

Pachydermoperiostosis with Myelofibrosis and Empty Sella

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Abstract

A case of pachydermoperiostosis presented to us in rheumatology clinic with complaints of pain and swelling in knee joints unresponsive to treatment, characteristic facial features, grade four clubbing of nails and broadening of distal parts of extremities. He also complained of fatiguability which was due to anemia. The natural history of the disease was reviewed and investigated.

Introduction

Pachydermoperiostosis (PDP) is the primary idiopathic form of hypertrophic osteoarthropathy (HOA) characterized by clubbing of the digits of the hands and feet, enlargement of the extremities secondary to periarticular and osseous proliferation and painful joints. It may be associated with additional features such as thickening of the skin of the face and scalp with coarsening of facial features, seborrhea and hyperhidrosis.

Case Report

A 32 year old male presented with complaints of enlargement of hands and feet, progressive swelling of knees and ankles, prominent skin folds and increased sweating on his face and easy fatigability from the age of 16 years. There was no history of fever, cough, dyspnea, arthralgia, backache, oral ulcers, bleeding tendency and weight loss. None of his family member had similar joint swelling but his father and younger sister were having enlargement of tips of fingers and toes.

On general physical examination, the patient was pale with coarse facial features, sebaceous hyperplasia and furrowing of forehead (Fig 1). His wrists and ankles were widened, nontender with grade four clubbing (Fig 2). Hands and feet were enlarged like as in acromegaly. Joint examination revealed nontender right knee effusion (Fig 3). He had undergone left knee synovectomy 2 years back for recurrent effusion. Systemic examination revealed 6 cm enlargement of spleen below left costal margin, which was firm and nontender. Rest of the physical examination was unremarkable.

Dermatological evaluation showed pachyderma, cutis verticis gyrate and sebaceous hyperplasia on forehead and palmo-plantar keratosis (Fig 1).

On investigations, his hemoglobin was 6.2 g/dl, corrected reticulocyte count of 1.2 %, ESR 56 mm in the first hour. The total leucocyte count and platelet count were within normal limits. Peripheral blood film showed microcytic hypochromic red blood cells with occasional fragmented, polychromatic cells and few teardrop cells. Serum iron studies were within normal limits. Upper GI endoscopy revealed no abnormalities. Stool examination for occult blood was negative. Both direct and indirect Coomb's test was negative. Liver and kidney function tests were normal. Ultrasound abdomen showed splenomegaly. Bone Marrow aspiration was dry and examination of the biopsy revealed hypocellularity of haematopoietic elements of all three

series and was suggestive of myelofibrosis (Fig 4).

Normal chest x-ray and 2D-echocardiography ruled out secondary cause for clubbing. X-ray bilateral lower legs showed periosteal reaction of long bones bilaterally with distal soft tissue swelling. X-ray forearm bones revealed cortical thickening noted in bilateral radius and ulna in diaphysis. X-ray both hands also showed increased cortical thickness but there was no evidence of acroosteolysis. Synovial fluid analysis was glucose 87 mg/dl, protein 2.7 g/dl, albumin 1.4 g/dl, white blood cell count 200/microlitre with 70% polymorphonuclear leucocytes, Gram stain and AFB stain were negative and culture was sterile. Crystals were not seen on polarized microscopy.

Screening test insulin like growth factor-1 (IGF-1) was done to rule out acromegaly. Age and sex matched level of IGF-1 was 123.8 ng/ml (Normal range for his age is 115-307 ng/ml), fasting growth hormone (2.89 ng/ml) was normal and was suppressed to 0.691 ng/ml after 1 hour of an oral glucose load of 75g. Visual perimetry was normal. Magnetic resonance imaging of brain showed an empty sella (Fig 5). But other pituitary hormones were also in normal limits (Cortisol-16.2 µg/dl, LH- 2.12 mIU/ml, FSH- 8.61 mIU/ml, Prolactin- 10.5 µg/L). Thyroid function tests were normal (T4 – 0.99 ng/dl, TSH – 3.161 mIU/l).

Hence the final diagnosis was pachydermoperiostosis with myelofibrosis and empty sella syndrome.

Discussion

Since the description in 1868 by Friedrich of pachydermoperiostosis in two young brothers, the disease has been better understood but is still uncommon.¹ In 1907, Unna described marked thickening of the skin of the forehead and its resemblance to the sulci and gyri of the brain and called it 'cutis verticis gyrata'. The association of cutis verticis gyrata and pachydermoperiostosis is sometimes referred to as Tourane-Solente-Gole syndrome. Hyperhidrosis and over activity of sebaceous glands of the skin, particularly of scalp and face is common. The skin of palms and soles is also thickened and rough, and the thenar and hypothenar areas will become prominent.^{2,3} The disorder is inherited as an autosomal dominant trait with variable expression. One-third of these patients have a positive family history. In our case, 2 family members have incomplete expression of the disease as they have clubbing but no skeletal or cutaneous features.

Hypertrophic osteoarthropathy (HOA) in childhood is an infrequent occurrence. When present, the abnormality is associated with congenital heart disease, bronchiectasis, pneumonia, cystic fibrosis, rarely with childhood malignancy, Hodgkin's disease and with undifferentiated epithelial cell carcinoma of the nasopharynx with metastasis to the lung and

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Fig. 1 : Facial features of pachydermoperiostosis patient



Fig. 2 : Photograph showing enlarged hands with grade four clubbing



Fig. 3 : Photo showing right knee effusion. Note scar of synovectomy done in past over left knee

the neck.

The clinical manifestations of PDP are somewhat variable with respect to skin and bone changes. The various clinical expressions include the complete form (pachydermia, periostitis, cutis verticis gyrata), the incomplete form (absence of cutis verticis gyrata) and forme fruste (pachydermia with minimal or absent periostitis). Patient under discussion had complete form of PDP.

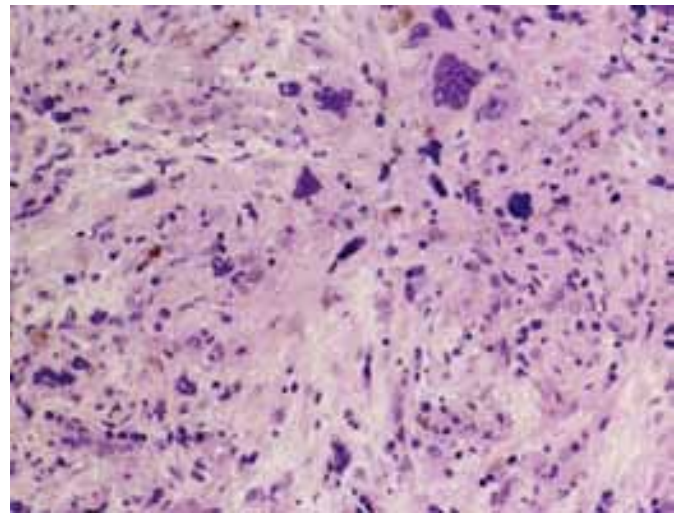


Fig. 4 : Bone marrow biopsy (H & E, X 400): Myelofibrosis showing collagen fibers and hematopoietic cells

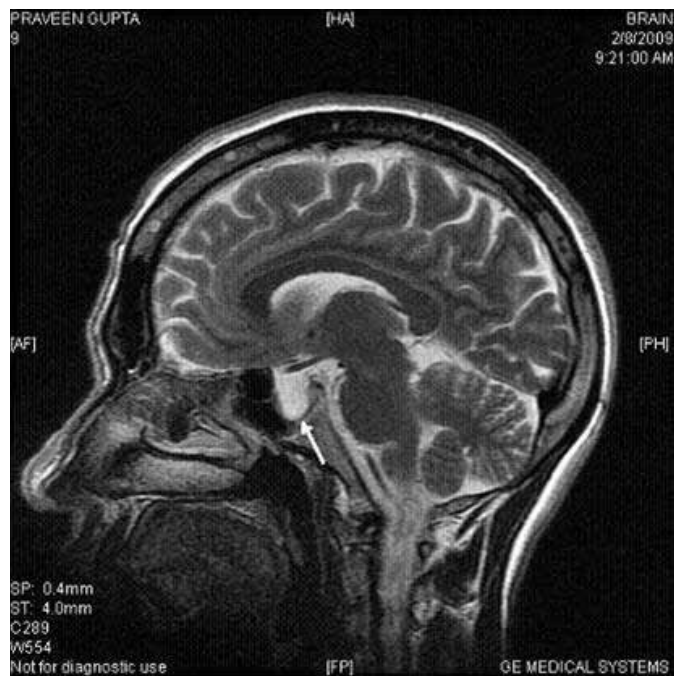


Fig. 5 : Sagittal section MRI brain (T2W), white arrow indicating empty Sella

Recent studies suggest a role for platelets in this disease. Aggregation and other activity of platelets and endothelial cells of peripheral vessels lead to the release of platelet drive growth factor and other factors, which induce the connective tissue and periosteal proliferation.⁴

PDP may be associated with sacroiliitis, psoriasis, rheumatoid arthritis, duodenal ulcers, hypertrophic gastritis, gynecomastia, anemia, myelofibrosis, juvenile polyps, gastric cancer, spondylolisthesis, and cutaneous squamous carcinomas. Our patient was found to be associated with anemia, myelofibrosis and empty sella.

The mechanisms of anemias associated with PDP are multifactorial including blood loss from the GI tract, bone marrow failure by myelofibrosis or narrowing of the medullary spaces, and possibly, the presence of an inhibitor for erythropoiesis. In our patient there was no evidence of blood loss as upper GI endoscopy was normal and stool occult blood was negative.

Myelofibrosis was revealed on bone marrow biopsy examination. To date there is no treatment for myelofibrosis in patients with pachydermoperiostosis.⁵ We advised him for bone marrow transplant but he refused. So, we discharged our patient on routine hematinics.

Nonsteroidal anti-inflammatory drugs (NSAIDS) or corticosteroids are used for skeletal symptoms. Also, Colchicine provides a beneficial response in both inhibiting increased chemotactic activity and in reducing tissue edema.⁶ Vagotomy may improve the articular pain and swelling associated with PDP. Plastic surgery may improve the appearance of the face and scalp by excising redundant skin and correcting the cutis verticis gyrate.

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