive hand sweatiness for the last 25 years. He denied having photosensitivity, oral ulcers, or alopecia. On examination, he had an oily face with coarse, thickened facial

skin and deeply furrowed forehead skin (part 1a in **Figure 1**). His eyelids were floppy, nearly hiding his eyes, and his scalp was cerebriform, with folds and furrows (cutis verticis gyrata) (part 1b in **Figure 1**). His eyelids were thickened, with bulging palpebral superiorem nearly hiding his eyes, giving the impression of eyelid ptosis (part 1c in **Figure 1**). Further eye examination showed the muscles of his eyelids were not lax, and there was no eyelid eversion. The conjunctivae were slightly erythematous, but no papillae were seen. The pupils' size and reaction were normal, as were the ocular movements, and his visual acuity was six/nine in both eyes. He had clubbing on both hands and feet (part 1d and part 1e in **Figure 1**). The cardiovascular, respiratory, and gastrointestinal examinations were also normal.

Blood investigations revealed a normal complete blood count and inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate were also normal. Additional tests including insulin-like growth factor-1 (IGF-1), thyroid, liver, and renal functions were also normal. Radiographic investigations were also ordered in view of the enlarged structures. X-ray of the right lower limbs showed periosteal hypertrophy and subperiosteal bone growth (part 2a in **Figure 2**) while bilateral hand X-rays showed soft tissue swelling at the distal phalanges, and periostosis at the metacarpal and proximal phalanges (part 2b in **Figure 2**). The skull radiograph revealed mild thickening of the cortex and subperiosteal tissue (part 2c and part 2d in **Figure 2**).

The clinical evaluation coupled with the blood investigations and radiographic imaging showed that his presentation may be connected to hypertrophic osteoarthropathy, and the diagnosis of PDP was made. The



Figure 1. Features associated with complete PDP: thickening of facial fold, eyelid ptosis, & deeply furrowed forehead skin (1a & 1c), cutis verticis gyrate (1b), & enlarged hands & finger clubbing on both hands (1c & 1e) (Reprinted with permission of the patient)

patient was counselled regarding his diagnosis and was treated symptomatically with non-steroidal anti-inflammatory drugs (NSAIDs) and oral steroids. His musculoskeletal pain responded well to the given treatment.

DISCUSSION & CONCLUSIONS

PDP, previously referred to as Touraine-Solente-Gole syndrome or primary hypertrophic osteoarthropathy, is an extremely uncommon medical condition characterised by a trio of distinctive features: digital clubbing, periostosis of tubular bones and pachydermia [1]. Other minor features include hyperhidrosis, arthralgia, gastric ulcer, cutis verticis gyrate, blepharoptosis, joint effusion, column-like legs, seborrhea and acne [9]. PDP can be classified into three forms based on the clinical features:

- (1) complete (digital clubbing, pachydermia, and periostosis),
- (2) incomplete (no pachydermia), and
- (3) fruste form (prominent pachydermia with few skeletal manifestations) [2, 10].

PDP is an uncommon genetic disorder whose exact incidence is not known; however, the estimated prevalence of the disease is 0.16% [11]. Among the reported cases, 30.00% of the patients with PDP show autosomal dominant inheritance with variable penetrance and men are more commonly affected than women, with a 7:1 ratio [10-12]. Complete PDP, with the presence of all the triads, accounts for 3.00% of all cases of primary hypertrophic osteoarthropathy [13]. The mutations that occur in HGPS gene or SLC02A1 gene may typically emerge as a clinical condition during adolescence



Figure 1. X-ray images of hands, right lower limb, & skull show cortical thickening, periosteal, & subperiosteal hypertrophy (2a, 2b, 2c, & 2d) (Reprinted with permission of the patient)

[12], as demonstrated by our patient, and progress insidiously for 5 to 10 years before remaining unchanged [10]. Clinical manifestations can vary according to the form of primary hypertrophic osteoarthropathy the patient suffers from [13]. In our case, the patient mainly exhibited joint pains resulting from a sympathetic response to periostosis.

Bilateral and symmetrical cortical thickening and periostosis in the long bones are the main radiographic characteristics that differentiate this condition from other possible diagnoses [10]. The periosteal reaction usually affects the shaft, often reaching the epiphysis of the long bones but sparing the joint spaces. The joint spaces are usually maintained due to the lack of erosion or periarticular bone loss [14]. These changes in the periosteal reaction may be due to the increased level of prostaglandin E₂ (PGE₂) because of mutation in HGPS gene, which can mimic the activity of osteoblasts and osteoclasts. The mutation in this gene may also cause dysregulation of mesenchymal cells, resulting in thickening of the facial skin and scalp, and can progress to the point of developing cutis verticis gyrate, leading to a leonine appearance characteristic of PDP [10]. Moreover, the ptosis often seen in PDP patients is a pseudoptosis due to sebaceous gland hyperplasia and excessive mucin deposition in the dermal layer [15, 16]. This mechanical dysfunction results in thickened and hypertrophic eyelids, mistakenly seen as ptosis. Previous literature has reported the finding of floppy eye syndrome in a PDP case [17] but our patient did not display significant eyelid laxity to fulfil the criteria of floppy eyelid syndrome.

PDP may be differentiated from acromegaly based on clinical features and laboratory results. Unlike those suffering from PDP, patients with acromegaly tend to have enlarged bones of the face, skull, and limbs in addition to jaw

prognathism [1]. Higher levels of IGF-1 and a positive oral glucose tolerance test are indicative of acromegaly [18].

Acromegaly is often due to pituitary tumors; hence, patients with acromegaly may also display signs of local compression and hormonal disturbances, which may aid in distinguishing it from PDP. The absence of these clinical features and inconsistent biochemical indicators for acromegaly enabled us to confidently eliminate this alternative diagnosis for our patient. Another potential differential that we considered was thyroid acropachy, a rare complication of autoimmune thyroid disease. Patients with thyroid acropachy may exhibit periostosis and joint pain, resembling some aspects of PDP [14]. However, there will also be other features of autoimmune thyroid disease, such as exophthalmos and pretibial myxedema [14]. The clinical history and examination of our patient suggested that he was euthyroid, and the subsequent thyroid function test was also normal and thus this diagnosis was eliminated.

For standard practice, the presence of a genetic mutation should be demonstrated to confirm PDP, as the severity of pachydermia correlates with serum PGE2 levels and *SLCO2A1* genotypes [8]. Unfortunately, genetic testing was not available at our center. After ruling out possible differentials, we made the diagnosis of complete PDP based on clinical-radiological findings. PDP is not treatable or reversible as it is a defect in genes. Thus, conservative symptomatic treatment is given as required. For PDP patients presenting with bone pain, NSAIDs and steroids are the medications of choice in the treatment of arthritis [14] since PGE2 is likely involved in periosteal bone growth and acroosteolysis.

This case highlighted the need for medical practitioners to be aware of rare diseases so that patients may be diagnosed and treated earlier. In the case of PDP, given its rarity and range of clinical manifestations, being aware of the condition is necessary for its diagnosis. This awareness is important since the majority of patients need only conservative treatment for their musculoskeletal problems, which can alleviate their anxiety and suffering. It is also important to remember that not all joint pains are due to arthritis, and a triad of digital clubbing, periostosis of tubular bone, and arthritis should raise the warning of possible cases of PDP.

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