Pachydermoperiostosis—Clinical Spectrum

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PACHYDERMOPERIOSTOSIS (idiopathic hypertrophic osteoarthropathy) is characterized by digital clubbing, periosteal bone changes, furrowing of the skin, and sebaceous gland overactivity. The fully developed case is easily recognized if there is an awareness of this entity. Milder cases in which only the musculoskeletal features are prominent are frequently unrecognized or are misdiagnosed as a form of secondary hypertrophic osteoarthropathy. While certainly not a common entity, our recent experience suggests that a failure to recognize this condition is partially to blame for its supposed rarity.

Pachydermoperiostosis is probably most frequently confused with that variety of secondary hypertrophic osteoarthropathy seen in association with certain malignant tumors, especially bronchogenic carcinoma. Because of the usually grave prognostic implications of hypertrophic osteoarthropathy, the physician must view this finding with great concern. However, in order to prevent undue mental anguish in those patients who present with hypertrophic osteoarthropathy and in whom no obvious cause can be found, one must be aware of the entity of pachydermoperiostosis. Since the internist is often called to see patients in whom the cause of hypertrophic osteoarthropathy is not readily apparent and because pachydermoperiostosis is frequently unrecognized as such, it is the purpose of this paper to describe six cases of this disease seen in one hospital in a 12-month period. The features of the entity will be reviewed and diagnostic criteria discussed. Furthermore, evidence for the existence of incomplete forms of this entity will be presented.

Report of Cases

CASE 1.—A 37-year-old Caucasian woman of Italian extraction presented with a history of clubbed fingers and toes dating back to early childhood. Arthritis involving the ankles, knees, wrists, and elbows with occasionally more objective findings of swelling, heat, and tenderness in the ankles, and less frequently the knees, had been noted for many years. Profuse perspiration of the hands and feet especially involving the fingers and toes had occurred episodically, commonly precipitated by emotional stress. This symptom was frequently associated with a marked subjective increase in skin temperature of the hands. Acne was noted at puberty and was considered severe enough in her adult life to require two dermabrasion procedures. A further plastic procedure was performed because of furrowing of the skin of the face and forehead.

The family history was noncontributory except that one sister had moderately severe acne which persisted to age 40 and her mother had rheumatoid arthritis with little deformity. There was no history of clubbing in the parents, three female and two male siblings, the paternal or maternal grandparents, three nieces, and three nephews. No known consanguinity was present.

Physical examination revealed furrowing of the skin, pitting from previous acne (Fig 1), evidence of the previous plastic procedures, and marked bulbous clubbing of fingers (Fig 2) and toes without cyanosis. Sweating began at the tips of the fingers and toes, there was marked cyanosis of the skin of the hands, and the subject had a chronic cough. Anemia was absent. A chest x-ray film showed no evidence of malignancy, and breathing studies were normal. The urine was normal, as were results of blood urea nitrogen, serum electrolytes, and complete blood count. The skin biopsy demonstrated changes consistent with pachydermoperiostosis.
The positive physical findings included marked furrowing of the scalp (cutis verticis gyrata), short spade-like hands, and marked clubbing of the fingers and toes without cyanosis. Periosteal proliferation was shown radiographically (Fig 3). No abnormalities were detected by cardiac catheterization.

Case 3.—A 43-year-old Negro man had noted the onset of digital clubbing, arthralgia of the small joints, and sweating of the distal ends of his fingers and toes in his early twenties. Excessive oiliness of his skin, sebaceous overactivity, and acne were present for an undetermined period of time. Several years prior to admission an effusion developed in the right knee which disappeared in about three to four months. The patient’s family included two parents, one brother with four children (three girls and one boy), and one sister with two children (one girl and one boy), all of whom were free of clubbing. The sister was, however, the only relative available for personal examination.

Physical examination demonstrated furrowing of the skin of the face, sebaceous overactivity, acne pits and bulbous clubbing of the fingers and toes without cyanosis. The findings of the remainder of the examination were within normal limits.

Laboratory studies revealed a normal carbon dioxide tension, pH, and oxygen tension in the arterial blood. The results of chest film were normal, and roentgenograms of his long bones did not show evidence of periosteal proliferation.

Comment.—This case illustrates an incomplete form of pachydermoperiostosis. Historical evidence of arthralgia, arthritis, sweating, acne, and sebaceous overactivity were present together with objective clubbing, furrowing, acne, and oily skin in the absence of roentgen evidence of periosteal bone changes (pachydermia without periostosis). The normal oxygen tension serves to eliminate cardiac or pulmonary arteriovenous shunting as a cause of clubbing.

Case 4.—A 69-year-old Negro man had a long history of arthralgia, increase in size of the knees and ankles, mild furrowing of the skin, and digital clubbing. The patient was unable to relate any family history.

On physical examination the only positive findings were mild furrowing of the skin of the face and moderate clubbing of the fingers and toes without cyanosis (Fig 4). Findings of a chest film were normal, but roentgenograms of the long bones revealed marked periosteal proliferation (Fig 5).

Comment.—In this patient the periosteal changes were severe, the clubbing only moderate, and the skin changes (furrowing, oiliness, and acne) were almost nonexistent. This illustrates that in addition to the variety of this entity in which clubbing and pachydermia may be seen without bone...
changes, severe periosteal proliferation may be seen with only moderate clubbing and equivocal skin changes (periostosis with equivocal pachydermia).

Cases 5 and 6.—A 46-year-old Negro man had a history of furrowed skin, clubbing, arthralgia, marked sweating of the palms and soles, sebaceous gland overactivity, and acne of many years' duration. Several years prior to admission an effusion in the left knee joint required an arthrocentesis. No information is available concerning the nature of the fluid; however, the effusion did not recur. Pertinent physical findings included furrowing, pitting and oiliness of the facial skin, marked clubbing without cyanosis of the fingers and toes, and persistent sweating of the palms.

Findings from a chest film were normal. Roentgen examination of the long bones revealed periosteal proliferation of one tibia (Fig 6).

The patient's father, age 76, was found to have similar skin changes (pachydermia) (Fig 7) but no sweating, clubbing, or periosteal bone changes.

The remainder of the family which includes the mother and 12 siblings had no historical evidence of clubbing.

Comment.—These two cases emphasize both the familial occurrence of the disease, previously reported in about 25% of the cases, and the incomplete form (pachydermia without clubbing or bone changes) in the father. The occurrence of the full syndrome in the son and only pachydermia in the father strengthens the current contention that forms frustes of this disease exist.

Comment

Since clubbing may be the first manifestation of either pachydermoperiostosis or secondary hypertrophic osteoarthropathy in individuals with this finding, roentgen examination for evidence of periosteal proliferation or new bone formation must be carried out. Documentation of the presence of bone changes is especially important since this finding is very rare in most conditions associated with simple clubbing such as suppurative lung disease, pneumoconiosis, emphysema, congenital heart disease with cyanosis, subacute bacterial endocarditis, chronic congestive heart failure, hypertrophic biliary cirrhosis, and chronic diarrheal states.

In pachydermoperiostosis the clinically apparent digital changes usually begin at or about the time of puberty. The condition is characterized by an insidious, progressive enlargement of the joints, especially the wrists, lower parts of the legs, and ankles not uncommonly accompanied by sterile joint effusions. The sites involved most commonly with periosteal changes are the distal one-third of the tibia, fibula, radius, ulna, and humerus. In these locations radiographic evidence of periosteal proliferation and even periosteal new bone formation with resultant cortical thickening may be seen.

Other prominent systemic features of this entity include malaise, profuse sweating especially over the hands and feet, with or without accompanying paresthesias, stiffness of the fingers, sebaceous overactivity on the
Fig 5.—Marked periosteal proliferation along the entire length of both tibiae and fibulae (case 4).

face resulting in excessive oiliness, acne, and marked thickening and furrowing of the skin of the face, forehead, scalp, hands, and feet. The most prominent of these folds are on the forehead, cheeks, and nasolabial region. Extreme furrowing of the scalp is designated cutis verticis gyrata. Some authors have reported secondary sex disturbances such as hypertrophy of the male breast, feminine distribution of hair, and scanty growth of beard as being common. However, most of the literature as well as our own experience fails to verify this finding.1,2,5

The disease may be relentlessly progressive or may become arrested spontaneously. In the former instance bone production may proceed to universal hyperostosis of the skeleton, ossification of ligaments, and fusion of certain joints, particularly those of the carpus, tarsus, and vertebral column. Functional joint changes may be permanent but life expectancy is not affected.5

Among the diseases to be considered in the differential diagnosis of pachydermoperiostosis are hypertrophic pulmonary osteoarthropathy, acromegaly, thyroid acropachy, syphilitic periostitis, osteopetrosis, and leprosy. Helpful diagnostic points in the differentiation of pachydermoperiostosis from pulmonary hypertrophic osteoarthropathy include the fact that the latter starts later in life, is more frequently painful due probably to the much more acute development of the musculoskeletal changes, and shows less skin involvement although this does occur in both states.1 A positive family history is also found in about one quarter of the cases of pachydermoperiostosis,2 a finding obviously not present in pulmonary osteoarthropathy.

One vexing problem in differential diagnosis is caused by the fact that the symptoms and signs of osteoarthropathy may precede the symptoms or roentgen evidence of a pulmonary tumor. To the best of our knowledge, the longest time interval recorded between onset of osteoarthropathy and onset of symptoms related to bronchogenic carcinoma is 18 months.6 It is possible that cases will be reported in which this interval is greater. However, while no specific figure...
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Fig 7.—Father of patient in case 5. Dilated pores of cutaneous glands and marked furrowing. This patient had no other features of the syndrome and his recognition as having pachydermoperiostosis depends on the presence of the full syndrome in his son.

can be given, it seems obvious that the longer osteoarthropathy has been present without evidence of lung tumor, the less likely will it be for this to be secondary pulmonary osteoarthropathy.

In acromegaly the mandible, nose, and supraorbital ridges are enlarged, but without periosteal proliferation, whereas in pachydermoperiostosis the periosteal proliferation involves the long bones. Other findings which may be seen in acromegaly and not in pachydermoperiostosis are enlargement of the sella turcica, visual field defects, macroglossia, and an elevation in the level of inorganic serum phosphorus. In thyroid acropathy malignant exophthalmos and pre-ribial myxedema may be present. This form of acropathy is usually seen following thyr-oidectomy for Graves' disease. Syphilitic periostitis is not symmetrical in distribution, occurs usually on the tibiae, not simultaneous on the fibulae, and seldom on the bones of the forearms. The serology will also help to differentiate this entity. In osteopetrosis there is narrowing of the medullary canal which is not seen in pachy-
dermoperiostosis. The skin changes and suggestive leonine facies bring leprosy into the differential diagnosis, but the clinical course, the lack of roentgenologic demonstration of calcific periositis, and the absence of clubbing rule out this possibility.

While the etiology of pachydermoperiostosis is not known, familial occurrence is seen, and the inheritance is mediated by a recessive or incompletely dominant gene. Recent articles have reviewed theories of pathogenesis as well as the vascular changes in the extremities of cases of simple clubbing and secondary hypertrophic osteoarthropathy. Another recent report has shown that peripheral blood flow in pachydermoperiostosis is reduced.7

No definitive therapy is known for this condition. Tarsorrhaphy may be required in those cases in which there is considerable hypertrophy of the eyelids. Sympathectomy may relieve the excessive sweating if this is a particularly troublesome complaint.2

Finally it should be reemphasized that the important entity to be ruled out before the diagnosis of pachydermoperiostosis is accepted is bronchogenic carcinoma, since hypertrophic osteoarthropathy occurs in 5%-10% of cases of carcinoma of the lung.8 Thus, digital clubbing and osteoarthropathy must be fully investigated with special reference to the chest before one can safely reassure both oneself and the patient that the correct diagnosis is pachydermoperiostosis.

Summary

Pachydermoperiostosis is considered to be rare. However, during the past 12 months six patients with this entity have been seen at this institution. The clinical features of the complete syndrome are clubbing with periosteal bone changes, skin furrowing, sebaceous gland overactivity, acne, and hyperhidrosis. Some subjects may have all these findings; in others, however, only some of these features are present.

Of six patients seen at this hospital, three had both pachydermia and periostosis, one had pachydermia and clubbing without periostosis, another had periostosis and clubbing.
but equivocal pachydermia, and the final subject had pachydermia without periostosis or clubbing.

Although the etiology of pachydermoperiostosis is unknown, familial occurrence is seen, and the inheritance is mediated by a recessive or incompletely dominant gene. No therapy other than symptomatic care is known. It must again be emphasized that the most important condition from which pachydermoperiostosis must be differentiated in hypertrophic pulmonary osteoarthropathy, which most commonly is secondary to bronchogenic carcinoma.

REFERENCES


