Gorham's disease with spontaneous recovery

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ABSTRACT

Gorham's disease is a rare benign cause of progressive massive idiopathic osteolysis. The clinician's acute awareness and high degree of suspicion are required for diagnosis because of its rarity and variable clinical presentation. Distinctive radiological and histopathological features may help in this regard. Though eventual stabilisation of the affected bone is the most common sequel, spontaneous recovery is very rarely reported in peer-reviewed literature. We report such a rare occurrence in a 17-year-old boy.

Keywords: disappearing bone disease, Gorham's disease, Gorham-Stout syndrome, idiopathic osteolysis, massive osteolysis

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INTRODUCTION

In clinical practice, osteolysis is commonly due to a variety of underlying diseases. From these secondary osteolyses, the rare entity of idiopathic osteolysis or disappearing bone disease can be differentiated. Gorham's disease, also known as Gorham-Stout syndrome or vanishing bone disease, is a very rare benign idiopathic osteolytic disorder characterised by progressive massive osteolysis due to proliferation of immature vascular channels in the form of lymphangioma or haemangioma. The precise aetiology is still unknown and the mechanism of bone resorption is unclear. The clinical presentation of Gorham's disease is variable. The shoulder, pelvis and mandible are commonly affected while the foot is rarely involved. A high index of clinical suspicion is needed to arrive at an early, accurate diagnosis. Progressive in most patients, the disease process is self-limiting in some cases, but spontaneous recovery is extremely rare. We report here the spontaneous recovery of Gorham's disease affecting the lower leg and foot in a boy aged 17 years.

CASE REPORT

A 17-year-old boy presented to our rheumatology clinic with mild pain and fluctuant swelling around the left ankle for the last four months. During the last month, he developed a discharging sinus over the medial aspect of the swelling, which exuded scanty whitish, odourless discharge intermittently (Figs.1a & b). He recounted one episode of blunt trauma in that region about a year and half ago. There was no history of fever, cough, sputum, haemoptysis, weight loss, consumption of uncooked milk, dysuria, oliguria, frequency, haematuria, nocturia, whole body swelling or periorbital puffiness, anorexia, nausea, vomiting, or tuberculosis. None of his family members had ever been afflicted with such type of disease or any haematological disorder.

Initial radiograph revealed soft tissue swelling around the left ankle region. A localised area of bone destruction breaching the overlying cortex, with adjacent

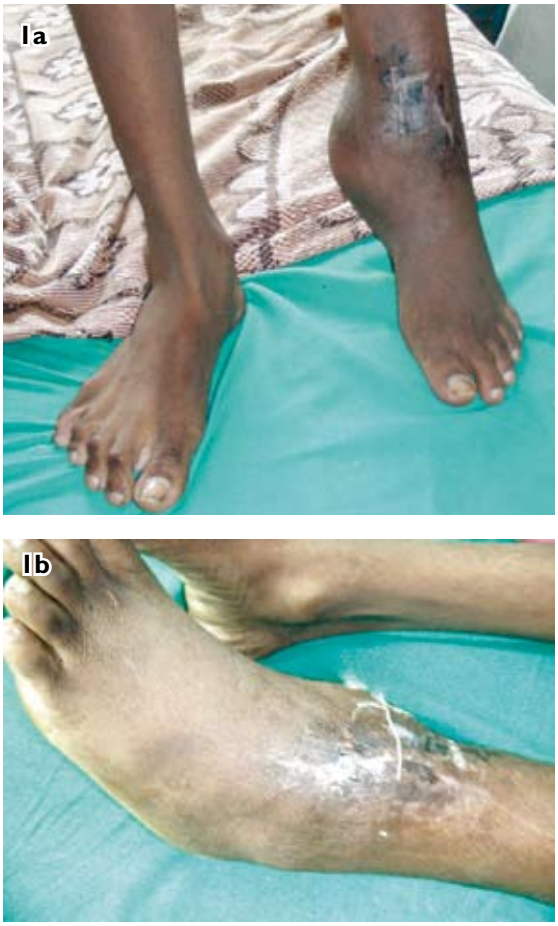

Fig. 1 (a, b) Photographs show a whitish discharge from the sinus over the medial aspect of swelling around the left ankle.

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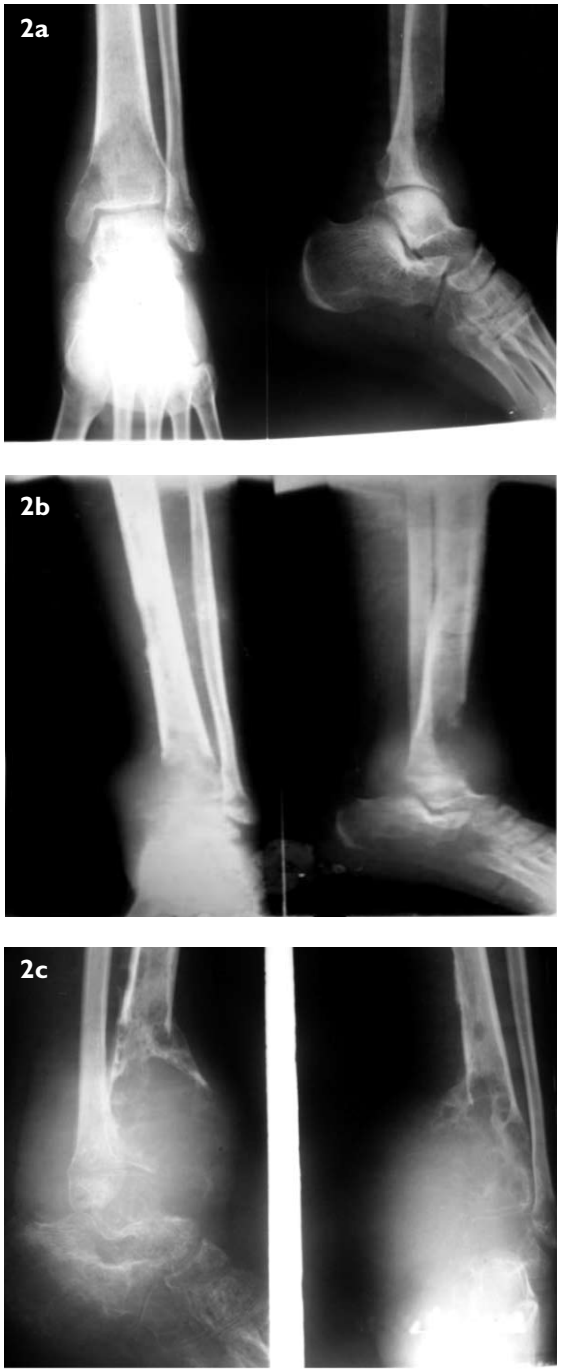


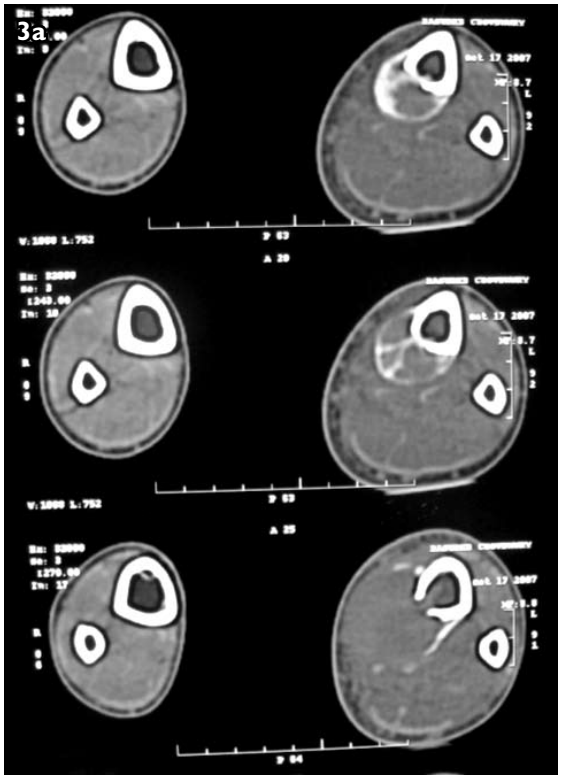
Fig. 2 (a–c) Sequential radiographs show progressive massive osteolysis of the left lower tibia and foot bones extending across the ankle joint with maintained joint spaces. Tibial cortical breakdown at several places with osteoporosis of the non-affected part of the foot bones was noted. Expansion of the bone and periosteal reaction are seen over the posteromedial aspect of left lower tibia (2c). Gross soft tissue swelling around the ankle was conspicuous.

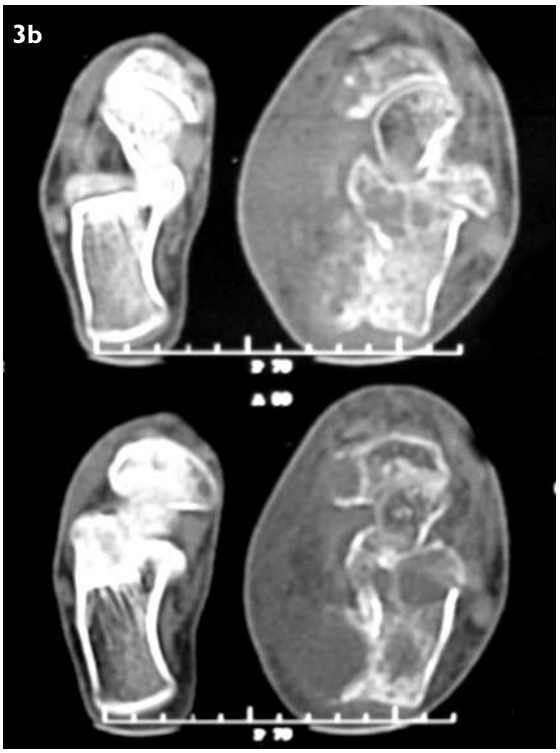
osteopenia, without any element of bone formation was noted in the lower end of the left tibia (Fig. 2a). Gram stain, Ziehl-Neelsen (ZN) stain and modified methylene blue stain failed to reveal any organism from the smear prepared from the whitish discharge of the sinus. No organism could be cultured from the discharge, even after prolonged anaerobic incubation.

Fine needle aspiration cytology of the swelling revealed moderate cellularity composed of neutrophils, few lymphocytes and some foamy macrophages in a necrotic background. No granuloma or malignant cell could be demonstrated. Gram stain, ZN and modified ZN stains were negative. Rapid (Bactec) culture for acid-fast bacillus, as well as culture for Gram-positive, Gram-negative bacteria and anaerobes, and the Mantoux test, were also negative. There was no anaemia or leucocytosis, but erythrocyte sedimentation rate was raised at 45 mm/1st hour. Liver function test, serum urea and creatinine were within normal limits. Serum alkaline phosphatase and parathyroid hormone levels were within normal limits. Chest radiograph was normal. Fasting true serum glucose was 71 mg/dL. Routine urinalysis as well as 24-hour urinary protein excretion rate was within normal limits. Serology for HIV-1 and 2 was negative. The patient was then no longer complaining of pain. He was treated with broad-spectrum antibiotics but the swelling gradually increased in size over the weeks.

Sequential radiographs at this stage revealed progressive massive osteolytic areas in the left lower tibia with expansion of the bone. The cortex was thinned out with breakdown at several places. Permeation of the disease process was seen in the medullary bone as well as the cortex in the visible part of the rest of the tibia without any sclerosis. Periosteal reaction was seen over the posteromedial aspect of the left lower tibia. Similar gross osteolytic areas could be seen in the talus, calcaneum, cuboid and navicular bone with osteoporosis of the non-affected part. The ankle joint was not subluxated. Gross soft tissue swelling around the ankle was conspicuous (Figs. 2b & c). Sagittal and axial contrast-enhanced computed tomography (CT) of the affected part revealed osteolysis of the bones around the left ankle without significant contrast enhancement. The left tibial cortical outline was deficient at places with soft tissue involvement and maintained joint spaces (Figs. 3a & b). CT reconstruction images beautifully illustrated the degree and extent of the lesion (Fig. 3c).

Incisional biopsy from the lesion revealed multiple congested thin-walled blood vessels with areas of haemorrhage and few multinucleated giant cells (Figs. 4a & b). No malignant cells could be found. During biopsy, the surgeon reported profuse bleeding from the biopsy site which needed prolonged local pressure. Differential diagnoses of the expansive bony lesion of the tibia and the foot, which included adamantinoma, aneurysmal bone cyst (ABC), fibrous dysplasia, sarcoidosis, familial expansile osteolysis, low-grade intramedullary or





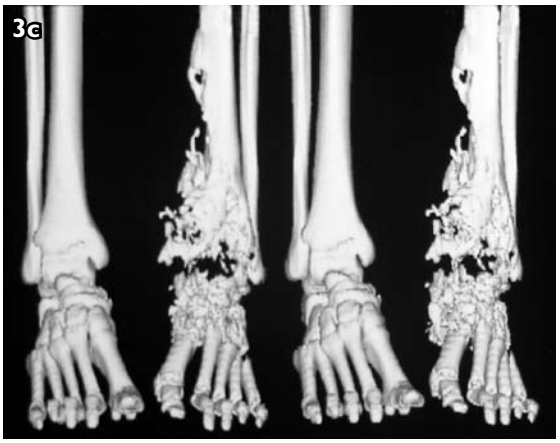


Fig. 3 (a) Sagittal and (b) axial CT images show osteolysis of the bones around the left ankle joint without significant contrast enhancement. Deficient cortical outline of the tibia with soft tissue involvement and maintained joint spaces are noted. (c) Sagittal reconstruction CT image beautifully demonstrates the osteolytic process.

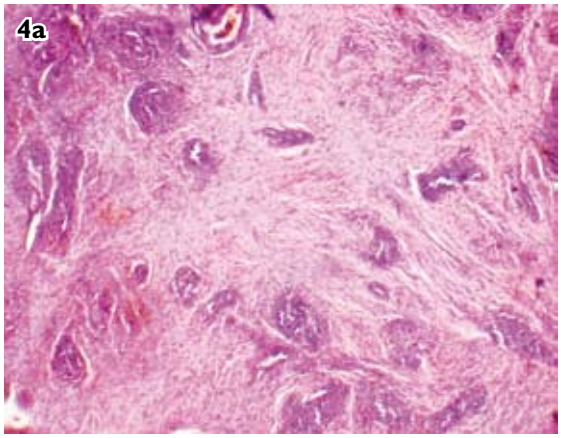
central osteosarcoma, were considered. The absence of typical histopathological features, like nests and bands of epithelial cells, peripheral palisading of the basaloid-appearing cells with a microcystic centre containing stellate-shaped tumour cells, or characteristic non-caseating granuloma, ruled out adamantinoma and sarcoidosis, respectively. The absence of cavity or fluid levels ruled out ABC. Similarly, fibrous dysplasia, low-grade osteosarcoma and familial expansile osteolysis were ruled out because of the absence of typical radiological or histological features or family history. Considering the clinical, radiological and histopathological features, a diagnosis of Gorham's disease was made.

The patient was asked to take bed rest and avoid weight-bearing. He was followed up fortnightly for the next three months. From the third month onwards, his sinus gradually stopped discharging, and the swelling subsided. Repeat radiograph at this stage revealed bony regeneration with exuberant callus formation in the region of the left lower tibia, talus, calcaneum, cuboid, and navicular bone, where the osteolytic lesion was previously present (Fig. 5). At this point of time, the patient was able to ambulate normally without a limp. The final diagnosis was Gorham's disease of the left leg with spontaneous recovery.

DISCUSSION

Jackson first described idiopathic osteolysis in 1838.[1] Many years later, in 1954, Gorham et al described two cases, with a review of the histological features of massive osteolysis.[2] Gorham and Stout recognised it as a syndrome in 1955.[3] Since then, over 175 cases of Gorham's osteolysis were reported under various eponyms, such as haemangiomatosis, disappearing bone disease, vanishing bone disease, massive osteolysis, Gorham's syndrome, Gorham-Stout syndrome and Gorham's disease.

Idiopathic osteolysis comprises a heterogeneous group of rare diseases, characterised by the spontaneous



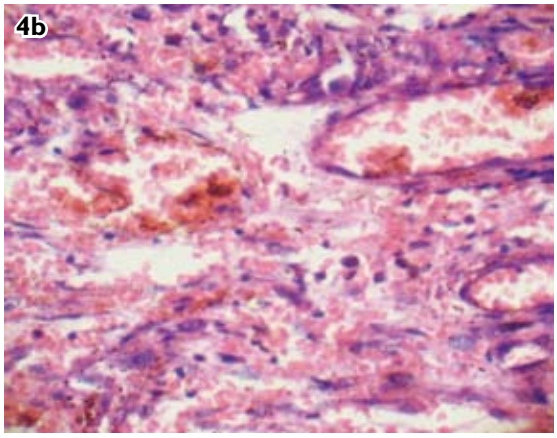


Fig. 4 (a, b) Photomicrographs of the biopsy from the affected site show multiple congested thin-walled blood vessels with areas of haemorrhage (Haematoxylin & eosin, [4a] × 100, [4b] × 400).

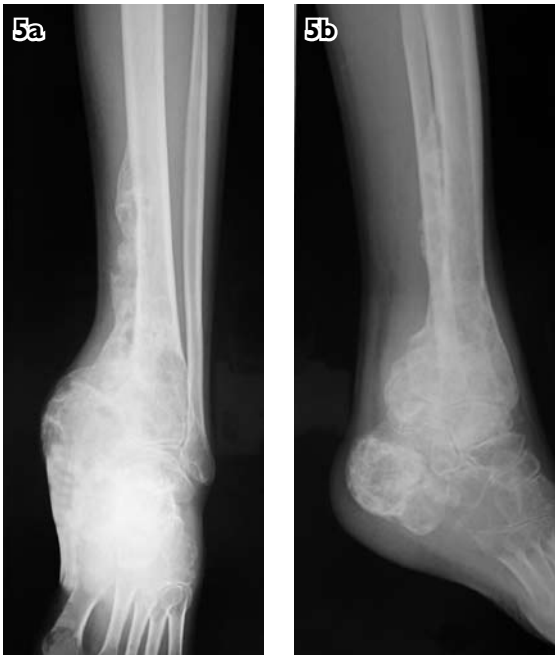


Fig. 5 (a, b) Radiographs show spontaneous bony regeneration with exuberant callus formation in the region of the left lower tibia, talus, calcaneum, cuboid and navicular bone.

onset of mostly peripheral osteolysis, without obvious reason. Torg et al first proposed the classification for idiopathic osteolysis.[4] It was later modified by Hardegger et al, who classified it into five types.[5] Idiopathic osteolysis has to be differentiated from familial and sporadic cases, and from multicentric and unicentric osteolysis. Multicentric osteolysis, usually presenting in childhood or adolescence, can either be hereditary (dominant or recessive) or a non-hereditary variety with nephropathy. Monocentric forms comprise the Gorham-Stout and Winchester syndromes.

Gorham's disease is a rare disease that can occur at any age, but is most often encountered in children and young adults. There is no clear gender or racial predilection, or any inheritance pattern. The lesion classically is without skip areas, multiple foci or metastases, but contiguous bony involvement is usual.[6] Both axial and appendicular skeleton may be involved. The shoulder and the pelvis are the most common sites of involvement.[7,8] Various other locations, such as the humerus, scapula, clavicle, ribs, sternum, pelvis, femur, skull, mandible, maxillofacial skeleton, spine and hand, can be affected by Gorham's disease. Foot involvement has been reported very rarely.[9]

The natural history of Gorham's disease is unpredictable. Clinical manifestations are variable, depending on the site of affection, thus making diagnosis of this uncommon disorder difficult. It may present acutely with pain and swelling, but a history of insidious onset of pain, limitation of motion and progressive weakness in the involved limb is more common. Soft-tissue weakness and/or atrophy may follow. Although idiopathic, some authors have noted onset after trauma to the affected area. This is most likely coincidental as frequently even minor trauma may cause a pathological fracture leading to early medical consultation. In spite of the severe degree of osseous deformity and protracted clinical course, the disease is rarely fatal, if at all, due to complications such as respiratory failure, obstruction of the airways or compression of the spinal cord. Rarely, bone infection and septic shock may also occur.

The disease is usually progressive, but eventual stabilisation of the affected bone is the most common sequel.[10] Spontaneous regression has been reported only in a few cases.[11,12] Chylothorax may occur from the direct extension of the lymphangiectasia into the pleural cavity or via invasion of the thoracic duct from diseases of the ribs, scapula, or thoracic vertebrae. This imparts a high rate of morbidity and mortality without surgical intervention.

Laboratory analysis is uniformly unhelpful.

Transient mild elevations of alkaline phosphatase and eosinophilia have been reported, but their significance is unknown. The hallmark of Gorham's disease is its distinctive radiographic and histopathological findings. Radiographically, Gorham's disease progresses through four stages.[13] Initially, the disease presents as radiolucent foci resembling patchy osteoporosis. Bony deformity progressively increases with further loss of bone mass and eventual disruption of the cortex with endothelial invasion into the adjacent soft tissues and/or across the joints. Finally, there is shrinkage of the ends of the affected bones, producing a "sucked candy" appearance. Pathological fracture may complicate any stage. Bony regeneration is rarely seen. The disease process can extend to contiguous bones; the intervening joints afford no protection to the extension of the disease. Such pattern of regional osseous destruction is distinctive of Gorham's disease and enables physicians to make an accurate diagnosis. The diagnosis, though, must be confirmed histologically from a generous biopsy of the affected bone, by identifying the vascular or lymphatic proliferation in early stages or fibrous tissue in late stages.[1]

Early on, the bone undergoes resorption due to aggressively-expanding, non-neoplastic angiomatous fibrous connective tissue composed of thin-walled vessels, which may be capillary, sinusoidal or cavernous. A clear aetiopathology of Gorham's disease is unknown. Slow circulation producing local hypoxia, hyperaemia and lowering of the pH, favouring the activity of various hydrolytic enzymes like acid phosphatase, alkaline phosphatase and leucine aminopeptidase, have been implicated. Activation and increased sensitivity of osteoclasts or mononuclear perivascular cells as well as deranged osteoblastic function have been proposed to stimulate osteolysis via increased IL-6 activity. New bone formation is absent or minimal. In later stages, due to unknown stimulus, the osseous tissue is replaced by fibrous tissue.

Despite the presumptive presence of angiomas, angiographical techniques have failed to demonstrate the lesions. Accumulation of lymphangiogram contrast in the regions of bone resorption has been able to document the lymphangiomatous lesions, which may cause soft-tissue abnormalities and visceral involvement.[14] Simultaneous and close embryological development of the venous and lymphatic systems may account for the confusion of identity.[15] Several therapeutic modalities have been tried with variable results. Bisphosphonates, alpha-2b interferon, radiotherapy and surgical resection with cortical bone grafting have moderate success in selected cases. Sympathectomy also has its proponents. Due to the variable clinical presentations of this disease, no standard treatment protocol can be advocated.

Our case fits the description of Gorham's disease according to Hardegger et al's classification. This case merits special attention because of several facts. Gorham's disease itself is a rare entity. The tibia and foot are rarely involved in Gorham's disease. During evolution, our patient presented with expansive osteolytic lesion which, to the best of our knowledge, has not been reported before. New bone formation and exuberant callus formation, signalling recovery, are again very rare. We hope to stimulate an early index of suspicion in fellow rheumatologists, physicians and orthopaedic surgeons by presenting this case.

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