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Pachydermoperiostosis : Trial with Isotretinoin

Yoon-Kee Park, Hyung Joo Kim and Kee Yang Chung

A 22-year-old male patient presented with typical features of pachydermoperiostosis. Thickening and oiliness of the facial skin, clubbing of the fingers, and hyperhidrosis of the palms and soles were the most prominent features. Osteosclerosis and hypertrophic osteoarthropathy were present in the bones of the hands, feet and tibia. We administered isotretinoin with the rationale that the drug inhibits sebum and collagen production. The patient was quite satisfied with the reduction of facial oiliness.

Key Words: Pachydermoperiostosis, isotretinoin

Pachydermoperiostosis (primary or idiopathic hypertrophic osteoarthropathy) is a rare disease first described by Touraine *et al.* in 1935. This syndrome is characterized by digital clubbing, periostosis of the long bones, thickening of the face and scalp, hyperhidrosis, and dyssebacea (Remoin 1965; Vogl and Goldfischer 1962). Treatment of pachydermoperiostosis is centered mostly around the improvement of the cosmetic appearance through plastic surgery. Reported here is a case of pachydermoperiostosis with histologically proven sebaceous hyperplasia. Oiliness of the face was markedly improved on a clinical trial with isotretinion

CASE

A 22-year-old male patient visited our department with chief complaints of facial skin thickening and accentuation of creases which gave him the appearance of being old. He also complained of difficulty in carrying out everyday work due to excessive hyperhidrosis of both palms and soles which developed 2 years ago. There was no contributing family history.

On physical examination, thickening, furrowing, and oiliness of the facial skin (Fig. 1) and bilateral palmoplantar hyperhidrosis with clubbing of the fingers were found (Fig. 2). His general condition was good, except that he looked older than his actual age. Chest X-ray, complete blood count, erythrocyte sedimentation rate, eosinophil count, urinalysis, SMA-12, STS, serum immunoelectrophoresis, serum

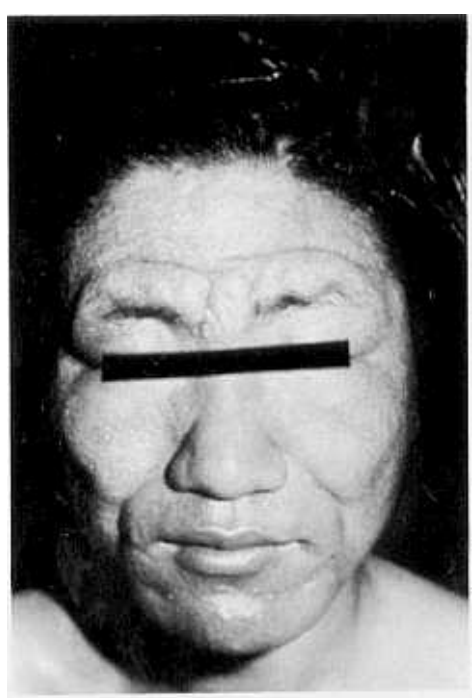

Fig. 1. A 22-year-old man presenting a deeply furrowed forehead, thickened eyelids, oiliness, and gaping sebaceous pore openings.

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Department of Dermatology, Yonsei University College of Medicine, Seoul, Korea
Address reprint requests to: Dr. YK Park, Department of Dermatology, Yonsei University College of Medicine C.P.O. Box 8044 Seoul, Korea, 120-140

T_3 and T_4, and growth hormone were all within normal limits or negative. Radiological examination of the hands, feet, and both tibias showed subperiostal new bone formation with widening of the width of the long and short tubular bones (Fig. 3).

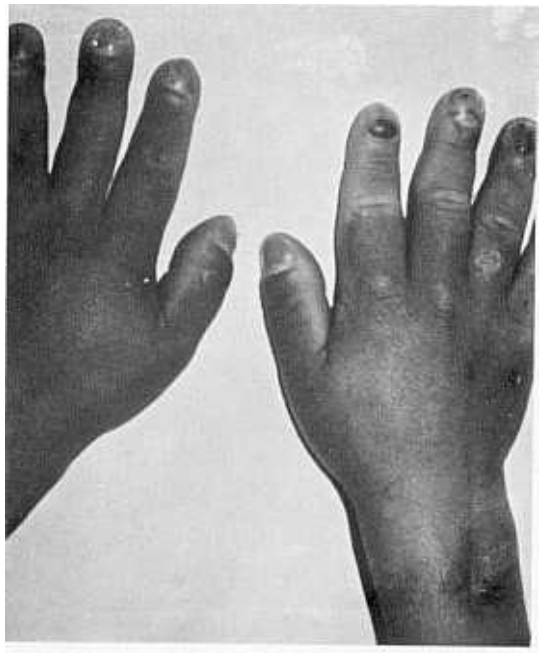

Fig. 2. *Thickened fingers and clubbing of the terminal phalanges.*

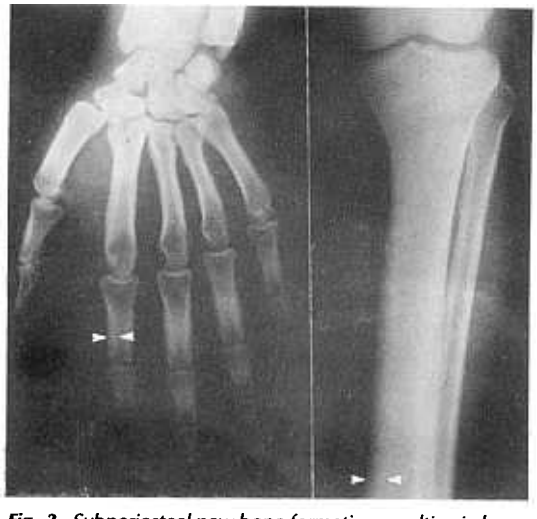

Fig. 3. *Subperiosteal new bone formation resulting in hypertrophic osteoarthropathy in the bones of the hands and legs.*

On facial skin biopsy with hematoxylin and eosin staining, mild acanthosis, marked sebaceous gland hyperplasia and perivascular and periappendageal infiltration of mononuclear cells were noted (Fig. 4). PAS,

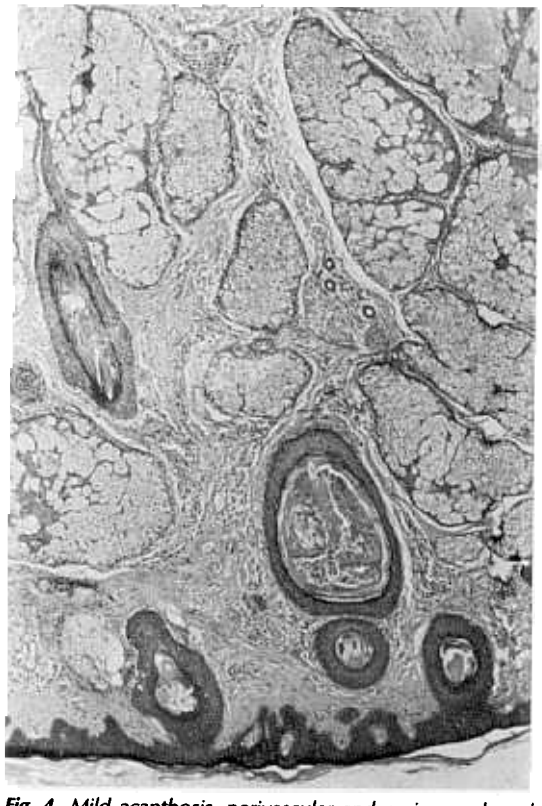

Fig. 4. *Mild acanthosis, perivascular and periappendageal lymphohistiocytic infiltration, and sebaceous gland hyperplasia are evident (H & E stain, x40).*

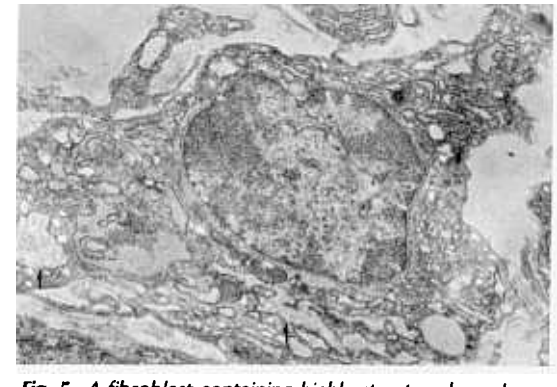

Fig. 5. *A fibroblast containing highly structured rough endoplasmic reticulum consisting of dilated cisternae filled with electron dense amorphous material (TEM, x15,000).*

alcian blue, and toluidine blue stains did not show mucin deposition in the dermis. Masson's trichrome stain also did not show any increase in collagen. On electron microscopy, the fibroblasts were rich in rough endoplasmic reticulum consisting of dilated cisternae filled with amorphous material characteristic of stimulated fibroblasts (Fig. 5).

Isotretinoin, 30mg daily, was given orally. When the patient 4 weeks later, he testified that he was quite satisfied with the marked decrease in the oiliness.

DISCUSSION

Pachydermoperiostosis was first described by Touraine, Solente, and Gole in 1935 as a characteristic syndrome. It is known to be transmitted autosomal dominantly (Remoin 1965).

Symptoms usually develop in males in their teens and become stationary in their late 20s and 30s. Characteristic clinical features are clubbing of the digits,coarsening of the facial features with thickening, furrowing and oiliness of the facial skin, and palmoplantar hyperhidrosis. Also, examination of the skin reveals marked sebaceous hyperplasia with wide open sebaceous pores filled with plugs of sebum. Massive thickening of the sclap and forehead in transverse folds results in a picture known as cutis verticis gyrata (Hambrick and Carter 1966).

Radiologic examination characteristically reveals irregular subperiosteal calcification of the long bones, primarily at the distal ends. The transverse diameter of the metacarpals, metatarsals, and the two proximal phalanges may be increased due to the formation of irrequlär, subperiosteal new bone (Remoin 1965). Clinical and laboratory features present in our patient are diagnostic of idiopathic pachydermoperiostosis.

Salient histopathological features usually found are slight hyperkeratosis or acanthosis with sebaceous gland hyperplasia, which may sometimes be absent. Increase in the number and size of eccrine glands and increase in connectivce tissue are also noted (Hambrick and Carter 1966). An increased number of collagen bundles and fibroblasts could not be seen in our case even though the sections were suitably stained, probably due to the pressure exerted by the massive sebaceous gland hyperplasia. However, electron microscopy of a skin biopsy specimen from the forehead before treatment showed the fibroblasts to be rich in rough endoplasmic reticulum. Dilated cisternae of the rough endoplasmic reticulum were filled with amorphous material, which consists of triple helical procollagen molecules.This picture was characteristic of stimulated fibroblasts undergoing active synthesis of collagen fibers Nigra *et al.*, 1972; Scarpelli and Goodman 1968; Uitto and Lichtenstein 1976).

As the typical course of this disease is self-limited, with most of the cases ceasing to progress before the patient reaches middle age, the treatment has been focused mainly on cosmetic improvement by plastic surgery. However, in patients with pulmonary hypertrophic osteoarthropathy, vagotomy or ligation of the pulmonary artery resulted in disappearance of the skeletal changes (Flavell 1956). However, as the facial features of the disease are brought about by an increase in the amount of connective tissue and hyperplasia of the sebaceous glands, improvement of the cosmetic features could well be expected by reducing the amount of both. Retinoids, be it etretinate or isotretinoin, were shown to reduce procollagen production by diminishing procollagen mRNA in fibroblasts. They are also known to inhibit the production of collagenase (Abergel *et al.* 1985). Even though not proven histopathologically or by sebum analysis in our case, sebaceous gland activity was assesed clinically to be reduced. Further evaluation of clinical effects by periodic skin biopsy, X-ray of the bones and by electron microscopy or biochemical methods is desired to elucidate the effect of the retinoids in the treatment of primary pachydermoperiostosis.

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