In June 1996, a 19-year-old male was referred to the Emergency Department of our hospital by his general practitioner. The patient complained of sudden-onset right-sided thoracic pain 2 days earlier, which increased on breathing. X-ray examination performed by the general practitioner had shown an osteolytic lesion of the 4th and 5th right ribs, as well as a fracture of the 3rd rib on the same side. No reactive sclerosis or callus formation was seen on the border of the lesions (fig. 1).

The patient was an otherwise healthy young man with no history of trauma to the upper thoracic region. He was a moderate smoker who had also taken drugs such as ecstasy and LSD over a period of 18 months up to 4 months prior to admission. His past medical and family history were unremarkable and he denied taking regular medication or having allergies. The initial physical examination was completely normal apart from an area in the ventral upper thoracic region on the right side in which, as expected, the bone could not be felt. The erythrocyte sedimentation rate was 1 mm in the first hour and the C-reactive protein levels, full blood count including differential white blood count, creatinine, calcium and alkaline phosphatase levels were all within normal limits.

A CT scan of the thorax confirmed the defect of the ribs as mentioned above (fig. 2). No tumour-like mass, lymph node enlargement or pleural effusion was seen.

A biopsy of the mass and of the end of the affected ribs was performed and showed hyperaemia and oedema of the bone marrow as well as a high degree of vascularisation and fibrosis of the adjacent periost. A ‘wait and watch’ approach was adopted.

After 3 months, a chylothorax had developed on the side of the affected ribs and the osteolytic lesions had spread to the 3rd, 4th, 5th and 6th rib (fig. 3). Interleukin-6 (IL-6) levels were measured after beginning therapy and found to be 6.7 times the upper normal limit.

What diagnosis should be considered in this young man who had disappearing ribs and a symptomatic chylothorax?
Diagnosis: Disappearing Bone Disease (Gorham-Stout Disease)

Jackson [1] was the first to describe massive osteolysis of the arm in 1838. Since then, several cases of spontaneous resorption of bone have been reported under a wide variety of names, for example, Gorham’s massive osteolysis [2], Gorham’s disease, Gorham-Stout syndrome, syndrome of the disappearing or vanishing bone or phantom bone. Since Gorham’s disease (GD) is exceedingly rare, with less than 200 patients recorded, and since there are currently no well-accepted therapeutic concepts, we present another case.

The disease may imitate a locally aggressive tumour involving bones and adjacent tissues; however, there are no attributes of malignant neoplastic disease. Gorham and Stout [2] first reviewed the disease in 1955 and presented 24 cases. In the pathological specimens of 8 cases, the lesions were described as abnormal proliferation of endothelium-lined thin walled capillaries or sinusoidal channels of vascular or lymphatic origin. These vessels formed an osteolytic haemangioma or lymphangioma with the potential to extend to adjacent bone and soft tissues. Despite obvious bone resorption, only few osteoclasts were noted [2]. More recent reports are inconsistent as to the presence or absence of osteoclasts in the regions of the vanishing bones [3–5]. The exact aetiology of GD has not yet been defined and there is no well-accepted treatment. It is non-hereditary and may occur at any age, although it is most commonly seen in young adults. The differential diagnosis includes other forms of osteolysis such as hereditary osteolysis, non-hereditary osteolysis with nephropathy, Winchester syndrome, syphilis and leprosy. The differential diagnosis of angiomatosis is important as it presents with multiple extraosseous lesions and, in contrast to GD, is frequently associated with visceral involvement [6].

The most common presentation of GD is a monocentric involvement of a single bone or adjacent bones separated by a joint space. The disease may occur in any bone but most reports describe involvement of the upper arm, shoulder and pelvic girdle, spine, thorax and, less frequently, the mandible [4, 5, 7–9]. In most cases, the clinical symptoms are comparatively mild and the disease follows a long, indolent course with no accompanying systemic symptoms, despite some localised bone pain from pathological fractures. GD has occasionally been diagnosed following a pathological fracture. The radiographic findings are distinct and have been divided into four stages [10, 11]. The first stage consists of diffuse intraosseous osteolysis, possibly accompanied by pathological fractures. This is followed by increasing deformity with loss of bone mass. In the third stage, the cortical bone is disrupted and adjacent soft tissue invaded. Lastly, the ends of the involved bone shrink, resulting in a ‘sucked candy’ appearance. Complete bone resorption may follow. Even though cases of spontaneous arrest have been reported, bone regeneration is exceptional [7, 12, 13].
Clinical, radiographic and histological findings together provide the diagnosis. Usually, histopathological diagnosis alone is not sufficient, as illustrated by the non-specific findings in our case (fig. 4). Microscopically, biopsy specimens may reveal vascular or lymphatic proliferation, which, in later stages of the disease, may be replaced by fibrous tissue. Histologically, there is no evidence of cytological atypia, malignant change or inflammation in the specimens reviewed in the literature [2, 5, 12] or, except for a few lymphocytic infiltrates, in our case. It is unclear how the benign hyperplasia of intraosteotic vessels causes the resulting osteolysis.

Regarding the prognosis, no general statements can be made. The survival and quality of life depend on the complications, such as pleural effusions, which often accompany osteolysis of the thorax or the vertebral column, and on the localisation. Involvement of the spine and thorax has been shown to dramatically increase mortality [14]. Quality of life is also affected by the fact that bone resorption may be complete, fractures rarely heal and grafts are often destroyed, resulting in significant functional deformity. However, as mentioned above, bone resorption may stop spontaneously, in which case life expectancy is generally unaltered when the extremities are involved. Especially in cases where vital structures are involved, we believe early diagnosis and appropriate therapy are essential for maximising survival and quality of life.

Due to the rarity of the disease, therapy is varied and few guidelines are available. The main strategies have included radiotherapy and/or surgical resection. Other treatments include vitamin D, vitamin B₁₂, parathyroid hormone, androgens, calcium, adrenal extracts, bisphosphonates and chemotherapy [15]. In cases of progressive disease, radiation therapy is an option that has met with varying success. The treatment volume should include not only the affected bones but also the surrounding soft tissue, with consideration of normal tissue tolerance. Doses of between 25 and 40 Gy have generally been effective at arresting osteolysis [15], and, rarely, at inducing calcification [12, 13]. The patient presented here received fractionated irradiation of the mediastinum (38 Gy) and right thorax (14.4 Gy) with a boost to the involved upper ribs (total dose of 30.6 Gy). In addition to radiotherapy, the patient also had surgical dissection of the thoracic duct and partial pleurectomy to avoid further pleural effusions. He was also treated with bisphosphonate infusions. Owing to the rarity of this disease, the long-term effectiveness and occurrence of late complications of radiation therapy cannot, as yet, be critically evaluated. The risk of radiation-induced cancer following modern treatment, although present, is extremely low. If amputation or local excision is undertaken, a bone graft may be inserted. Such procedures are not universally successful either and resorption of the grafts has been described [16].

In contrast to other investigators, Devlin et al. [17] strongly suggest a role for osteoclasts in the resorption that is characteristic of this disease. They found increased levels of IL-6, which, as in vitro studies have shown, indirectly enhances osteoclast formation and bone resorption [18, 19]. Devlin et al. [17] conclude that patients with GD may benefit from therapeutic modalities which affect IL-6 production or activity. Therefore, we measured the IL-6 serum levels of our patient both during radiotherapy and follow-up. IL-6 levels that were increased to 6.7 times the upper limit of the normal range were detected early in the course of treatment. After completion of radiotherapy, the IL-6 levels fell to 3.2 times this limit. A further reduction to 1.9 times was noted up to 9 months after the radiotherapy treatment was terminated, which provides a strong argument in favour of the patient having re-
responded well to our treatment. In addition, radiographic (fig. 5) and clinical examinations have indicated arrest of the bone resorption in this patient.

In conclusion, GD is a rare, serious disease that might be mutilating or even life-threatening despite the fact that spontaneous arrest can occur. Its aetiology is unclear, and currently no treatment is generally accepted; however, early irradiation may be able to prevent the further spread of the osteolytic lesions. Serum IL-6 levels could be a promising marker for tracing the course of the disease as well as evaluating the arrest of the bone destruction. We recommend further investigation in any newly diagnosed patients.

**Key Words**

Gorham-Stout disease  
Radiotherapy  
Interleukin-6

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