MAK HILL Publications Research Journal of Medical Sciences

Case Study
doi: 10.59218/makrjms.2023.7.1145.1148

Primary Hypertrophic Osteoarthropathy (Pachydermoperiostosis): Clinical Insights From a Case Report

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Key Words
Pachydermoperiostosis, primary hypertrophic osteoarthropathy, case report, clubbing, hyperhidrosis

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Received: 18 March 2023
Accepted: 28 March 2023
Published: 29 March 2023

Citation: Zubin Vaid and Dilip Karnad, 2023. Primary Hypertrophic Osteoarthropathy (Pachydermoperiostosis): Clinical Insights From a Case Report. Res. J. Med. Sci., 17: 1145-1148, doi: 10.59218/makrjms.2023.7.1145.1148

ABSTRACT
Primary Hypertrophic Osteoarthropathy, also known as Pachydermoperiostosis (PDP) is a rare syndrome characterized by distinct features, including clubbing of fingers and toes, thickening of facial skin, hyperhidrosis and new bone formation associated with joint pain. It was first identified in 1935 and can manifest in three forms complete, incomplete and forme fruste. A 40 year old male presented with a 15 year history of progressive joint pain involving wrists, knees and ankles, along with dyspnea on exertion. He also noticed enlargement of extremities, had a history of severe anemia requiring blood transfusion and a family history of similar skeletal deformities. Physical examination revealed coarsening of facial features, skin furrowing, deep nasolabial folds and severe hyperhidrosis. Grade 4 clubbing of fingers and toes, soft tissue and bony enlargement over extremities were observed. Hemoglobin was 6.4 g dL^{-1} with a hypochromic microcytic smear. Radiographic findings showed symmetrical calcification along long bones, periosteal bone formation and cortical thickening. PDP was initially described in 1935 and is also known as the Touraine Solente Golé syndrome. It primarily affects males and often has a familial component. The syndrome presents with hyperhidrosis, extremity enlargement, arthritis, coarse facial features and more. The pathogenesis is not fully understood but is associated with specific genes and elevated prostaglandin E2 levels. Severe anemia and bone marrow issues have been reported in some cases, potentially due to bone encroachment on the medullary cavity. Pachydermoperiostosis is a rare syndrome with characteristic clinical and radiological features. Diagnosis can be challenging due to its rarity and overlapping symptoms with other conditions like acromegaly. Clinicians should consider PDP in patients with these unique features for accurate diagnosis and management.

INTRODUCTION

Pachydermoperiostosis (PDP) is a rare condition characterized by several distinct features, including clubbing of the fingers and toes (acropachy) thickening of facial skin (pachyderma) excessive sweating (hyperhidrosis) and the development of new bone associated with-joint pain[1]. It was initially identified by dermatologists Touraine, Solente and Gole in 1935, and it can present in three forms complete (periostosis and pachyderma) incomplete (lacking pachyderma) and forme fruste (minimal skeletal changes with pachydermia)[2].

Diagnosis of PDP typically involves the presence of at least two of the following. A positive family history, clubbing, hypertrophic skin changes and bone pain or radiographic changes. This condition is quite rare with an estimated prevalence of around 0.16% and it primarily affects males, with a male to female ratio of 7:1[3,4]. The exact cause of PDP is not fully understood but it is associated with specific genes, including the 15-hydroxyprostaglandin dehydrogenase gene and the solute carrier organic anion transporter family member 2A1[5]. The pathogenesis involves elevated levels of prostaglandin E2 (PGE2) resulting from impaired uptake and degradation. This increased PGE2 is believed to lead to tissue remodeling, vascular stimulation, and the characteristic symptoms observed in PDP patients, including hyperhidrosis, acro-osteolysis, periostosis, arthritis, and pachyderma[6].

In clinical practice, PDP can be challenging to diagnose and may be mistaken for other conditions like acromegaly due to its overlapping symptoms. However a thorough evaluation and the presence of specific criteria can lead to an accurate diagnosis of PDP.

Case Report: A 40 year old male presented with progressively increasing joint pains for the last 15 years involving the wrists the knees and the ankles bilaterally, without any morning stiffness. He also had dyspnoea on exertion. He had noticed a change in his features with an enlargement of his extremities in the last few years.

There was a history of blood transfusion received for severe anemia in the past. His brother had similar but milder skeletal deformities. On examination, he had coarsening of the facial features, folding and furrowing of the skin over the face and scalp with deep nasolabial folds and hypertrophy of the sebaceous glands over the face (Figure 1). Hyperhydrosis of the palms was severe, with a greasy appearance on the face. There was grade 4 clubbing of the fingers and toes with soft tissue and bony enlargement over the hands and feet (Figure 2). The extremities had a columnar configuration with thickened skin. He was pale. The systemic examination was within normal limits. On investigations, his haemoglobin was 6.4 g dL^{-1} reticulocyte WBC and platelet count being normal. The peripheral smear showed hypochromasia and microcytosis. A review of his previous reports 2 years back revealed a haemoglobin of 4.3g% with a hypochromic microcytic peripheral smear. Iron studies showed normal iron and TIBC values. A marrow examination showed mild hypocellularity but was otherwise normal. Sugars, liver and renal function tests were normal. A radiographic skeletal survey was done. The radiographic findings were more or less symmetrical, with calcification all along the long bones. There was also a lot of new periosteal bone formation with cortical thickening and soft tissue hypertrophy.

DISCUSSIONS

The first reported cases of this syndrome were the Hagner brothers, who were described by Freidreich in 1868. However, they were considered to be variations of either acromegaly or pulmonary osteoarthropathy[7]. Pachydermoperiostitis was first described as a distinct clinical entity by Touraine, Solente and Golé in 1935. The major characteristics of the syndrome, including the skin and bone changes, were described in their paper[8]. Since then, pachydermoperiostitis has also come to be known as the Touraine Solente Golé

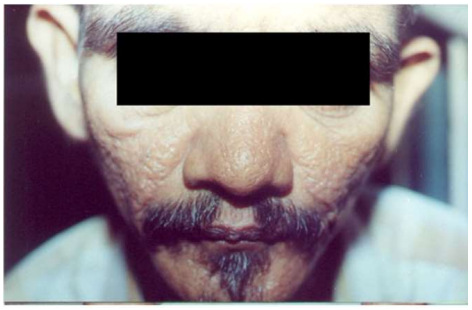

Fig. 1: Typical facial appearance in our case of pachydermoperiostitis: coarsening of the facial features, folding and furrowing of the skin over the face with deep nasolabial folds and hypertrophy of the sebaceous glands over the face

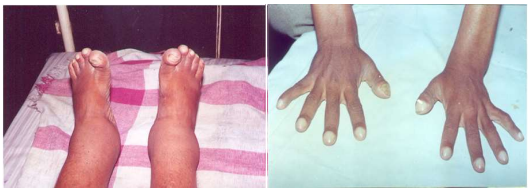

Fig. 2: Grade IV clubbing in a case of pachydermoperiostitis

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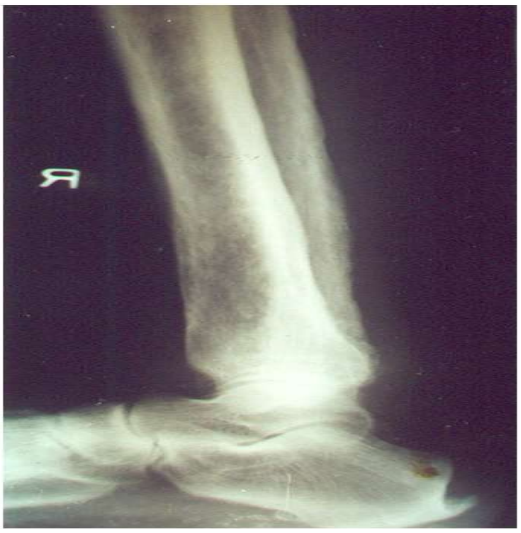

Fig. 3: Calcification of the long bones with cortical thickening in pachydermoperiostitis

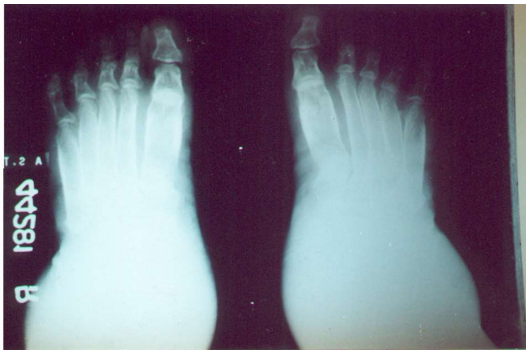

Fig. 4: Cortical thickening with new periosteal bone formation with evidence of soft tissue hypertrophy

syndrome. The other less commonly used synonyms for this syndrome are idiopathic familial generalized osteophytosis, achropachyderma with pachyperiostitis, chronic idiopathic hypertrophic osteoarthropathy and osteodermatopathia hypertrophicans[9]. The condition is more common in males and the familial nature of this condition has been well recognized the nature of transmission being autosomal dominant, with approximately 40% of the cases reported giving the history of a first-degree relative being affected with some or all features of the syndrome like in our patient. It has been postulated that hereditary clubbing may well be an incomplete form of this syndrome. The principal features are hyperhydrosis of the hands and feet, enlargement of the fingers and toes and later the forearms and legs, arthritis, nonspecific neuromuscular symptoms, coarse facial features with an increase in the bulk of the skin, depression and furrowing of the skin over the scalp (cutis vertices gyrata) thickening of the skin over the palms and soles and ptosis. The coarseness of the facial features can be very severe and there have been reports of patients undergoing plastic surgery for the same[10]. Dermatosis papula nigra (premature seborrheic keratosis) has been found only in Negroes. The symptoms start around puberty and progress for about 10 years, being self limited thereafter[11]. The pathogenesis of this condition is ill understood. Though angiography has demonstrated increased blood flow to the digits in secondary forms of clubbing, it has, in fact, shown decreased blood flow in pachydermoperiostitis[9].

Touraine *et al*. divided this syndrome into the complete form the incomplete form and the forme fruste. Patients with all features of pachyderma and pachyperiostitis were called complete. Patients with all features of the syndrome, excluding cutis vertices gyrata, were labeled incomplete and patients with skin changes but with minimal or absent periosteal changes comprised the forme fruste[7]. The radiological changes demonstrate the thickening of the soft tissues of the forearms, fingers and legs, formation of new periosteal bone with ragged outlines, calcification along the long bones and, in severe cases, thickening of the cortex of long bones (Figure 3 and 4).

Besides the musculoskeletal features, our patient also had chronic hypochromic microcytic anemia with normal Iron studies and hypocellular bone marrow. The development of severe anemia has been reported in only three cases of pachydermoperiostitis[9-11]. Though mild anemia with haemoglobin values of 10.5-12.5 g dL^{-1} has been reported in at least four other instances[12]. The severe anemia has been demonstrated to be because of bone marrow failure (a dry aspirate and bone sclerosis being demonstrated on bonemarrow biopsies). There has also been demonstrable extramedullary haematopoiesis in one of the cases via ferrokinetic studies showing the concentration of the isotope primarily in the spleen rather than in the bone marrow[12]. It has also been postulated that the anemia and bone marrow failure could be due to the thick cortical bone encroaching upon the medullary cavity, as demonstrated in the X-rays of our patient. The differential diagnosis includes a secondary form of the disease, which can be excluded by ruling out a malignant or suppurative lung disease. Acromegaly, thyroid acropachy, syphilis and pagets disease need to be kept in mind while examining a patient with presumed pachydermoperiostitis. These conditions will never have the soft tissue and bone changes described above.

CONCLUSION

Pachydermoperiostosis (PDP) is a rare syndrome characterized by distinctive features like clubbing of fingers and toes, thickening of facial skin and new bone formation with joint pain. It was first recognized by dermatologists in 1935 and can manifest in complete, incomplete or forme fruste forms. Diagnosis involves specific criteria, including a positive family history and clinical signs. In a case report a 40 year old male with PDP presented with joint pain, facial changes and severe anemia. Radiographic findings showed symmetrical calcification along long bones and periosteal bone formation. PDP is more common in males and has a genetic association with specific genes. Besides musculoskeletal symptoms, some patients may experience anemia and bone marrow issues. The exact pathogenesis remains unclear and PDP can be challenging to diagnose due to overlapping symptoms with other conditions like acromegaly. Clinicians should consider PDP in patients presenting with these unique features, as it can help guide accurate diagnosis and appropriate management.

REFERENCES

1. Merwe, J.L.V., D.R. Hall, C. Wright, P. Schubert and D. Grové, 2010. Are Early and Iate Preeclampsia Distinct Subclasses Of the Disease-What Does the Placenta Reveal. Hypertens. Pregnancy., 29: 457-467.
2. Barker, D.J., S.P. Bagby and M.A. Hanson, 2006. Mechanisms Of Disease: In Utero Programming In the Pathogenesis Of Hypertension. Nat. Clin. Pract. Nephrology., 2: 700-707.
3. Jajic, I. and Z. Jajic, 1992. Prevalence of primary hypertrophic osteoarthropathy in selected population. Clin. Ex. Rheum., Vol. 10.
4. Barker, D.J.P., 1995. Fetal Origins Of Coronary Heart Disease. B.M.J., 311: 171-174.
5. Uppal, S., C.P. Diggle, I.M. Carr, C.W.G. Fishwick and M. Ahmed et al., 2008. Mutations in 15-hydroxyprostaglandin dehydrogenase cause primary hypertrophic osteoarthropathy. Nat. Genet., 40: 789-793.
6. Bergmann, C., M. Wobser, H. Morbach, A. Falkenbach and D. Wittenhagen et al., 2011. Primary hypertrophic osteoarthropathy with digital clubbing and palmoplantar hyperhidrosis caused by 15-pghd/hpgd loss-of-function mutations. Exp. Dermatol., 20: 531-533.
7. Freidreich, N., 0. Hyperostose des gassamten. Arch. J. Path. Anat., 43: 83-87.
8. Rimoin, D.L., 1965. Pachydermoperiostosis (idiopathic clubbing and periostosis). New. Engl. J. Med., 272: 923-931.
9. Bashiri, A., T. Lazer, E. Burstein, A. Smolin, S. Lazer, Z.H. Perry and M. Mazor, 2007. Maternal and neonatal outcome following cerebrovascular accidents during pregnancy. J. Maternal-Fetal and Neonatal Med., 20: 241-247.
10. Vogl, A. and S. Goldfischer, 1962. Pachydermoperiostosis. J. Med., 33: 166-187.
11. Metz, E.N., 1965. Bone marrow failure in hypertrophic osteoarthropathy. Arch. Internal Med., 116: 759-764.
12. Neiman, H.L., B.M. Gompels and W. Martel, 1974. Pachydermoperiostosis with bone marrow failure and gross extramedullar hematopoiesis. Radio., 110: 553-554.