THE SYNDROME OF IDIOPATHIC OSTEOLYSIS
CLASSIFICATION, REVIEW, AND CASE REPORT

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Idiopathic osteolysis is characterised by a spontaneous onset without previous causative factors, followed by rapid destruction and resorption of the involved bones. This process can result in severe deformities with joint subluxation and instability. In certain forms an associated malignant nephropathy may develop. A case report is presented which illustrates the destructive nature of the process.

Primary idiopathic osteolysis is rare. It is characterised by the spontaneous onset of bone resorption without known causative factors. Bones which previously appeared normal begin to undergo partial or complete resorption. This process continues for years, until eventually it ceases spontaneously. The end results of this destructive phenomenon are severe deformities and serious functional disabilities. The exact pathogenetic mechanism of the osteolysis is unknown. In some forms of the disease malignant nephropathies can occur.

CLASSIFICATION

Different terms have been used to describe the primary osteolytic process. These include: essential osteolysis (Neyroud, Baumgartner and Lenoir 1956; Mahoudeau et al. 1961; Torg and Steel 1968; Macpherson, Walker and Kowall 1973); progressive essential osteolysis (Marie et al. 1956); idiopathic acro-osteolysis (Marie et al. 1963); hereditary osteolysis (Shurtleff et al. 1964; Kohler et al. 1973); hereditary multicentric osteolysis (Torg et al. 1969); carpal tarsal agenesis (McKusick and Scott 1971); familial carpal dysostosis (Coleman, Litton and Christensen 1965); and bilateral carpal necrosis (Caffey 1967). Tyler and Rosenbaum (1976) differentiated between the multicentric and the monocentric types of idiopathic osteolysis. In the multicentric variety there is, as the name implies, more than one osteolytic focus; thus, both wrists and both feet may be involved. By contrast, monocentric osteolysis involves only one bone or one group of bones. Both varieties may be similar in appearance, but they represent completely different disease processes. The idiopathic multicentric osteolysis syndrome has been divided into two principal groups by Tyler and Rosenbaum (1976): multicentric osteolysis with nephropathy and multicentric hereditary osteolysis.

McKusick and Scott (1971) also differentiated two groups of idiopathic osteolysis: the well-known acro-osteolysis, and the multicentric variety. Acro-osteolysis is further divided into a phalangeal form and a carpotarsal form; the latter may be associated with nephropathy. Edeiken and Hodes (1973) described the hereditary autosomal dominant form of idiopathic osteolysis and a non-heriteditary form with malignant nephropathy.

Torg et al. (1969) classified the osteolyses into four types: idiopathic multicentric osteolysis with dominant transmission, idiopathic multicentric osteolysis with recessive transmission, idiopathic non-heriteditary multicentric osteolysis with nephropathy, and Gorham's massive osteolysis. Macpherson et al. (1973) added a fifth type, namely the Winchester syndrome. These varieties are described in the account which follows.

Type 1: hereditary multicentric osteolysis with dominant transmission. Approximately 25 cases have been described in the last 20 years (Omer and Mossman 1958; Thieffry and Sorell-Dejerine 1958; Normand, Dent and Smellie 1962; Shurtleff et al. 1964; Coleman et al. 1965; Caffey 1967; Gluck and Miller 1972; McManus et al. 1972; Kohler et al. 1973; Tyler and Rosenbaum 1976). The progression of the disease process is characteristic. Between the age of two and seven spontaneous pain and swelling begin in the hands and feet. These initial symptoms can at times be associated with previous minor trauma. Over the period of a few years, partial or complete resorption of the involved bones can be seen. In the majority of cases, the carpal and tarsal bones are affected. For this reason, Beals and Bird (1975) have referred to this disease as carpotarsal osteolysis. However, a high proportion of cases also have osteolytic involvement of the metacarpals, as well as the distal epiphyses of the radius, ulna and humerus. This leads to shortening and ulnar deviation of the carpus with instability. If the elbows are involved, they subluxate and severe limitation
of mobility ensues. The disease process normally stops in the adolescent period, but can reappear in the third decade (Tyler and Rosenbaum 1976).

**Type 2: hereditary multicentric osteolysis with recessive transmission.** Torg *et al.* (1969) found this recessive variant of the syndrome in three siblings. The clinical appearance is similar to that described for the dominant form. In addition to the specific osteolysis, a generalised severe osteoporosis with cortical thinning and enlargement of the tubular bones is present.

**Type 3: non-hereditary multicentric osteolysis with nephropathy.** Five cases of this form have been described (Marie, Salet and Lévêque 1951; Neyroud *et al.* 1956; Derot *et al.* 1961; Mahoudeau *et al.* 1961; Marie *et al.* 1963; Lagier and Rutishauser 1965; Torg and Steel 1968; Macpherson *et al.* 1973). In two of these five, the onset occurred at two years of age with pain and swelling of the wrist. In this variety there is primarily a gradual disappearance of the carpus, with the tarsal bones involved to a lesser degree. The adjacent metacarpals also are involved in the osteolytic process and the radiological appearance resembles the sucked end of a candy-sugar stick. The osteolysis also crosses the epiphyseal growth centres of the distal radius and ulna, resulting in growth disturbance and severe ulnar deviation. At the same time as the onset of the osteolysis, a proteinuria, reflecting pathological renal function, can also be found. In three of the five cases, death occurred in adolescence from renal failure and malignant hypertension. Post-mortem histology revealed severe chronic glomerulonephritis. In addition to the renal pathology, other manifestations of this particular form of osteolysis were found. In three cases there were deformities of the feet. In one case, Torg and Steel (1968) noted atrophy of the shoulder girdle and a systolic heart murmur; in another, Lagier and Rutishauser (1965) noted skull deformity, cervical spine asymmetry, and a thoracic scoliosis; and Huke (1978) also reported a case with an associated thoracic scoliosis and skull deformity.

**Type 4: Gorham’s massive osteolysis.** In 1955 Gorham and Stout reported 24 cases with a monocentric, massive osteolysis. This variety, known as Gorham’s osteolysis, is associated with a vascular abnormality, angiomatosis or hemangiomatosis, and Gorham demonstrated that a hemangioma in the region of a bone could cause osteolysis. Unlike multicentric osteolysis, this type may start at any age. It has neither a hereditary pattern nor an associated nephropathy. The monocentric pattern of osteolysis may develop not only in the carpaltarsal area, but also in any part of the skeleton. This disease has a benign character, and the osteolytic process stops after a few years.

**Type 5: the Winchester syndrome.** This rare disease, of autosomal recessive inheritance, has been known since the publication of two cases by Winchester *et al.* in 1969. These started in childhood with carpaltarsal osteolysis; other findings included contractures, shortness of stature, skin lesions, corneal clouding, and osteoporosis. No nephropathy was present.

At first this disease was thought to be a new form of mucopolysaccharidosis, but Hollister *et al.* in 1974, reported three other cases and suggested reclassifying it as a non-lysosomal collagenosis. He found an abnormality of fibroblastic function with abnormal collagen production. On electron microscopy, the fibroblasts showed swelling and degeneration of the mitochondria and the endoplasmic reticulum. It is not known if the osteolysis is directly related to the abnormal fibroblastic function.

**CASE REPORT**

A six-year-old boy was first brought to outpatients with pain and swelling of the right wrist. Two months previously he had had a minor fall. Radiologically there were osteolytic changes of the carpal bones and the distal radial and ulnar epiphyses (Fig. 1). A biopsy of the joint capsule and the hamate showed non-specific fibrous inflammation with normal cartilaginous and bony tissue.

![Figure 1](bank/t5247/Fig1.jpg)

**Figure 1**—The right wrist when the boy was six years old. Osteolytic changes are present in the proximal metacarpals, the carpal bones, and the distal radial and ulnar epiphyses. Figure 2—Six months later the carpus has collapsed further.

Bacteriological tests, including tests for tuberculosis and fungal cultures, were negative. Six months later the carpus was virtually destroyed by resorption (Fig. 2). All the adjacent epiphyses showed irregular lytic zones.

One year after his initial visit, the osteolytic process had begun in the left wrist. Both feet also showed isolated acro-osteolysis of the great toes (Fig. 3). At the age of eight, the osteolysis began to involve both elbows. Six years later, partial osteolysis of the entire distal humeral epiphysis, the radial head, and the olecranon was present (Figs 4 and 5), resulting in severe subluxation and limitation of movement; both elbows were similarly affected. By this age (14) the carpal bones had totally dissolved except for small remnants, resulting in severe deformities of both wrists with ulnar deviation and instability (Figs 6 and 7). The shoulders remained completely normal. Both feet had mild osteolytic changes in the metatarsals, cuneiforms, and the os calcis, but the knees and hips remained normal. Active, progressive bone destruction stopped at the age of 14.
The patient is now eight years old. Isolated acro-osteolysis is seen in the right great toe; similar changes were present in the left great toe.

Fig. 3

Fig. 8

Appearance at the age of 14.

Fig. 9

Age 14 years. The severe osteolysis of the distal humerus, the radial head, and the olecranon seen here was present in both elbows.

Fig. 4

Fig. 5

Aged 18 years. Right wrist: as with the other affected areas there has been no significant progression since the age of 14.

Fig. 10

The patient's facial appearance was distinctive (Figs 8 and 9), with skull dysplasia, a flat lateral facies with micrognathia, narrow lid opening and hypertelorism. The shoulder girdle and arm musculature were minimally hypoplastic. His mother and three siblings had a similar appearance but no osteolysis was present in any other member of the family.

Laboratory investigations at the ages of 8 and 14 showed slight proteinuria and a remarkably elevated alkaline phosphatase, reflecting active bone turnover. The differential blood count and the blood chemistry were normal. Further tests including metabolic, rheumatologic and chromosomal profiles were all negative.

A recent follow-up, when the patient was 18 years old, showed the results of 12 years of the disease process.
His physical appearance had not changed significantly since the age of 14, at which time all the pain in his wrists, elbows, and feet ceased. He was of normal intelligence and employed full time as a watch-maker. Physical examination revealed normal shoulder function, but both elbows moved only from 60° to 115°. There was foreshortening of the forearms with significant ulnar deviation of the wrists. Full movement of all metacarpophalangeal and interphalangeal joints was present without deformity. His strength of grip and his dexterity were remarkably good, considering the degree of deformity. His feet had no significant deformity. Radiographs of the elbows, wrists, and feet showed that progression of the osteolysis had virtually halted after the age of 14 (Fig. 10).

DISCUSSION

It is difficult to be sure which of the five types our patient belongs to. We believe he fits best into the third group (multicentric osteolysis with nephropathy), although hereditary multicentric osteolysis with dominant transmission is a possibility. His radiographs are consistent with both of these groups, and his slight albuminuria at an early age might represent a nephropathy. It is known that the nephropathy can be latent over a period of years (Marie et al. 1956; Weiss 1957; Derot et al. 1961; Berthoux et al. 1971), and then later result in hypertension and uraemia. Further follow-up will help to clarify the extent of renal involvement in our patient.

With regard to treatment, at an early age he was given orthotic appliances and had active mobilisation of the involved joints, as well as exercises to strengthen the shoulder and arm muscles. Nevertheless, there are some activities which he cannot perform because of the instability of his wrists. This raises the question as to whether operative stabilisation of the wrists with bone grafts should, in such cases, be undertaken. It is uncertain if the bone grafts would also undergo osteolysis, though it seems likely that grafting would be relatively safe now that the osteolytic activity has ceased and the increased bone turnover is no longer present. An involved unstable wrist was successfully arthrodesed by Kohler et al. (1973), and Huke (1978) performed successful arthrodeses in a patient with osteolysis affecting both ankles.

Differential diagnosis. First one must exclude malignant osteoclastic tumours and inflammatory disorders of bone. Secondly, arterial vascular disease, neurogenic arthropathies, and other neurological diseases must be ruled out. Thirdly, the better known post-traumatic osteolyses must be considered; these can present a similar picture to idiopathic osteolysis because of the absence of neurological dysfunction and trophic changes (Weiss 1957). Multiple destructive foci of bone are also present in the Farber syndrome or granulomatosis disseminata (Bierman et al. 1966). This disease also starts in early childhood with joint swelling; contractures, multiple subcutaneous granulomata, and progressive dyspnoea secondary to laryngeal constriction occur.

Other conditions which must be differentiated are aseptic bone necrosis and lipodermal arthritis (Bortz and Vincent 1961). The latter begins in the third decade with symmetrical peripheral polyarthritis and subcutaneous nodules. This is followed by bone resorption, especially of the distal interphalangeal joints, and deformities of the shoulder, elbow, hip and knee joints. Francois and Detroit (1950) reported two siblings with the following triad: subepithelial central corneal dystrophy, xanthoma of the skin, and osteochondral dystrophy of the extremities; this latter feature is similar to that seen in the carpotarsal osteolysis.

Pathogenetic hypotheses. The pathogenetic mechanism is, in all types of idiopathic osteolysis, unknown. The clinical and radiological progression of the three multicentric osteolyses would seem to indicate a common pathogenesis. Tyler and Rosenbaum (1976) suggested a hereditary immunological defect as the cause. They also proposed that in multicentric osteolysis with nephropathy a similar pathogenetic mechanism exists as in Goodpasture's syndrome. In this syndrome (Beeson and McDermott 1971) antibodies interacting with the basement membrane are present concurrently in the lung alveoli and in the renal glomeruli; in the kidney this leads to a proliferative glomerulonephritis. Because of the concurrent involvement of the nephropathy and osteolysis in the idiopathic multicentric osteolytic syndrome with nephropathy, a similar pathogenetic mechanism as in Goodpasture's syndrome is supposed.

With regard to Gorham's monocentric massive osteolysis, Gorham and Stout (1955) suggested that in the presence of a haemangioma, an active hyperaemia with proliferation of peristeal capillaries ensues; this distorts the bone turnover balance in favour of osteoclastic resorption. Knoch (1963) suggested that a previously silent hamartoma becomes active because of the influence of microtrauma; this association with microtrauma would correlate well with the sites most commonly involved in the syndrome. The rapid growth of an angiomatous tumour could distort the bone metabolism or by direct infiltrative influence lead to osteolysis.

REFERENCES


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