Touraine-Solente-Gole’ syndrome, Crohn’s disease, and primary hypothyroidism presenting as anaemia

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Abstract

Pachydermoperiostosis or TSGS is a rare familial inherited autosomal dominant disorder characterised by digital clubbing, subperiosteal new bone formation with pain, polyarthritis, cutis verticis gyrata, seborrhoea, hyperhidrosis, thickened skin of the face with furrowing, thick and corrugated scalp with primary hypertrophic osteoarthropathy. Rheumatological manifestations in form of joint pain, effusion, acroosteolysis, and periosteal calcification are also seen. Association with various systemic diseases has been reported. Penetrance is variable, though autonomic recessive forms have also been reported. Three forms of the disease, i.e., complete, incomplete, and the fruste form are described. A rare case of TSGS in a 40-year-old young male who was admitted for evaluation of severe anaemia is presented. Detailed evaluation revealed iron deficiency anaemia, Crohn’s disease, and primary hypothyroidism. The case is highlighted and presented for its rarity of association which probably is the first such reported case from India.

Key words: Idiopathic hypertrophic osteoarthropathy, pachydermia, periostosis, clubbing, Crohn’s disease, hypothyroidism.

Introduction

TSGS or pachydermoperiostosis (PDP) is a familial disorder inherited as an autosomal dominant trait with variable expression. Freidreich described – in 1868 – a familial case of hypertrophic osteoarthropathy (HOA) that he called hyperostosis of the entire skeleton. Touraine, Solente, and Gole in 1935 first individualised the PDP as the primary form of HOA. They proposed a classification, namely, the complete form, the fruste form, and the incomplete form. The complete form includes pachydermia, clubbing, and periostosis. The fruste form includes prominent pachydermia with minimal skeletal changes, and the incomplete form has no pachyderma.

Case report

A 40-year-old young male born of a consanguineous marriage presented to the medical emergency of SMHS Hospital, Srinagar, Jammu & Kashmir State, India, with complaints of loss of appetite, easy fatiguability, palpitations, constipation, and a history of occasional evening rise of temperature of six months duration. There was no history of weight loss, haematemesis, haemoptysis, bleeding per rectum, mucus with stools, loose motions, jaundice, vomiting, or drug intake. No addiction to cigarette, hookah, alcohol, or ganja was recorded. General physical examination revealed a pale, young male of average build with coarse facial features and increased wrinkling of the folds of the skin of forehead, narrowed palpebral fissures with thick eyelids, mechanical ptosis with hyperaction of frontalis muscle (Fig. 1 a, b). Scalp examination revealed a typical gyrate appearance with prominent multiple ridges. The patient had grade V clubbing with osteoarthropathy of both hands. The skin of both palms and soles was rough and thickened particularly on both hypothenar eminences (Fig. 2 a, b, c, d). Hands and feet were spindle shaped with thickened extremities. No palpable enlarged lymph nodes were found. Vitals were: Pulse 100/minute, regular. BP was 120/70 mm Hg. Abdominal examination revealed a palpable lump in the right iliac fossa 3 x 3 cm in size,

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non tender, without any enlargement of the liver and spleen. CNS examination was normal except for bilateral hung up ankle jerks. A provisional diagnosis of anaemia, pachydermoperiostosis, and an abdominal lump was made. Investigations revealed: Haemoglobin 6 gm%, TLC 5,100/cmm, DLC (Poly 66, Lym 21, Mix 13), Hct 23%, MCV 76, MCHC 27, MCH 20, platelets 2,90,000/cmm, ESR 40 mm/1^st^ hr, reticulocyte count 5%. Peripheral blood film revealed a microcytic hypochromic type with no abnormal cells. Iron profile was: Serum iron 54 μg%, TIBC 328 μg% and transferrin saturation of 16%. Biochemical investigations including kidney function tests, liver function tests, blood sugar, electrolytes, and uric acid were normal. Routine urine examination was normal. ELISA for HIV, hepatitis serology, and VDRL for syphilis were negative. Stool for occult blood done thrice after proper preparation was positive. ECG showed sinus tachycardia. X-ray chest PA view was normal. Upper GI endoscopy was normal. Ultrasonography of the abdomen showed an ill-defined caecal mass of 2.7 x 3.0 cm with absence of para-aortic nodes or ascites. A contrast-enhanced CT scan of the abdomen revealed thickening of the terminal ileum and ileo-caecal junction with adjacent nodes suggestive of ? ileo-caecal TB, ?? Crohn’s disease, ??? Behcet’s disease (Fig. 3 a, b) Full length colonoscopy revealed a deformed caecum, ulceration around the ileo-caecal valve, a narrowed ileo-caecal valve with a fistulous opening suggestive of ? ileo-caecal TB, ?? Crohn’s disease (Fig. 4 a, b). Colonic biopsy of the tissue from the ileo-caecal region showed ulcerated ileal mucosal fragments with chronic inflammatory granulation tissue suggestive of a chronic
inflammatory disease likely to be ileo-caecal TB. Sputum for AFB done thrice was negative. TSH was 18 μIU/ml with negative anti-TPO antibodies. Skin biopsy revealed epidermal hyperkeratosis with follicular plugs with round cell infiltration, hypertrophied sebaceous glands, and dilated infundibuli in the dermis. X-ray skull including the pituitary fossa was normal. X-rays of both forearms and wrists revealed periosteal reaction at the lower ends of both radial bones without erosions. Diaphyseal thickening of radius/ulna, metacarpals and phalanges associated with cortical soft tissue swelling was also seen (Fig. 5 a, b, c, d). Serological evaluation for antineutrophil cytoplasmic antibodies, and human leukocyte antigen as well as genetic testing for tumour necrosis factor were negative. Since ileo-caecal TB is common in the third world countries, particularly India, it was decided to treat the patient empirically with the standard anti-tubercular regimen which was given for nine months. The patient was started on replacement therapy with iron, folic acid, l-thyroxine, and calcium. Anti-

tubercular treatment with a four-drug regimen of INH, rifampicin, PZA and ethambutol along with pyridoxine was also given. The patient continued to be on regular follow-up with improvement of anaemia, constipation, and lassitude. Haemoglobin at the end of the 2-month intensive phase of ATT was 10 gm% with normal MCV and a decrease in reticulocyte count to 1.5%. Features of PDP could not be controlled though there was an overall improvement in his general condition. A repeat colonoscopy done at the end of one year treatment with anti-tubercular drugs showed a partially healed ulcer around the ileo-caecal valve with a deformed narrowed caecum (Fig. 6 a, b). A colonic biopsy taken at this point of time revealed a focal ulcer in the caecum with patchy, moderate, non-specific typhilitis and focal pyloric metaplasia. No granuloma was seen in the biopsy (Fig. 7). A revised diagnosis of pachydermoperiostosis (Touraine-Solente-Gole’ syndrome), Crohn’s disease,
primary hypothyroidism, and anaemia was made keeping in view the history, investigations, and response to treatment. Sulphasalazine and corticosteroids were added to the patient's treatment with marked improvement in symptoms on follow-up as evidenced by normalisation of TSH, rise in the haemoglobin level, and normalisation of complete blood count, and no bleeding with stools. A detailed family survey of the patient's siblings, children, and relatives failed to reveal a similar disorder in any of them.

Discussion

TSGS or pachydermoperiostosis (PDP) is a familial disorder inherited as an autosomal dominant trait with variable expression. Freidreich described – in 1868 – a familial case of hypertrophic osteoarthropathy (HOA) that he called hyperostosis of the entire skeleton. Touraine, Solente, and Gole in 1935 first individualised the PDP as the primary form of HOA. They proposed a classification, namely, the complete form, the fruste form, and the incomplete form. The complete form includes pachydermia, clubbing, and periostosis. The fruste form includes prominent pachydermia with minimal skeletal changes, and the incomplete form has no pachyderma. Cutis verticis gyrata or cutis verticis et frontalis gyrata – a form of pachydermia of the face and scalp – was described by Unna and Jadassohn in 1906-1907. PDP is a rare syndrome and the precise incidence is unknown. According to one study its prevalence is 0.16%. It usually manifests in adolescence occurring almost exclusively in males with a male: female ratio of 9:1 and has been reported in many races with significant morbidity at advancing ages. Rarely, as happened in our case, it may remain undiagnosed for long until there are significant facial, joint, digital deformities, or systemic manifestations which prompt the patient to seek medical attention. HOA is a syndrome characterised by finger clubbing, periostosis, and mono-or polyarthritis. PDP is a rare form of HOA with no known cause and is hence called as idiopathic or primary HOA to distinguish it from secondary osteoarthopathy or pulmonary osteoarthopathy which occurs in association with several diseases and sometimes as a part of the para-neoplastic syndromes. PDP occurs in 3 - 5 % of cases of hypertrophic osteoarthopathy.

Diagnostic criteria for primary PDP

Major: Pachydermia, periostosis, finger clubbing.

Minor: Hyperhidrosis, arthralgias, gastric ulcer, cutis verticis gyrata, blepharoptosis, joint effusion, oedema, seborrhoea, acne, and flushing.

Secondary form of hypertrophic osteoarthopathy

The secondary form of hypertrophic osteoarthopathy results from cardiopulmonary diseases (bronchiectasis, cystic fibrosis, congenital heart diseases, tuberculosis), hepatic diseases (portal and biliary cirrhosis), gastrointestinal diseases (inflammatory bowel disease and polyposis), malignancies (Hodgkin’s disease, carcinoma nasopharynx, and chronic myeloid leukaemia). Secondary form of HOA occurs predominantly in men aged 30 - 70 years with bone changes that develop rapidly and are painful.

PDP is often familial in up to 1/3rd of patients, and hereditary affecting several members of the same family with autosomal dominance and variable penetrance. PDP has been described in siblings of consanguineous marriages. Some case reports suggest that it may be an X-linked disease. There is no difference in the severity of symptoms but growth retardation, early ulcers, and acrolysis of distal parts of the extremities have been reported. PDP is associated with thickening of the facial and scalp skin (pachydermia), periarticular and subperiosteal periostosis, or bone formation with consequent enlargement of hands and feet with joint deformities and neurological manifestations. Associated clinical manifestations like clubbing, seborrhoeic dermatitis, mechanical ptosis of thickened eyelids, periodontal disease, palmoplantar keratosis, and
hyperhidrosis have also been described and which were found in our case also, reflecting it as a classic complete form of the disease as described by Touraine et al.1 Facial involvement in late stages causes prominence of folds on the forehead and cheek giving a leonine look. Thickening and undulating appearance of the scalp resembling sulci and gyri of the the brain (the so-called ‘bulldog appearance’ or cutis verticis gyrata) affecting 24% of patients is a prominent feature which was seen in our case also. Cutis verticis gyrata is also seen in a variety of other disorders like neurofibromatosis, diabetes mellitus, myxoedema, cretinism, amyloidosis, acromegaly, tuberous sclerosis, and in syndromes like Noonan’s, Turner’s, and therefore is not pathognomonic for PDP15. Skeletal findings include symmetric shaggy subperiosteal bone formation in long bones (forearms/legs), metacarpals, metatarsals, and phalanges. Epiphyseal involvement is seen in primary HOA to distinguish it from secondary HOA metatarsals, and phalanges. Epiphyseal involvement has been described in the literature by Compton et al. No genetic link has been found to account for the same26. The authors believe that the patient described in this case report had primary HOA accompanied by Crohn’s disease. Association of Crohn’s disease and primary hypothyroidism as seen in our case is a very rare association thus making this case unique which has probably not been reported from India till now. Squamous cell carcinoma, papular mucinosis, pyoderma gangrenous, basal cell carcinoma, and acromegaly are other associations described with PDP.16

Treatment of PDP is multifactorial with NSAIDs, colchicine being the mainstay of treatment for articular symptoms. Pamidronate for rheumatological symptoms, isotretinoin for seborrhea, acne, folliculitis, and pachydermia. Retinoids inhibit procollagen formation by decreasing procollagen mRNA in fibroblasts and inhibit production of collagenase. Proton pump inhibitors (PPIs) for gastrointestinal symptoms like gastrointestinal bleeds are helpful. Plastic surgery like frontal rhytidectomy, correction of ptosis and finger clubbing reduction, besides symptomatic treatment of various associated diseases as seen in our case is helpful16.

References

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“It is never too late to be what you might have been.”
– GEORGE ELIOT.