Case Report

Pachydermoperiostosis with Chronic Diarrhoea: A Case Report

Khan MSA[1], Shazzad MN[2], Ahmed S[3], Haq SA[4]

Abstract

Pachydermoperiostosis (PDP) is a rare autosomal disorder characterized by periostosis, clubbing, thickening of the skin (pachyderma) of the face and scalp, seborrhea and hyperhydrosis. It is the primary form of hypertrophic osteoarthropathy (HOA), the other name of which is Touraine-Solente-Golé syndrome. PDP has various organ involvements and there are some rare associations of PDP with other disorders. Here we describe a 16-year-old boy who presented with skin and skeletal manifestations typical of PDP who also had chronic diarrhea, abdominal pain and weight loss. After giving treatment with risedronate sodium and mesalazine he got significant improvement in his skeletal and abdominal complaints.

Keywords: *Pachydermoperiostosis, chronic diarrhea, Crohn's disease,*

INTRODUCTION

Pachydermoperiostosis (PDP) is a rare disorder inherited as autosomal dominant trait with variable expression. In 1935, Touraine, Solente and Golé first described the PDP as the primary form of hypertrophic osteoarthropathy (HOA) and thus it has been referred to as "Touraine-Solente-Golé syndrome".[1] The disease is characterized clinically by periostosis, digital clubbing and hypertrophic skin changes (pachydermia) that includes coarse facial features and cutis verticis gyrata. Arthralgia, seborrhea, hyperhidrosis, gastrointestinal (GI) and endocrine abnormalities are also reported. Among the GI abnormalities diarrhea, gastric and duodenal ulcers, chronic gastritis, hypertrophic gastropathy, abdominal ache, multiple polyps in duodenum are found. Association of PDP with other disorders like Crohn's disease is also reported.[2,3,4,5] No treatment is curative, symptomatic treatment with NSAIDs, steroids, colchicine are used. Bisphosphonates are found to be effective in the treatment skeletal abnormalities of PDP.[6]

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CASE PRESENTATION

A 16-year-old boy presented with painful swelling of distal end of long bones for 5 years which increased in severity for 3 months. The pain and swelling used to increase during activity and partially relieved by taking rest and NSAIDs. The patient had the complaints of progressive acral enlargement from the beginning of his illness. He also had gradual coarsening of skin of face and scalp which became more prominent for one year. The skin change in the scalp became progressively furrowed and convoluted. There was no history of other skin lesions suggestive of psoriasis and no history of urethral discharge, painful red eye or low back pain.

The patient also had the complaints of frequent passage of loose stool for one and half years. He had the propensity to defecate in the morning and sometimes at night. Stool was of various forms and consistency- sometimes watery and voluminous, foul smelling, floated on water and sometimes became sticky to pan which was difficult to flush away. The patient also had abdominal cramps which used to subside following defecation. He lost 7 kg of his body weight over the period of 1½ years.

General physical examination revealed characteristics of leonine face and there was cutis verticis gyrate (Figure 1). Clubbing was present involving fingers of both hands. Musculoskeletal system examination findings included broadening of distal end of both forearms and all fingers of both hands (Figure 2) with grade II tenderness. Both the elbows, knees and ankles were also found swollen symmetrically with grade II tenderness.

(a) (b)

Fig.-1: Cutis verticis gyrate

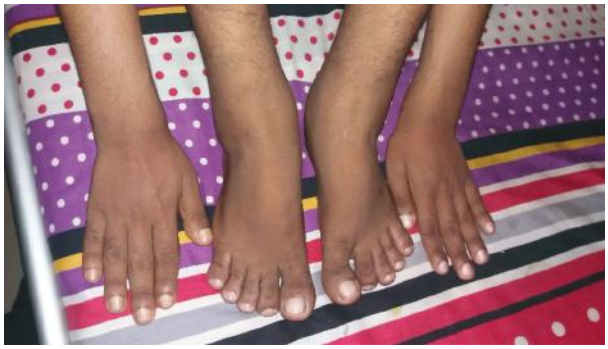

Fig.-2: Broadening of distal end of both forearms and all fingers of both hands

Laboratory reports showing Hb%-122 g/L, WBC-9.6 × 10^9/L, Platelet count-240×10^9/L, ESR- 30 mm in 1st hr, CRP-12 mg/L, Serum creatinine-1.13 mg/dl, RA factor, anti-CCP antibody-negative, S. TSH- 3.05 mIU/L, insulin hypoglycemic test showing: GH 1 hour after 100 gm glucose- 0.05 µg/L (0.05-5.0 µg/L), chest X-ray and X-ray skull (both view)–normal, X-ray both sacroiliac joints-normal. X-ray both hands anteroposterior view showed marked sclerosis, cortical thickening with obliteration of the medullary cavity involving the distal radius and ulna causing loss of normal cavity of bones on both sides. Sclerosis and minimal obliteration of medullary cavity was also seen involving the mid-shaft of proximal phalanges of both hands: findings suggestive of pachydermoperiostosis (Figure 3).

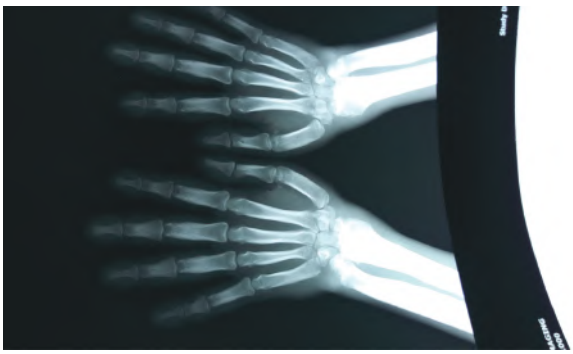

Fig.-2: Sclerosis and minimal obliteration of medullary cavity of radius and ulna

Fecal calprotectin was raised; the value was 322.63 µgm/gm (normal <50 µgm/gm). Ileoscopy revealed few superficial ulcers in the terminal ileum. Biopsy was taken and the report showed infiltration of chronic inflammatory cells in lamina propria. No granuloma or malignancy was found.

Initially, the patient was treated with risedronic acid 150 mg monthly along with calcium 1000 mg daily for skeletal involvement of PDP. Subsequently, he was prescribed with anti-tubercular four-drug regimen for a therapeutic trial, as he was suspected to have intestinal tuberculosis considering the ulceration in the terminal ileum with chronic diarrhea and weight loss. The anti-TB drugs were stopped at the end of three weeks because of a lack of clinical response.

After the failure of anti-TB therapeutic trial, we considered other entities as our differentials that mimic PDP associated gastrointestinal (GI) lesions. These included Crohn's disease (CD), chronic enteropathy associated with *SLCO2A1* gene (CEAS) and cryptogenic multifocal ulcerous stenosing enteritis (CMUSE). Due to the financial constrain we could not proceed for genetic study to see the mutations of *HPGD* and *SLCO2A1* genes of our patients that might be related to PDP. However, clinical presentation, morphological characteristics of the GI lesions guided us to differentiate PDP associated GI lesions from other entities,

Since there is no consensus for the treatment of PDP associated GI lesions, we treated the patient with mesalazine (3 gm/day) and discharged him with the advice for follow up. In the follow-up visits at one and three months, the patient was found to have Grade I tenderness on both knee joints only and he got almost normal bowel habit along with weight gain of two kg.

DISCUSSION

Our patient presented with progressive painful enlargement of the acral parts, coarsening of the skin of face and scalp giving the appearance of cutis verticis gyrata and digital clubbing which are classic symptoms of primary hypertrophic osteoarthropathy; the other name of which is pachydermoperiostosis (PDP). For the exclusion of secondary HOA, we performed physical examination and did relevant laboratory tests and imaging; none of which revealed any abnormality. Though recent genetic studies pointing towards the relation of mutations of *HPGD* and *SLCO2A1* genes to PDP, the diagnosis is still clinical.

Pachydermoperiostosis (PDP) is a rare syndrome and its precise incidence is unknown. One study has shown the prevalence to be 0.16%.[8] It usually manifests in adolescence and occurs predominantly in male with a male: female ratio of 9:1.[9] A mutation linked to X chromosome in association with testosterone-dependent proliferation may be involved in the disease distribution by gender.[10] Three forms of pachydermoperiostosis have been described, the complete form, the fruste forme and the incomplete form. The complete form comprises pachyderma, clubbing and periostosis; the fruste forme includes prominent pachyderma and minimal-to-absent skeletal changes and the incomplete form with evidence of bone abnormalities but lacking pachyderma.[10] Our patient appeared to be a case of complete form of PDP since he has had pachyderma, clubbing and periostosis altogether. As other family members were not involved, it might be due to incomplete penetrance and variable expressivity in other family members.

The pathogenesis of PDP has not been fully elucidated. There are evidences that increased level of prostaglandin E2 (PGE2) and impaired metabolism of PGE2 plays an important role in PDP. Inflammation and malignancies may lead to an increase in the PGE2 levels. Mutation in the human gene that encodes the 15-hydroxyprostaglandin dehydrogenase, a key enzyme responsible for the degradation of prostaglandins, leads to high level of prostaglandins especially PGE2 and thereafter excessive formation of collagen through fibroblast hyper-activation.[11] Circulating factors like platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF) may have some role in the pathogenesis of secondary hypertrophic osteoarthropathy. Bisphosphonates have been shown to decrease the level of plasma VEGF that has the function in angiogenesis and osteoblastic differentiation.[5]

The PDP should be distinguished from secondary hypertrophic osteoarthropathy. Secondary form of HOA occurs predominantly in men aged 30-70 years and the bony changes develop rapidly and are painful. The secondary form of HOA results from several conditions including cardiopulmonary diseases (bronchiectasis, cystic fibrosis, congenital heart diseases), gastrointestinal (GI) diseases (inflammatory bowel disease and polyposis), hepatic diseases (portal and biliary cirrhosis), malignancies (e.g., bronchial carcinoma, Hodgkin's disease, nasopharyngeal carcinoma, chronic myeloid leukemia).[12]

Our patient had GI manifestations that included chronic diarrhea, abdominal cramp and weight loss. His fecal calprotectin was raised and he had superficial ulcers in terminal ileum with infiltration of cells in lamina propria (part of intestinal mucosa). Literature review reveals there are few case reports of PDP which were found to be associated with inflammatory bowel disease in particular with Crohn's disease[2,13] The GI symptoms of our patient appeared long after the appearance of cutaneous and skeletal abnormalities and IBD-associated arthritis could not explain the skin changes. Moreover, In CD, the ulcers are typically longitudinal, commonly present on the

mesenteric site and the lesions are usually transmural. We also considered other differentials like chronic enteropathy associated with *SLCO2A1* gene (CEAS) and cryptogenic multifocal ulcerous stenosing enteritis (CMUSE). In CEAS, females are predominantly affected and the lesions spares the terminal ileum.[14] In CMUSE, the CRP level is usually normal and there is skipping ulceration and stenosis restricted to mucosa and submucosa. CMUSE responds well to steroid therapy.[15] Our patients had the history of treatment with NSAID and prednisolone for few months before presenting to us without substantial improvement of his GI symptoms. Intestinal tuberculosis was also excluded by the therapeutic trial of anti-tubercular drugs.

Due to rarity of this condition, it is difficult to make standard therapeutic modalities for PDP. The proposed treatment is multi-prong with NSAIDs, colchicine for articular symptoms; bisphosphonates for rheumatological symptoms; isotreninoin for seborrhea, acne, folliculitis and pachyderma. Our patient was treated with risedronic acid 150 mg monthly along with calcium 1000 mg daily for PDP. As colchicine could lead to diarrhea, it was not the preferred drug for our patient. Due to lack of consensus for the treatment of PHO associated GI lesions, we treated the patient with mesalazine (3 gm/day) and he got substantial improvement of his GI symptoms. As mesalazine does not have proven value in Crohn's disease, this drug might be effective in PDP associated GI lesions in the small gut.

CONCLUSIONS

Secondary hypertrophic osteoarthropathy (HOA) is relatively more frequently addressed in clinical practice. However, it is important to identify the primary hypertrophic osteoarthropathy (pachydermoperiostosis) and its various associations. Mesalazine may be effective in treating pachydermoperiostosis associated GI manifestations involving the small gut.

Conflict of interest:

The authors have no conflict of interest to declare.

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