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FAMILIAL NEUROGENIC ACRO-OSTEOLYSIS, TYPE GIACCAI —REPORT OF TWO FAMILIES—

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Summary Two families with familial neurogenic acro-osteolysis are reported. According to the classification of Spranger *et al.*, these cases fall into the category of Giaccai type idiopathic osteolysis. In all cases, the primary site of the osteolytic process was at the phalangeal regions with skin ulceration and sensory disturbance. In kindred I, two siblings born to the parents of consanguineous marriage were affected, indicating autosomal recessive inheritance. In kindred II, cousin affection was observed. The terms "familial neurogenic acro-osteolysis" used in human genetics and orthopaedic surgery and "a recessive form of hereditary sensory radicular neuropathy" used in neuro-medicine seem to indicate the same disease.

INTRODUCTION

In the recent International Nomenclature of Diseases of the Bone (Special report, 1978), a category entitled "Idiopathic Osteolysis" was described. This classification includes phalangeal, tarsocarpal, and multicentric forms. On the other hand, Spranger *et al.* (1974) classified idiopathic osteolysis into eight types.

The purpose of this paper is to report two families with idiopathic osteolysis, Giaccai type, or familial neurogenic acro-osteolysis, and to discuss the relationship between familial neurogenic acro-osteolysis and hereditary sensory radicular neuropathy.

CASE REPORTS

Kindred I

Proband. A 29-year-old male

Chief complaints. Painful swellings and ulcerations of the tips of the fingers and toes.

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Present history. The patient had suffered from painful swellings and skin ulcerations of bilateral fingers and toes for seven years. Five years ago, he was treated with sympathectomies of the thoracic and lumbar regions, but to no avail. Three years ago, he was treated with amputation at the level of the base of the middle phalange of the right middle finger because of suppurative inflammation of the middle and terminal phalangeal bones.

Present illness. Clinical investigation revealed that the terminal phalanges of the right thumb and index, ring and little fingers and the left thumb and, index and middle fingers were shortened and atrophied with ulcerations and/or scar formations due to ulcerations and deformities of the nails. The right middle finger was amputated at the level of the base of the middle phalange (Figs. 1, a and b). The

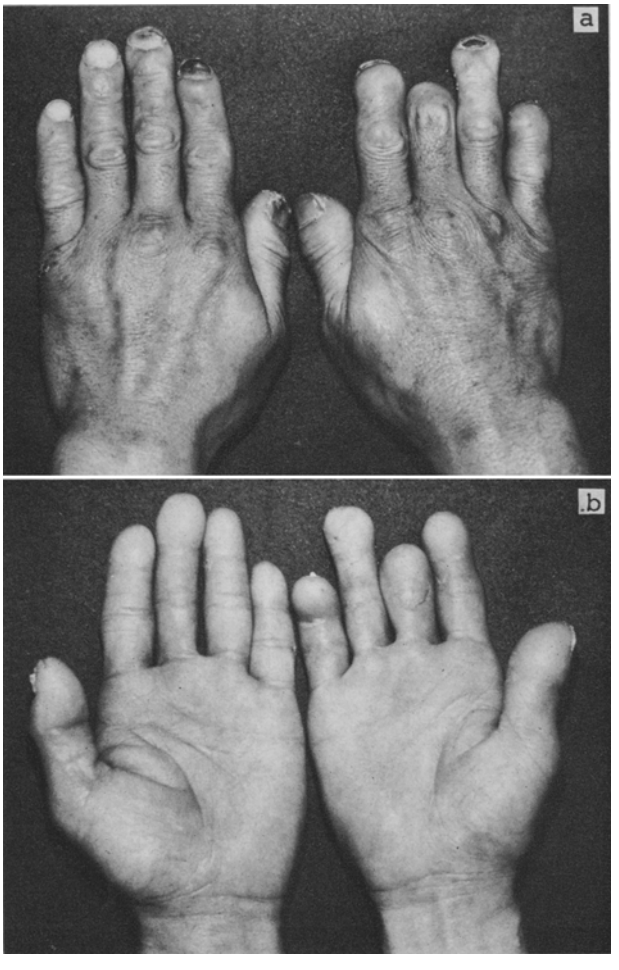


Fig. 1. External appearance of the hands. a, dorsal aspect; b, volar aspect.

terminal phalanges of all of the bilateral toes were shortened and atrophied with ulcerations or scar formations and deformities of the nails (Fig. 2, a and b). There was definite degree of hypesthesia bilaterally below the forearms and lower legs. Degree of hypesthesia was distally dominant. Tendon reflexes of extremities were lacking. X-ray examinations revealed acro-osteolytic shortening and deformities of the terminal phalanges of bilateral thumbs and all fingers, except the amputated right middle finger, and of all the toes (Fig. 3, a and b).

Family study. The pedigree of the patient is shown in Fig. 4. The maternal and paternal grandfathers of the proband were brothers. In addition, the paternal and maternal grandmothers of the proband were cousins. The eldest brother of the proband was affected by the same disease and was treated with bilateral lower

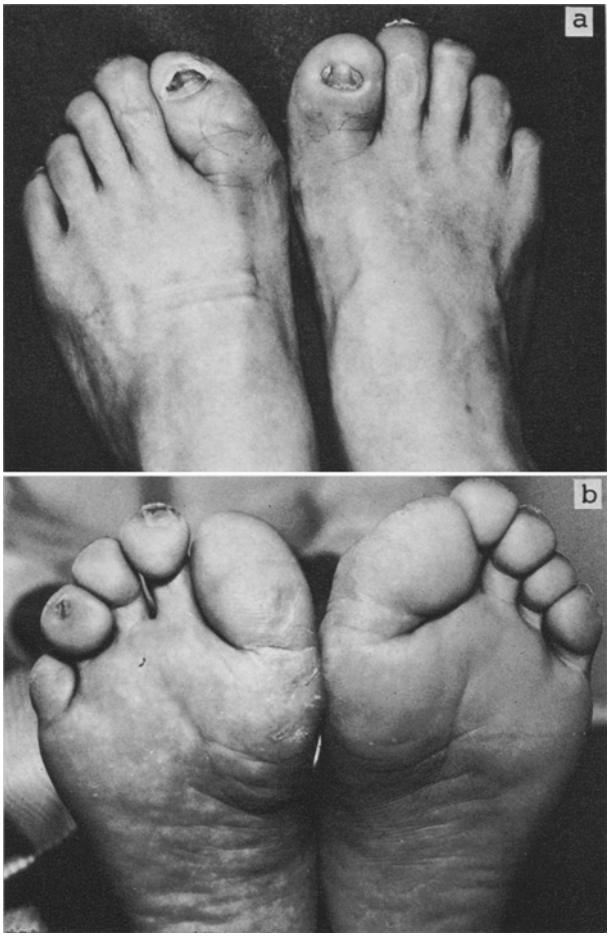


Fig. 2. External appearance of the feet. a, dorsal aspect; b, plantar aspect.

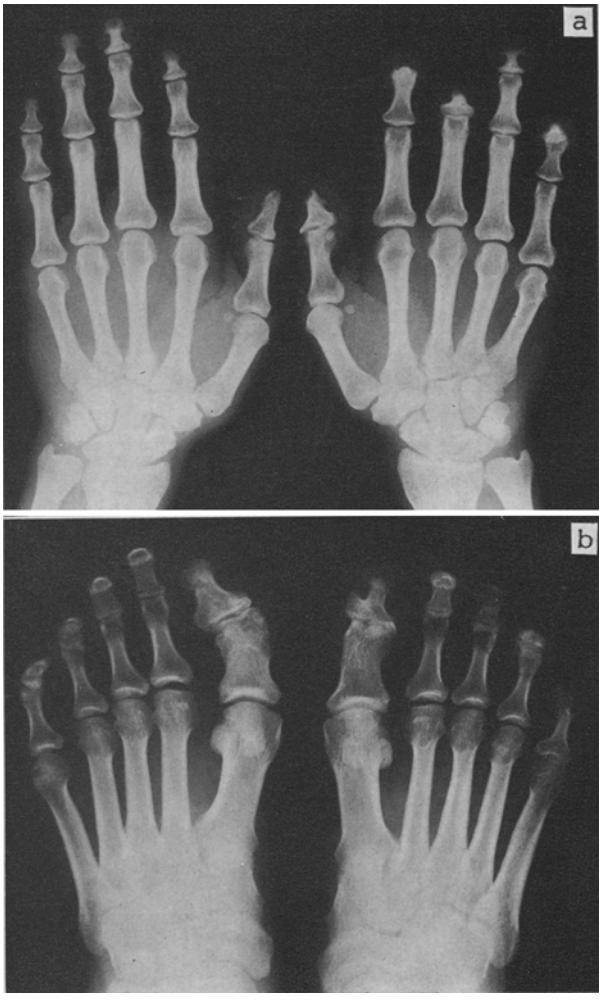


Fig. 3. X-ray findings of the hands and feet. a, hands; b, feet.

leg amputations because of severe suppurative osteomyelitis of the tarsal and toe bones secondary to the deepening of the skin ulceration.

Kindred II

Proband. A 30-year-old female

Chief complaints. Deformity and pain of both feet.

Present history. She had suffered from severe pain, swelling, redness and functional disturbance of the tip of the right index finger at the age of six, of the tips of both little fingers at the age of 10, of the metatarsophalangeal joint of the left great toe at the age of 13 and thereafter of the metatarsophalangeal joint of the right fifth

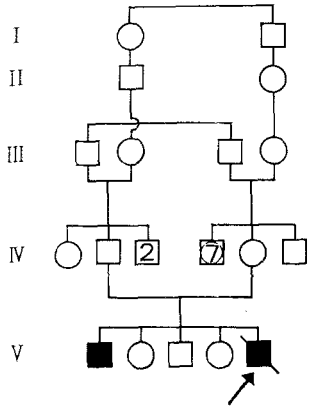


Fig. 4. Pedigree tree of kindred I.

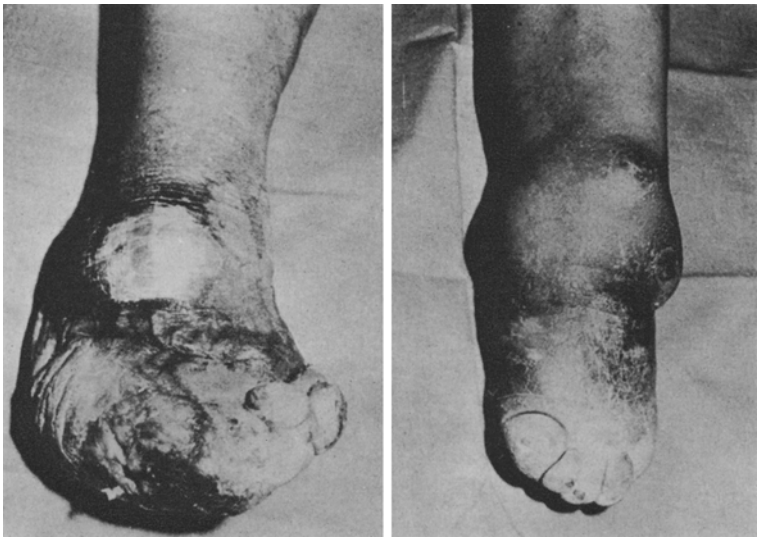


Fig. 5. External appearance of the feet.

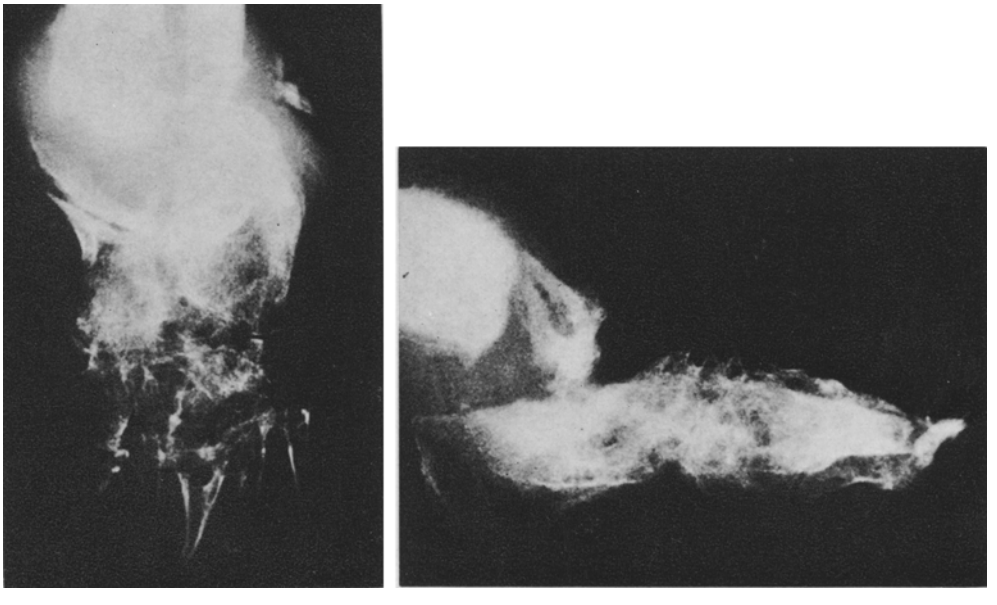
toe. These affections had been diagnosed as chronic suppurative osteomyelitis by surgeons and orthopaedic surgeons. After these acute inflammatory episodes, both feet gradually showed shortening and deformities, which were accompanied by deepened skin ulcerations at bilateral plantar aspects. At the age of 28, she suffered from intermittent fever and pus discharge from bilateral plantar aspects of the feet and was hospitalized for four months.

Present illness. The right foot was markedly shortened and deformed. At the plantar aspect of the tarsal region, there was ulcer formation with conspicuous pus

discharge. The markedly shortened and deformed great and second toes remained, while the third, fourth and fifth toes were completely missing. The left foot was also obviously shortened and deformed (Fig. 5). In the upper limbs, hypesthesia was observed below bilateral elbow joints. The degree of hypesthesia was distally dominant. The tendon reflexes were markedly weak. X-ray findings revealed that all the toes were missing, and the metatarsal bones showed marked distal taper and bone atrophy of the right foot. On the left foot, however, all the toes were faintly visible and the metatarsal bones showed conspicuous distal taper with a mixture of rarefied and condensed bone shadows and marked bone resorption at the talar and navicular regions (Fig. 6, a and b).

Clinical course. Continuous administration of high dosage of antibiotics was not successful in relieving pyrexia caused by suppurative osteomyelitis secondary to the deepening of the soft tissue inflammation. Therefore, amputation of the left lower leg was performed.

Pathohistological findings. Most of the bone tissue in the destroyed area of the distal part of the left tibia was necrotic with fibrosis of the bone marrow and suppurative inflammatory cell infiltration. In the nervus tibialis, the epineural tissue disclosed marked necrosis of collagen fibers and the perineurium grew thicker, indicating a tendency to fibrosis among the nerve fibers as observed through H and E staining. Luxal fast blue staining revealed that the myelin was swollen, partly showing waving and tear with a tendency to demyelination (Fig. 7, a and b).



a b

Fig. 6. X-ray findings of the left foot. a, AP view; b, lateral view.

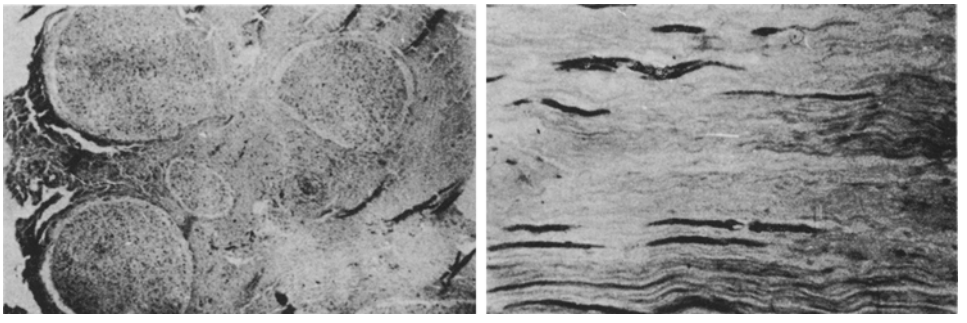


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Fig. 7. Pathohistological findings of the tibial nerve. a, H.E. stain; b, luxal fast stain.

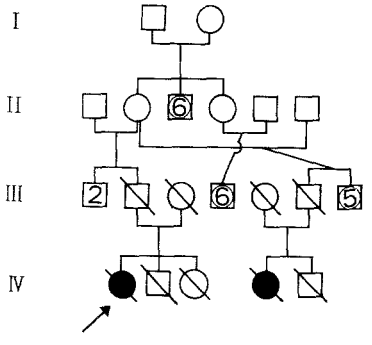

Fig. 8. Pedigree tree of kindred II.

Family study. The pedigree of this patient is shown in Fig. 8. A paternal cousin was also affected by the same disease and was treated with curettage and bone graft of the affected right calcaneus by the authors. The fathers of the two patients were half brothers and had the same paternal grandmother.

DISCUSSION

Hitherto, a number of case reports on idiopathic osteolysis have been published. Spranger *et al.* (1974) reviewed them and classified the disease into eight groups on the basis of inheritance, primary location of the affection of the osteolytic process and associated features. The disease groups indicated as 1b and 2b in this classification are believed to be neurogenic ones because of the feature of sensory disturbance and skin ulceration. According to the classification of Spranger *et al.* (1974), the cases presented here fall into the category 2b, Giaccai type, because the primary site of the osteolytic process was at the phalangeal regions with skin ulceration and sensory disturbance, and because autosomal recessive inheritance was indicated by sibling

affection born to the parents of consanguineous marriage in kindred I. The authors prefer to use the term "familial neurogenic acro-osteolysis," postulated by Giaccai (1952) for this type of idiopathic osteolysis.

Denny-Brown (1951) postulated the term "hereditary sensory radicular neuropathy" for the disease which is very similar to the disorder described here, from the viewpoint of neuro-medicine. He reported the clinical and autopsy findings of a 53-year-old woman, a member of the family reported by Hicks and Camp (1922). The most severe changes found in the autopsy were a marked loss of ganglion cells in the sacral and lumbar dorsal root ganglia (Denny-Brown, 1951). Hereditary sensory radicular neuropathy is considered as autosomal dominant disorder (McKusick, 1983; Axelrod, 1983). On the other hand, Ogden *et al.* (1959) reported cases of younger patients with similar clinical findings; these may have recessive inheritance. In Japan, Kuroiwa and Murai (1964) reported two families with heraditary sensory radicular neuropathy for the first time. According to their description, hereditary sensory radicular neuropathy is characterized by the familial occurrence of severe, relapsing foot ulceration of neurogenic origin, progressive destruction of the terminal digits of the feet and hands and a loss of sensation and tendon reflexes in the extremities. These characteristics are observed in the present cases. Familial neurogenic acro-osteolysis and a recessive form of hereditary sensory radicular neuropathy seem to be the same disorder.

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