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Pachydermoperiostosis: A Rare Clinical Entity

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Pachydermoperiostosis is an autosomal dominant disorder characterized by periosteal new bone formation, and involves the distal extremities. This disorder presents as clubbing, hyperhidrosis, progressive enlargement of hands and feet, and thickening of the skin. Symptoms usually appear during adolescence, get worse over the next decade, and then stabilize. Progressive enlargement of the hands and feet is also observed in acromegaly (1).

A 26-year-old male was referred to our clinic with the enlargement of hands and feet since the age of 12 years (Figure 1). In addition, he was suffering from widespread pain and swelling of both ankles and knees. He noticed that enlargement was insidious in onset, and got worse over the years until presentation. He gave a history of excessive sweating in his hands. His elder sister and father were suffering from similar, but milder, complaints. The other sister and brother were asymptomatic. There was agnation between his parents. Physical examination revealed a height of 177 cm, weight of 86 kg, and body mass index of 27.4. He had severe clubbing of all fingers and toes with enlargements of the distal parts of extremities, and he had thickened skin of both hands and feet (Figure 1). He had arthritis of both ankles and knees. Clinical examinations of the other systems were normal. Radiological imaging showed hypertrophic osteoarthropathy and acro-osteolysis. Magnetic resonance imaging of the knee showed synovitis. Laboratory values, including serum calcium, phosphorous, alkaline phosphatase, complete blood count, and blood glucose levels, were normal. The serum growth hormone (GH) level and the serum insulin-like growth factor 1 (IGF1) level were normal. Serum cortisol, adrenocorticotrophic hormone, free thyroxine (T4), thyroid stimulating hormone, testosterone, and prolactin levels were normal as well. The erythrocyte sedimentation rate and C-reactive protein levels were high (104 mm/h and 21 mg/L, respectively). After excluding excess GH secretion, the patient was diagnosed as pachydermoperiostosis because of the presence of clubbing, thickening of the skin, hyperhidrosis, hypertrophic osteoarthropathy, arthritis, and acro-osteolysis. Treatment with colchicine, acemetacin, and bisphosphonates was started. Symptoms of arthritis decreased dramatically, and the other symptoms ameliorated remarkably in a short period.

In 1868, Friedrich described pachydermoperiostosis in two young brothers. It is inherited as an autosomal dominant trait with variable expression. One-third of affected patients have a positive family history (2), similar to the present case. It differs from the majority of well-known secondary hypertrophic osteoarthropathies, which are usually associated with heart and lung diseases. The onset is usually in adolescence, and symptoms usually get progressively worse in next 5-20 years. The pattern of onset and progression in this case were similar. Enlarged hands and feet in late childhood or early adulthood can be caused by different pathologies, including GH excess. Pathologies of the somatotrophic axis must be excluded in a young patient with an acromegalic phenotype, before considering other differential diagnoses, such as pseudoacromegaly associated with severe insulin resistance or pachydermoperiostosis (3). In the absence of insulin resistance, pachydermoperiostosis should be kept in mind, especially in the patients with the thickening of periosteum or skin, clubbing, acro-osteolysis, or alopecia. Acromegaly was ruled out with the finding of normal GH and IGF-1 levels in this patient. The clinical features of pachydermoperiostosis

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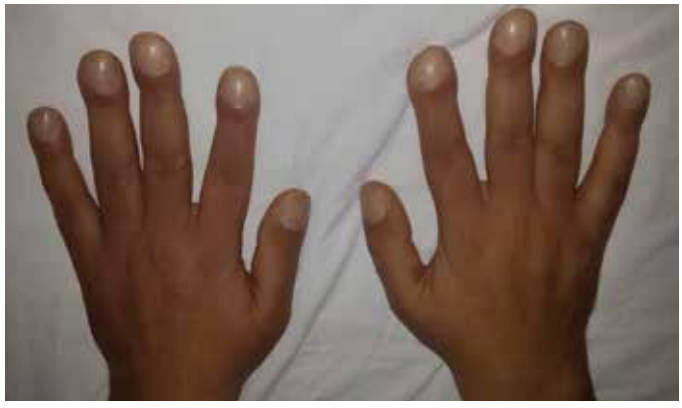

Figure 1. Enlargement of hands

are variable. Clinical presentation is classified into the complete form (pachydermia, clubbing, and periostosis), the fruste form (prominent pachydermia with minimal skeletal changes), and an incomplete form which has no pachydermia (4). Our case had thickening of the skin over hands and feet. He also had severe clubbing, with radiological evidence of periostosis and acro-osteolysis. Thus, we classified the patient with the complete form of pachydermoperiostosis. A common radiological finding affecting terminal phalanges of fingers called acro-osteolysis was observed in our case. Arthritis and joint effusions have been noted in 20%-40% cases, similar to our case (5). However, no complications, including neuropathies due to compression of spinal cord or nerve roots, entrapment neuropathies, and osteonecrosis of the femur, were noted in our case.

Current treatment modalities for pachydermoperiostosis are limited. Conventional drugs like non-steroidal anti-inflammatory drugs and colchicine (6) are usually the first-line drugs. Some studies have reported that bisphosphonates can decrease pain and other symptoms related to hypertrophic osteoarthropathies (6-8). In one study, pamidronate resulted in a significant reduction of pain in three patients with hypertrophic osteoarthropathies. In some other studies, zoledronic acid was shown to be effective (9,10). The mechanism of action of bisphosphonates in hypertrophic osteoarthropathies remains unclear; however, it is commonly accepted that they have both antiresorptive, and anti-inflammatory benefits (9). In our patient, colchicine 3×0.5 mg/day, acemetacin 2×60 mg/day, and alendronic acid 1×70 mg/week treatment were started. Arthritis improved dramatically in a week, whereas the erythrocyte sedimentation rate and C-reactive protein levels were decreased (12 mm/h, 1,1 mg/L, respectively) and the bone pain ameliorated in a month. This is the first paper reporting the promising result of combination therapy of colchicine and alendronic acid in the treatment of pachydermoperiostosis.

In cases of enlarged hands and feet, i.e., in the differential diagnosis of acromegaly, the possibility of pachydermoperiostosis has to be kept in mind, because treatment modalities differ between these two diseases. Acemetacin, colchicine, and alendronic acid seem to be effective in the treatment of pachydermoperiostosis.

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