

CASE REPORT

## Pachydermoperiostosis (Touraine-Solente-Gole Syndrome): A Case Report of Primary Hypertrophic Osteoarthropathy

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### ABSTRACT

Pachydermoperiostosis (PDP), or primary hypertrophic osteoarthropathy (PHO), also known as the Touraine–Solente–Gole syndrome, is an autosomal dominant genetic disorder that is rare and is identified by finger clubbing, skin thickening, and periosteal growth. This case study details the case of a 21-year-old man with PDP to raise awareness, improve diagnosis, and enhance management strategies for the condition. The individual showed common signs like digital clubbing, pachydermia, and periostosis, as well as related symptoms like hyperhidrosis. Radiological imaging supported the diagnosis by revealing periosteal reactions and cortical thickening in multiple bones. Other conditions with comparable clinical characteristics were considered in the differential diagnosis, however, the diagnosis of PHO was confirmed by the specific radiological results and normal hormonal levels. The treatment primarily targets alleviating symptoms with drugs like Non steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, along with newer options such as bisphosphonates. Timely detection and correct treatment are essential to enhance the well-being of people with PHO. This case study emphasizes the significance of tracking symptoms and offering thorough care to those with PDP/PHO.

**Keywords:** Digital Clubbing, Primary Hypertrophic Osteoarthropathy, Pachydermoperiostosis, Periostosis, Touraine-Solente-Gole Syndrome.

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### INTRODUCTION

Pachydermoperiostosis (PDP), also referred to as primary hypertrophic osteoarthropathy (PHO), is a rare genetic condition that was first described in 1868.<sup>1</sup> The precise frequency of PDP is still uncertain,<sup>2</sup> but it is significantly more common in teenage boys, with a male-to-female ratio of approximately 7:1.<sup>3,4</sup> It is characterized by finger and toe clubbing (acropachy), skin thickening (pachyderma) mainly on the face, increased sweating, and the formation of new bone linked to joint pain.<sup>5</sup> In 1935, doctors Touraine, Solente, and Gole pinpointed this ailment as a genetic issue with three forms: full (involving periostosis and pachyderma), incomplete (without pachyderma), and forme fruste (minimal skeletal changes with pachyderma). As a result, PDP is also known as the Touraine-Solente-Gole syndrome.<sup>6</sup>

The pathogenesis of PDP is still partially understood. The connection between PDP and the 15-hydroxyprostaglandin dehydrogenase gene and the solute carrier organic anion transporter family member 2A1 has been identified. It is thought that increased

levels of prostaglandin E2 (PGE2) are caused by disrupted specific intake through the cell membrane by solute carrier organic anion transporter family member 2A1 and/or insufficient breakdown by 15-hydroxyprostaglandin dehydrogenase (HPGD), contributing significantly to the progression of PDP.<sup>7,8</sup> Research has shown a correlation between serum PGE2 levels and the severity of pachydermia and its associated histological changes. It is believed that increased PGE2 levels in PDP patients can cause tissue remodeling and vascular activation via cytokines, resulting in symptoms such as excessive sweating, bone erosion, bone overgrowth, joint inflammation, and thickening of the skin. Instances have been recorded showing an autosomal recessive pattern of inheritance caused by harmful alterations in the HPGD gene, which codes for an enzyme that breaks down PGE2, and in the SLCO2A1 gene, which codes for the prostaglandin transporter that aids in PGE2 absorption. However, there have been families that showed autosomal dominant inheritance with incomplete penetrance.<sup>9,10</sup> This case study offers important information on primary PHO, a rare genetic condition known for digital clubbing, periostosis, and

joint issues, and focuses on a detailed case of a 21-year-old male in order to increase awareness, enhance diagnostic accuracy, and improve management strategies for those with primary hypertrophic osteoarthropathy.

## CASE REPORT

A 21-year-old man visited the outpatient department seeking medical help for symptoms that had been getting worse over the last five years. He talked about a clear increase in the size of his hands and feet, along with nail changes marked by deformities but no change in color or loss. Additionally, he mentioned a shift in his skin, observing a rise in greasiness and extra perspiration. Throughout the past year, he had been dealing with joint pain in larger joints like his knees and ankles, but he claimed he did not feel any morning stiffness or joint swelling. Surprisingly, his pain improved with the use of painkillers on occasion.

The patient's brother had a history of nail deformities that were similar. Upon assessment, medical results showed severe digital clubbing in hands and feet (Figure 1), as well as excessive sweating particularly in the hands. Radiological imaging showed symmetrical periosteal reactions and new bone formations in different areas such as the occipital bones, both clavicles, and long bones in the upper and lower limbs. Thickening of the cortex was noted in various bones including the humerus, radius, and ulna, as well as in the long bones of the hands and feet (Figure 2-4). Also, osteoarthritic alterations were observed on both sides. Laboratory investigations showed that alkaline phosphatase (ALP) was high because of periosteal new bone formation, while initial all laboratory and radiological investigations, such as blood count, kidney and liver function tests, viral markers (hepatitis B and C), thyroid function tests, IGF-I, growth hormone, prolactin, follicle stimulating hormone, testosterone, magnetic resonance imaging brain, high-resolution computed tomography, Doppler ultrasonography of hands and feet, and rheumatological panel (Antinuclear Antibody, Extractable Nuclear Antigen, Anti-Cyclic Citrullinated Peptide, and Rheumatoid Factor), showed normal results.

Based on a thorough assessment of the patient's medical history, family background, physical examination, and radiological findings, the diagnosis of Primary Hypertrophic Osteoarthropathy (Pachydermoperiostosis) or Touraine-Solente-Gole Syndrome was made. Symptomatic treatment was initiated with Etoricoxib 60mg once daily. The patient had follow-up

appointments scheduled at one month and six months to evaluate response of the treatment. In the subsequent appointments, it was observed that the clubbing and swelling stayed consistent and did not deteriorate. At first, Etoricoxib was given every day for two months before being changed to be taken only when necessary. He was followed up at 3 month and 6 month for symptoms improvement, no adverse effects of treatment and no adverse events or recurrence were noticed. This case was managed as a multidisciplinary approach, mainly the rheumatologist managed disease, along with the opinions from radiology, dermatology, Orthopedic surgery and Physiotherapy team.

## DISCUSSION

PDP is a genetic condition characterized by three main characteristics: clubbing of the fingers, thickening and wrinkling of facial and/or scalp skin (pachydermia), and periosteal growth (an increase in tissue surrounding the joints and new bone formation underneath the periosteum).<sup>11</sup> Other possible symptoms could involve rough facial characteristics, inflammation of multiple joints, a condition called cutis verticis gyrata occurring in 24% of cases, excessive oiliness of the skin, drooping eyelids, excessive sweating, skin breakouts, joint disease, and bone erosion in the extremities.<sup>12,13</sup> The case study illustrates a complete manifestation of the syndrome in a male patient, with a history that began in adolescence (as expected), presenting both consistent clinical and radiological proof. The patient exhibits all three main characteristics as well as other associated symptoms, such as excessive sweating. Although it is recognized that 33% of PDP cases have a family history, the genetic predisposition associated with consanguineous marriages is further confirmed by the positive family history in our patient's older sibling, as reported in the literature. The typical amount of IGF-1 provides strong indication that excludes acromegaly, a crucial factor in the differential diagnosis.<sup>13,14</sup> Radiological assessment was crucial in confirming our diagnosis of PHO. The X-ray images of the skeleton showed similar periosteal reactions, thickening of the outer layer, and signs of early osteoarthritis in different bones such as the occipital bones, clavicles, long bones in the arms and legs, and metacarpals and metatarsals. These imaging findings are typical of PHO and have been extensively recorded in prior research.<sup>15,16</sup> The differential diagnosis of PHO involves considering other conditions that could exhibit similar clinical characteristics. In this case, acromegaly, thyroid acropachy, syphilitic periostosis, and lepromatous



Figure 1: Digital Clubbing of hands and toes

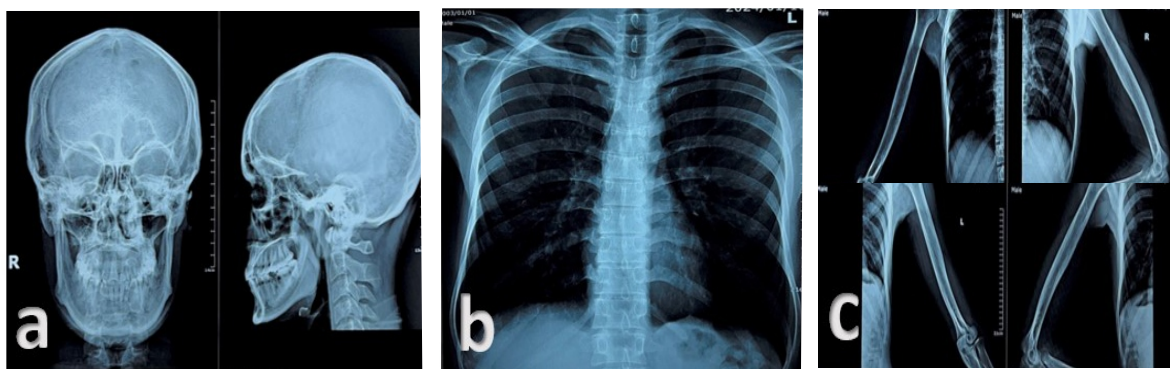


Figure 2: a) Diffuse cortical thickening of occipital bone. b) Bilateral symmetrical diffuse periosteal reaction (distal shafts of both clavicles). c) Bilateral symmetrical periosteal reaction with thickened cortex in shafts of humerus (mid-diaphysis region).



Figure 3: a) Bilateral thickened cortex in shafts of radius and ulna. b) Mild cortical thickening in shaft of long bone of hand (more obvious in 4th metacarpal). c) Bilateral early osteoarthritic changes (sharpening of tibial spines and periarticular sclerosis).



Figure 4: a) Bilateral symmetrical shaggy periosteal reaction in shaft of both tibia and fibula. b) Mild cortical thickening in shaft of long bones of feet. c) Bilateral mild cortical thickening in shaft of long bones of feet (more obvious in 4th metatarsal).



leprosy were all taken into consideration. Nevertheless, despite the normal hormonal levels and negative laboratory results, the specific radiological findings in our patient's clinical presentation ultimately confirmed the diagnosis of PHO.

Due to the important role played by PGE<sub>2</sub> in the development of PHO, the treatment of PHO mainly aims to provide relief from symptoms through different medications. Non steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and colchicine are often used to reduce pain and inflammation related to PHO. Recent developments in treating PHO involve research investigating the effectiveness of oral etoricoxib, a selective COX-2 inhibitor, and bisphosphonates. These trials have demonstrated encouraging outcomes in alleviating arthritis symptoms. Furthermore, arthroscopic synovectomy has been studied as a possible way to treat joint problems in PHO. The goal of these therapeutic methods is to enhance the quality of life for individuals with PHO by addressing pain relief and symptoms related to joints. One of the previous study's findings revealed that oral etoricoxib may reduce inflammation and slow the evolution of pachydermia, as well as alleviate face skin furrowing, but had limited efficacy for arthralgia. However, oral aescin was effective in treating arthralgia. Thus, combining etoricoxib with aescin is a safe and effective therapy for PDP. Meanwhile, arthroscopic synovectomy can alleviate joint effusion but has little impact on arthralgia. As a result, postoperative oral drugs would be required as a follow-up treatment for joint issues.<sup>16-18</sup> Literature shows that early diagnosis and proper management are important in PHO to reduce symptoms and enhance the quality of life for those affected.<sup>19,20</sup> Although there is no definite cure for PHO, providing symptomatic treatment centered on pain control and supportive actions can be helpful. It is crucial to closely monitor symptoms like thickened skin, joint pain, and nail deformities in order to address complications and provide the best possible care.

## CONCLUSION

This case report underscores the critical importance of early recognition and multidisciplinary management in PDP. Prompt diagnosis facilitated by a thorough clinical evaluation, radiological assessment, and exclusion of differential diagnoses enables targeted and effective management, reducing symptom progression and improving patient quality of life. The collaborative approach involving rheumatology, dermatology, radiology, orthopedics, and physiotherapy played a

pivotal role in addressing the complex manifestations of this condition. As our understanding of PDP evolves, integrating advancements in genetics, pharmacological therapies, and supportive care will further enhance outcomes for patients. This case highlights the need for continued research and awareness to optimize care strategies for this rare disorder.

**PATIENT'S CONSENT:** The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his clinical information to be reported in the journal. The patient understand that his name and initials will not be published.

**CONFLICT OF INTEREST:** The authors declared no conflict of interest.

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