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Short Communication

Touraine–Solente–Gole syndrome: Clinical manifestation with bilateral true eyelid ptosis

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ABSTRACT

Touraine–Solente–Gole syndrome (pachydermoperiostosis [PDP] or primary idiopathic hypertrophic osteoarthropathy [HOA]) is a rare hereditary disorder that is characterized by a triad of manifestations that consists of skin changes (pachydermia), abnormal bone and joint manifestations (periostosis and/or artritis), and digital clubbing (acropachia). Here, we report the case of 24-year-old male who presented with severe bilateral true eyelid ptosis. Physical examination revealed severe ptosis with poor function of the levator palpabrae superioris muscle, thickening of and deep grooves in facial skin (especially at the frontal region), and abnormal appearance of the scalp with accentuating folds and deep furrows (cutis verticis gyrata). Abnormal bone enlargement of the hands, knees, and feet was also observed. Frontal rhytidectomy and levator resection and advancement were performed to alleviate symptoms. At the short-term follow-up, the patient described being satisfied with the outcome of treatment. This patient will be routinely followed over the long term to evaluate disease progression. Although the cause of ptosis in most PDP is mechanical process or dysfunction, this case of PDP had bilateral true eyelid ptosis due to poor levator palpabrae superioris muscle excursion with coexisting signs and symptoms of complete form PDP. This finding highlights the need to investigate for bilateral true eyelid ptosis caused by abnormal

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levator palpabrae superioris muscle function in patients diagnosed with PDP.

Introduction

Touraine–Solente–Gole syndrome (pachydermoperiostosis [PDP] or primary idiopathic hypertrophic osteoarthropathy [HOA]) is a rare hereditary disorder that was first described in 1868 by Nikolaus Friedreich, who called it "Hyperostosis of the entire skeleton".[1] In 1935, three dermatologists named Albert Touraine, Gabriel Solente, and Laurent Gole described this condition as a familial disorder that is inherited in an autosomal dominant fashion with variable expression and three forms of penetration.[2] The first is referred to as *complete form*, which comprises pachydermia (thick or elephant-like skin), periostosis (abnormal bone manifestations), and acropachia (digital clubbing). The second is referred to as *incomplete form*, which includes periostosis and digital clubbing without dermatologic changes. The third is referred to as *forme fruste*, which includes pachydermia with minimal-to-absent skeletal manifestations.

Onset of PDP usually begins with clubbing that normally starts during adolescence, followed by gradually progressive changes in the skeleton and skin that results in significant lifelong morbidity.[3] The estimated prevalence of PDP is 0.16%, it more commonly affects males (male to female ratio: 7 to 1), and disease severity is greater among males than among females.[4,5] Ptosis is a less commonly reported presenting symptom in PDP, and the cause of ptosis is usually due to mechanical process or dysfunction, such as thickened or hypertrophic eyelids (pseudoptosis).[6] Here, we report a case of complete form PDP that presented with bilateral severe eyelid ptosis.

Case presentation

A 24-year-old male presented with complaint of progressive bilateral eyelid ptosis for 8 years. He and his parents noticed his progressive eyelid ptosis, abnormal facial skin thickening with subsequent development of deep furrows, and broadening of his fingers and toes since age 16, but they never went to the hospital for medical evaluation. He described having no history of joint or bone pain, and he did not recognize the change in contour of both of his knees and ankles. In October 2018, he visited our center for the first time to seek treatment for his bilateral ptosis to improve his appearance. None of his other family members exhibited the same symptoms and signs.

On physical examination, the scalp showed a cerebriform appearance with accentuating folds and deep furrows (cutis verticis gyrata) (Figure 1). Abnormal facial features with thickening of facial skin, furrowing of forehead skin and deepening of nasolabial folds, and seborrheic hyperplasia are shown in Figure 2. Enlargement and clubbing of the fingers and toes were observed in addition to skin thickening and hyperhidrosis of the palm and sole (Figures 3 and 4). Swelling of both knees and ankles was also observed (Figure 5). Ophthalmologic examination revealed normal visual acuity, normal visual field, and no increase in intraocular pressure. He had ptosis of both upper eyelids, with vertical palpebral fissure heights of 3 mm on the right side, and 2 mm on the left side. Upper eyelid ptosis of 5 mm and 6 mm with marginal reflex distance 1 (MRD1) of 1 mm and 0 mm was found at the right eye and left eye, respectively. Levator palpebral excursion was poor on both sides (5 mm in both eyes), but no abnormal Bell's phenomenon was observed.

Investigations

Laboratory investigations, including complete blood counts with peripheral smear, erythrocyte sedimentation rate, liver and renal function tests, thyroid function test, serum calcium, phosphate,

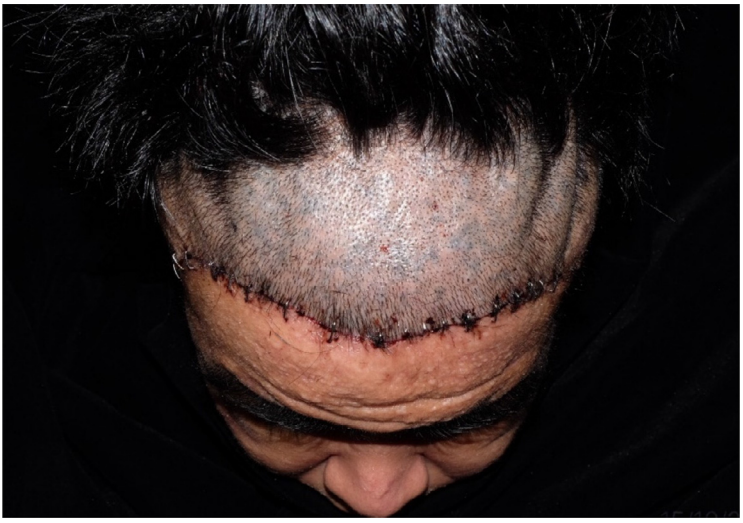

Figure 1. Cutis verticis gyrata.

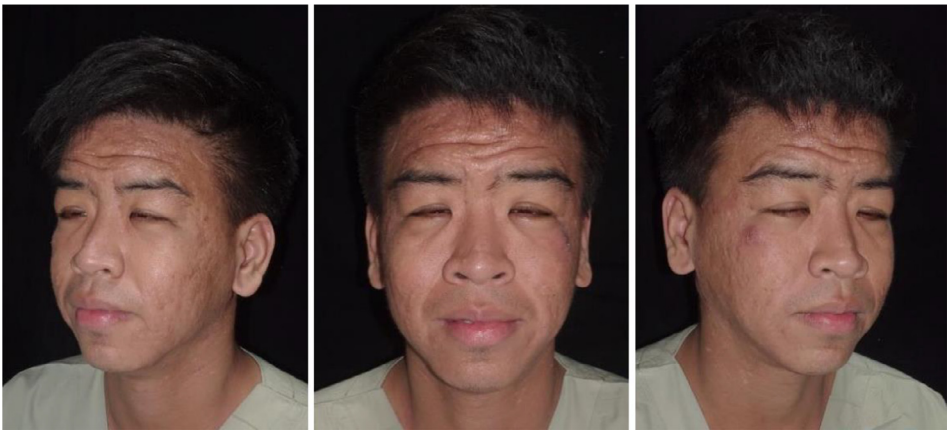

Figure 2. Thickening and furrowing of facial skin with seborrheic hyperplasia.

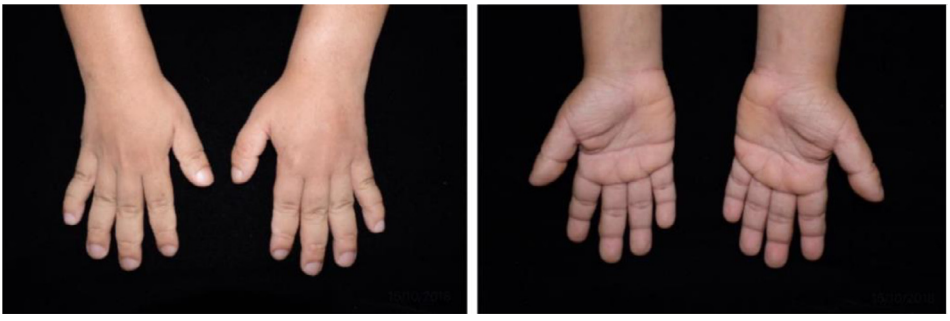

Figure 3. Enlargement and clubbing of fingers.

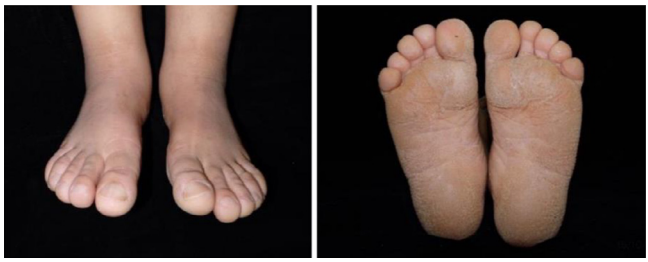

Figure 4. Enlargement and clubbing of toes.

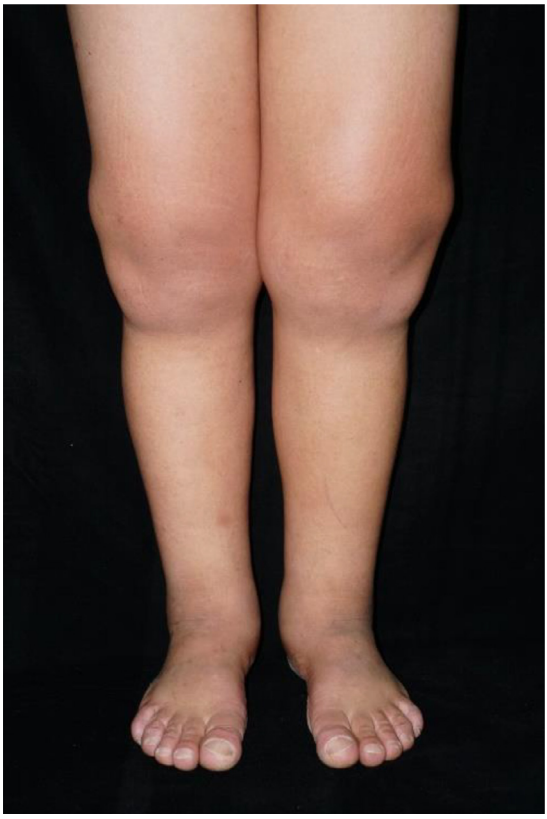

Figure 5. Bilateral knee and ankle swelling.

magnesium, serum alkaline phosphatase, blood glucose, HbA_{1C}, IGF1 (Insulin-like growth factor 1), growth hormone assay, and parathyroid hormone assay, were normal. Rheumatoid factor, C-reactive protein, ANA, Anti Ds DNA antibody, anticentromere antibody, anti-Scl 70, and anti-CCP were all negative. Urinalysis results were also within normal limits. A genetics work-up was performed, but the outcome is still pending.

Radiographic imaging of the hands and feet revealed periosteal thickening in all metacarpal and metatarsal bones. Periostitis of both distal radiuses, distal ulnas, distal tibias, distal fibulas, and navicular bones is shown in Figure 6. No significant change in the long bones of both legs, no abnormal joint spaces, and no evidence of joint effusion was observed. X-rays of the skull and chest were unremarkable.

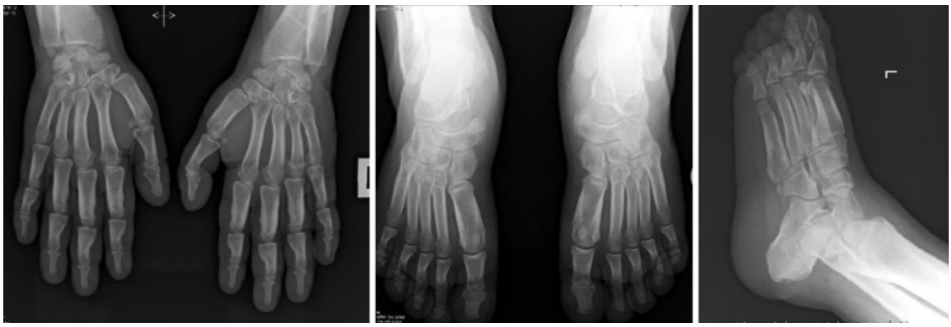

Figure 6. Radiographic images showing periosteal thickening of all metacarpal and metatarsal bones, and periostitis of the distal tibia, the distal fibula, and the navicular bone.

Skin biopsy at the forehead revealed sebaceous gland hyperplasia and dermal edema with mucin deposition in the deep dermis and subcutaneous fat (Figure 7(A)–(D)). Alcian Blue pH 2.5 staining showed dermal mucin deposition (Figure 7(E) and (F)). Dermal fibrosis with elastic fiber degeneration was also detected (Figure 7(E)). Verhoeff–van Gieson stain revealed loss of elastic fiber in dermis (Figure 7(F)). The histopathologic findings were compatible with PDP.[13]

Surgical management

Frontal rhytidectomy was simultaneously performed with levator resection and advancement under general anesthesia to correct the furrowing of forehead skin and bilateral eyelid ptosis. Frontal rhytidectomy was performed via pretragal incision with subgaleal and subsequent subperiosteal dissection. The forehead skin was lifted, excess skin was excised, and the forehead skin then sutured layer by layer with tensionless repair. Levator resection and advancement was performed via upper blepharoplasty incision at 7 mm above the grey line. Excess skin and soft tissues were excised, after which the levator palpabrae superioris muscle and its aponeurosis were identified. Intraoperative finding showed thinning and attenuation of the muscle, and aponeurosis bilaterally. We resected 10 mm of aponeurosis bilaterally, and then advanced to suture fixation at the upper border of the tarsal plate. Bleeding was checked and stopped, and wound closure was performed. At 2 weeks after surgery, the patient reported satisfaction with the treatment outcome of both forehead and eyelid surgery (Figure 8). On examination, vertical palpebral fissure heights were 7 mm for both sides with a marginal reflex distance 1 (MRD1) of 3 mm and 4 mm in the right eye and left eye, respectively. The patient will be reevaluated at 3 months postoperatively to assess surgical outcomes after the treatment-related edema subsides.

Discussion

Touraine–Solente–Gole syndrome (pachydermoperiostosis [PDP] or primary idiopathic hypertrophic osteoarthropathy [HOA]) is a rare hereditary disorder, accounting for only 3–5% of all cases of HOA.[6] This condition is characterized by a triad of manifestations that consists of skin changes (pachydermia [defined as thick elephant-like skin], which is observed in 30–40% of cases), abnormal bone and joint manifestations (periostosis and/or artritis, which is/are observed in 80–97% of cases), and digital clubbing (acropachia, which is observed in 89% of cases).[11] The pathogenesis of PDP is still unclear, but association with an abnormal level of vascular endothelial growth factor is suspected. Mutation in the HPGD gene (Hydroxyprostaglandin dehydrogenase gene), which is located on chromosome 4q33 4q34, leads to an increased level of Prostaglandin E2, which is the substance that is thought to be associated with the processes of digital clubbing, skin thickening, and periostosis.[7] Mutations in the SLCO2A1 gene (Solute Carrier Organic Anion Transporter Family Member 2A1 gene) encodes a prostaglandin transporter that is a member of the 12-membrane-spanning superfamily of transporters. The encoded

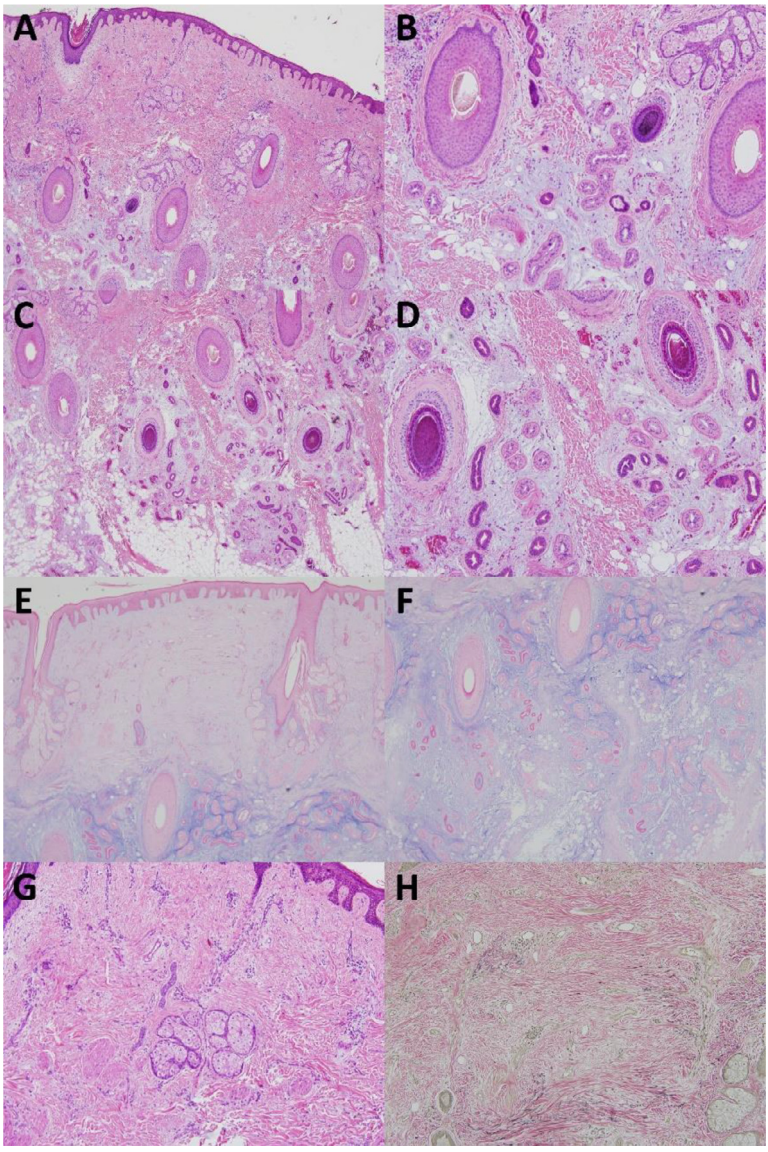

Figure 7. Slight increase in sebaceous lobules and thickening of dermis. Increase in dermal mucin noted (H&E stain) (A–D). Mucin highlighted by Alcian Blue pH 2.5 stain in deep dermis and subcutaneous fat (E, F). Focal dermal fibrosis (H&E stain) (E). Elastic fiber degeneration (Verhoeff–van Gieson stain) (F).

protein may be involved in mediating the uptake and clearance of prostaglandins in numerous tissues.[8] Regarding the eyelid ptosis that is found in PDP, it usually evolves from mechanical dysfunction, such as sebaceous gland hyperplasia and dermal mucin deposition that promotes thickening of eyelid.[6–10] PDP manifestations usually start with digital clubbing during adolescence, followed by gradually progressive and changes of the skeleton and skin over the next 5–20 years that cause significant lifelong morbidity and adverse effect on quality of life.[3]

In this case, we found bilateral true eyelid ptosis caused by poor levator palpebral excursion that was surgically corrected with levator resection and advancement procedure. We were not able to

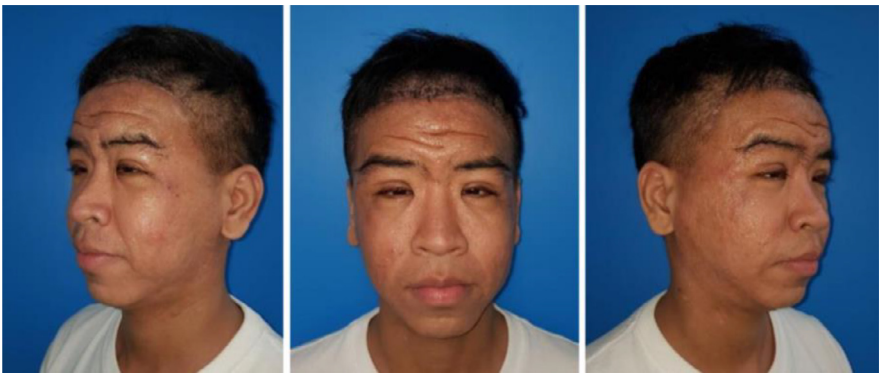

Figure 8. Two-week postoperative images.

ascertain the exact cause of the thinning and attenuation of the levator palpabrae superioris muscle, but we suspect prolonged downward force caused by the increased weight of thickening upper eyelids.

Potential differential diagnoses in patients presenting with PDP-like signs and symptoms include acromegaly, thyroid acropachy (a rare presentation of Graves' disease), intraabdominal or intrathoracic disease (e.g., lung, liver, and intestinal malignancy), and syphilitic periostitis.[6–10]

Until now, there is still no definite treatment for PDP. Corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDS) are used to control osteoarthropathic changes and relieve symptoms.[6,7,9] Colchicine inhibits neutrophil chemotaxis and tissue edema, which improves joint symptoms, pachyderma, and folliculitis.[3] Bisphosphonates, such as pamidronate and risedronate, have been used extensively in PDP due to their antiresorptive and osteoclast inhibitory properties.[11] Isotretinoin has been used to improve skin changes, with variable results reported.[12]

The role of the plastic surgeon in most previously reported PDP patients was limited to facilitating aesthetic improvements, such as changing the facial appearance with frontal rhytidectomy, and correcting blepharoptosis. In this case, the primary concern of our patient was bilateral eyelid ptosis. Examination revealed true ptosis due to poor function of the levator palpabrae superioris muscle on both sides. At the short-term follow-up, the patient expressed satisfaction with the surgical outcome. He will continue to be routinely followed at long-term intervals to evaluate disease progression.

Conclusion

Although the cause of ptosis in most PDP is mechanical process or dysfunction, this case of PDP had bilateral true eyelid ptosis due to poor levator palpabrae superioris muscle excursion with co-existing signs and symptoms of complete form PDP. This finding highlights the need to investigate for bilateral true eyelid ptosis caused by abnormal levator palpabrae superioris muscle function in patients diagnosed with PDP.

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Conflict of interest

Both authors declare no personal or professional conflicts of interest, and no financial support from the companies that produce and/or distribute the drugs, devices, or materials described in this report.

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