Gorham’s disease of femur

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ABSTRACT

Gorham’s disease is a rare condition of bones characterized by spontaneous massive and progressive osteolysis. Less than 200 cases have been reported so far. Femur is an uncommon site of Gorham disease. We report a young female, presenting as pathological fracture of the femur, wherein rapid osteolysis of femur occurred. The clinical, pathological, and radiological picture suggested a diagnosis of Gorham’s disease. The patient was subjected to radiotherapy (40 Gys) and put on bisphosphonates. At a follow-up of 2 years, the disease process had stopped and partial recalcification of the bone had occurred.

Key words: Femur, Gorham’s disease, osteolysis, radiotherapy

INTRODUCTION

Gorham’s disease is a rare disease characterized by proliferation of thin-walled vascular structures in the bones, resulting in progressive osteolysis which also extends into the surrounding soft tissues. Since the first report in 1838 and the description of the disease by Gorham and Stout only about 200 cases have been reported till date. Although the disease is known from quite some time, the etiology remains speculative; the prognosis unpredictable and effective therapy still not determined. The common sites of the disease include skull, mandible, rib cage, and pelvis. Exclusive involvement of the femur is uncommon. We report Gorham’s disease in a young female, presenting as a pathological fracture in femur which responded to radiotherapy.

CASE REPORT

A 20-year female sustained fracture of the right proximal femur following trivial trauma [Figure 1a]. The patient had occasional pain in the thigh for one year prior to the fracture for which she had been managed with NSAIDs. The patient underwent open reduction and internal fixation with large fragment dynamic compression plate and autogenous bone grafting. The postoperative period was uneventful. The patient reported after 8 weeks with a sudden history of acute pain and deformity in the thigh with inability to bear weight. Radiographs revealed resorption of the graft and the bone with loosening of screws and bending of the plate [Figure 1b]. The systemic examination was normal. Renal ultrasound examination, parathyroid assay, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were normal. A whole body bone scan with 99mTc-MDP (Technecium methylene diphosphate) demonstrated increased focal concentration of radiotracers in the involved femur. The implant was removed, tissue biopsy taken and the limb splinted in a Thomas splint. Intraoperative findings showed partial replacement of the bone by fibrous tissue with absence of signs of infection. Histopathological examination revealed fibromyxoid tissue with highly vascularized collagenous tissue and small capillary-like vessels [Figure 2]. MRI showed destructive changes in femur

Figure 1: (a) Radiograph of the femur showing fracture of the proximal femur (b) Radiograph shows osteolysis at fracture site with bending of plate and loosening of the screws
extending from head into the whole shaft, bone being replaced by multiple cystic areas with fluid levels. The lesion was hypointense on T1-weighed, hyperintense on T2-weighed and STIR (Short TI inversion recovery) with enhancement after intravenous contrast. The lesion extended into the soft tissue reaching up to the subcutaneous fat [Figure 3]. Based on the clinical, radiological, and histological findings a diagnosis of Gorham’s disease was made. The patient refused both surgery (free fibular grafting) and radiotherapy as treatment option. She was managed with oral bisphosphonate (risedronate 35 mg weekly) and mobilized nonweight bearing with a brace. Radiographs after 1 month revealed rapid progression of the osteolysis which now involved the whole of the femur [Figure 4]. The patient received radiotherapy in two stages, initial dose of 25 Gy, followed by a second phase of 15 Gys after 12 weeks (total 40 Gy). Following radiotherapy, the osteolytic process halted and partial recalcification of the bone occurred with bridging across the fracture site [Figure 5]. The patient was mobilized on brace with partial weight bearing and bisphosphonates were continued for two years. At follow up of 2 years the patient was symptomatically better with no complaint of pain in the limb. There was no abnormal mobility at the fracture site but the knee was stiff (ROM 0°-40°) and the patient had a shortening of 1.5 cm. The patient continued to bear partial weight on the limb while using the brace. There was no further osteolysis nor was a further increase in the recalcification noted [Figure 6].

**Discussion**

Gorham’s disease is a rare condition of the bones with less than 200 cases reported so far.² The condition occurs predominantly in the upper extremity and the maxillofacial region in children and young adults, although the disease has been described in patients as young as one month and as old as 77 years.³ The pathological process involves replacement of the normal bone by an aggressively
expanding angiomatous or lymphatic tissue, sometimes both.\(^5\) Pathologically, there are two stages of the disease process: the first with vascular proliferation followed by a second stage in which residual fibrous tissue replaces resorbed bone.\(^5\) Although the normal levels of serum calcium and alkaline phosphatase seen in the disease suggest lack of osteoclastic activity, recent studies showing elevated levels of IL-6\(^6\) suggest that osteoclasts do play an important role in the disease process.\(^6\)

Exclusive involvement of the femur is extremely rare. Since the first reported case of exclusive femoral involvement by Richard in 1937, only 24 cases (including our case) involving femur has been described in literature.\(^2,7\) To the best of our knowledge this is the second report of Gorham’s disease of the femur from India.\(^8\) Gorham’s disease of the femur is notorious for the propensity to have a fracture either at presentation or during the disease course. Because union is very difficult to achieve in these patients, severe disability results.

The presenting symptom of Gorham disease is localized dull aching pain, or more commonly acute pain arising after a pathological fracture.\(^7\) Occasionally, there is some soft tissue swelling. In the present case, the patient presented with a pathological fracture in a limb with chronic pain. Although the preoperative radiograph did not reveal any gross abnormality, the osteolytic process increased rapidly following the fracture. Trauma has been mentioned as a triggering factor for osteolysis.\(^9,10\) A high index of clinical suspicion is needed to arrive at an early, accurate diagnosis. The diagnosis is based on clinical examination; absence of hereditary, metabolic, infectious, immunogenic or neoplastic etiology; radiological examination and histological examination. Histological features include intraosseous growth of vessels, absence of tumor/cellular atypia, minimal or no osteoblastic response and absence of dystrophic calcification. Radiographs are the best tools for detecting vanishing bone disease.\(^11\) The initial radiological features of Gorham disease may reveal radiolucent foci in the intramedullary or subcortical regions (patchy osteoporosis). Subsequently, the characteristic picture of progressive dissolution and disappearance of a portion of the bone may occur in the absence of a sclerosing or osteoblastic reaction, soft-tissue calcification and coarse trabeculation. Magnetic resonance imaging (MRI) is especially helpful in Gorham’s disease as it clearly delineates the soft tissue component. MRI usually shows low-signal intensity on T1-weighted images, high-signal intensity on T2-weighted images, and enhancement after intravenous contrast.\(^12\)

The treatment of Gorham’s disease is controversial. Medical treatment with estrogens, magnesium, calcium, vitamin D, vitamin B12, fluoride, calcitonin, cisplatin, actinomycin D, thalidomide, somatotrophin, interferons, amino acids, placental extracts, and transfusions of placental blood have proved unsuccessful.\(^13,14\) Long-term bisphosphonates, although a therapeutic option, have not been found to have any significant effect on the disease process.\(^15\) Our patient did not show any response with bisphosphonates. Surgical treatment generally involves resection of the affected bone, with or without replacement prostheses or bone grafts.\(^8,16\) Amputation has also been done in a number of patients. Since femoral involvement is usually proximal, extending to the hip and associated with a fracture, resection and total hip arthroplasty has been the favored treatment. Diaphyseal involvement poses a challenge to the treating surgeons. The treatment of diaphyseal disease has been either amputation or radiotherapy followed by bone grafting. Despite the fact that bone grafts have been found to resorb, some studies have shown promise with fibular grafting.\(^8,17\)

Our patient had involvement of the whole femur and responded well to radiotherapy. Results obtained with radiation therapy have been equivocal, although in a few cases, apparent arrest has been produced.\(^18\) Radiotherapy acts by accelerating sclerosis of the proliferating blood vessels and prevents re-growth of these vessels which have been found to be extremely radiosensitive. The different results with radiotherapy are probably related to the different doses given. Total radiation doses up to 20 Gy have been found to be ineffective, although Fontanesi showed excellent results using a total dose of 15 Gy in a case that involved the upper extremity.\(^19\) Where a higher total dose was applied: up to 30 Gy or more, the effect was quite remarkable, as with our patient. Since the disease has been known to arrest spontaneously the exact role of radiotherapy is difficult to prove. Despite this fact, radiation therapy, especially when used early in the course of the disease, appears to be the only
accepted form of treatment with a greater chance of success and to prevent disastrous consequences resulting from rapid osteolysis. The long-term effectiveness of radiotherapy and the risk of radiation induced cancer is not known. The chances of latter seem to be very low as the dose used is same as that in juvenile angiofibroma.

This case was a clinical diagnostic dilemma, as the initial radiological picture pointed to infection. A combination of clinicoradiological findings, evolution and histological findings helped us reach the diagnosis. Due to the rarity of the condition a high index of clinical suspicion is needed to arrive at an early, accurate diagnosis. Radiation therapy early in the disease course prevents disease extension, halts the process and may even result in calcification.

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