

Case Report

Bisphosphonates use in a Case of Pachydermoperiostosis

Jagdish RK^{1*}, Bhatnagar MK¹, Malhotra A¹, Aggarwal R¹ and Shailly²

¹Santosh Medical College & Hospital, Santosh University, Ghaziabad, India

²Chest and TB Hospital, Govt. Medical College, Patiala, India

*Corresponding author: Rakesh Kumar Jagdish, Department of Rheumatology Clinic, Santosh Medical College & Hospital, Santosh University, Ghaziabad, India

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Abstract

Pachydermoperiostosis is a rare Autosomal disorder, which commonly presents with clubbing, bone pains and skin changes. The treatment is unsatisfactory. We tried bisphosphonates in its treatment with encouraging results. We suggest that injectable bisphosphonates should be tried early in treatment of Pachydermoperiostosis.

Keywords: Pachydermoperiostosis; Primary osteoarthropathy; Touraine-Solente-Gole´ syndrome; Treatment; HOAP (Hypertrophic Osteoarthropathy); Bisphosphonates

Introduction

Pachydermoperiostosis, also known as Touraine-Solente-Gole´ syndrome, primary or idiopathic Hypertrophic Osteoarthropathy (HOAP). It is a rare autosomal disorder with variable expression. Pachydermoperiostosis is characterized by bilateral and symmetrical grade IV clubbing, periosteal new bone formation, thickening of skin (pachyderma) and excessive sweating (hyperhidrosis). No treatment is curative, symptomatic treatment such as NSAIDs, Steroids, colchicines are used. There are case reports of bisphosphonates use with good results in secondary HOAP [1,2]. The uses of bisphosphonates in primary HOAP/Pachydermoperiostosis are only few [3].

Case Presentation

A 31 years old, male patient, non smoker, non alcoholic, resident of Bihar, presented to us with history of pain and swelling in hands and feet, followed by involvement of ankle, knee and wrist joints, of 15 years duration, this was associated with hyperhidrosis of palms and soles. There was no history of fever, palpitation, bluish discoloration, backache, haemoptysis, haemetemesis, hematuria, haematochezia, cough, expectorations, dyspnea, oral ulcers, weight loss and bleeding tendency. Family history of similar complains positive in paternal cousin brother.

On physical Examination, He was a febrile, Pulse-70/min, Respiratory rate-16/min, BP-122/80 mmHg, SpO₂-98% at room air, there was no cyanosis, pallor, lymphadenopathy and oedema. On systemic examination-respiratory, cardiovascular, abdominal and neurological examination were normal, on skin examination there was furrowing on the forehead, skin is oily and shiny in appearance (Figure 1), Hyperhidrosis of hands and feet. Musculoskeletal examination shows-grade IV clubbing along with widening of wrist and ankle joint, swelling of both the knee joint (Figures 3-6).

On investigation his haemoglobin, ESR, CRP, leukocyte count and platelet count were within normal limits. Peripheral blood film showed normocytic norm chromic picture. Liver function test, kidney function test and thyroid function test were normal. Blood sugar was within normal range. Urine examination was also within normal range. Stool for occult blood, chest X-ray PA view, Contrast enhanced CT chest [2], Echocardiography, USG abdomen and

pelvis were normal. Other radiological investigations, X- ray of ulna, radius, tibia and fibula showed wavy periosteal reaction along the distal meta-diaphyses (Figure 2). On the basis of history, physical examination and investigations we made diagnosis of Primary HOAP (Pachydermoperiostosis).

His main problem was of bony pains and swelling, We started him on NSAID, steroids, colchicines, added one after the other to relive pain over six months without much relief, we gave bisphosphonates infusion (pamidronic acid) 60 mg over 2 hours slowly, after hydration with 500 ml normal saline, patient responded well in the form of pain relief in 3-4 days of treatment and decrease in swellings of hand, feet and knee in 7-10 days, patient was better for 3 months of follow up but again same symptoms and signs reappear then a long acting bisphosphonates zoledronic acid 4mg given with prior hydration which resulted in marked improvement as shown in images and it is persisting till date after 6 months of infusion during follow up. Oral glycopyrolate was given for hyperhidrosis with good result.

Images comparison before bisphosphonates treatment and after bisphosphonates treatment given below (Figures 3-6).

Discussion

Primary HOAP/Pachydermoperiostosis is an autosomal dominant disease with incomplete penetrance and variable expression, in few cases autosomal recessive and X-linked inheritance can be there [1] and family history present in 1/3rd of cases only. The disease begins insidiously at puberty and nine times more common in males. Symptoms usually disappear at adulthood but in our patient symptoms persisted and patient did not respond to usual treatment.



Figure 1: Facial features-furrowing on the forehead with oily and shiny skin.



Figure 2: Periosteal reaction-wavy periosteal reaction along the distal metaphyses of ulna, radius, tibia and fibula and around knee joint.



Figure 3: Hands-soft tissue swelling significantly reduced post treatment.



Figure 4: Feet and ankle swelling reduced significantly post treatment.

Exact pathology is unclear but it is suggested that abnormal production of growth factors [2] like VEGF (Vascular Endothelial Growth Factor) and PDGF (Platelet Derived Growth Factor) are playing central role. It is a rare disease and should be differentiated from other causes of clubbing like chronic suppurative pulmonary diseases, bronchogenic carcinoma and lung metastases, cystic fibrosis and cyanotic congenital malformations of the heart, thyroid acropachy, acromegaly and chronic inflammatory rheumatic diseases [2]. Long term prognosis of Pachydermoperiostosis is generally non fatal. No treatment is curative. Various symptomatic treatment strategies are there for Pachydermoperiostosis, including NSAIDS, Steroids, colchicine, vagotomy for skeletal symptoms, botulinum toxin type A, Isotretinoin [4] and plastic surgery for dermatological manifestation, Beta blockers, glycopyrolate or neurotoxins for hyperhidrosis, Newer therapies [2] are emerging like octreotide, gefetinib (EGFR inhibitor), bisphosphonates (pamidronate or zoledronate) [2,3]. Bisphosphonates exert their therapeutic effects through potent inhibition of osteoclastic bone resorption. They also have anti-inflammatory, antiangiogenic effects and also reduce vascular endothelial growth factor [7]. Bisphosphonates [3] had also been tried in painful bony conditions in Rheumatoid Arthritis



Figure 5: Knee Effusion-decreased significantly post treatment.



Figure 6: Hands, Wrist, Feet and Ankle swelling significantly reduced post treatment.

(RA), Spondyloarthritis (SpA) [2,4,5] bony metastasis, bone pain in secondary HOAP [6,7], multiple myeloma.

We have earlier experience of using injectable bisphosphonates in painful Ankylosing Spondylitis (AS) patients. In primary HOAP3, there is few case report of use of bisphosphonates therapy with good result. We tried bisphosphonates in its treatment with encouraging results, with maximal effect on pain followed by effusions and no effect on bone deformities and clubbing. We suggest that injectable bisphosphonates should be tried early in pachydermoperiostosis. Consistent effect was seen with long acting zoledronic acid than pamidronate.

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