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Case report of vanishing bone disease (Gorham's Disease) of humerus and proximal radius managed with radiotherapy

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Abstract

Gorham's Disease or massive osteolysis is one of the rare entities with unpredictable prognosis. This vanishing bone disease has predilection for femur, mandible, ribs, scapula, humerus and pelvis. Although much research has been done regarding etiopathogenesis, no conclusive evidence exists regarding single best modality for treatment. Here we present a case of 17 year old female with pain and swelling of right arm following a history of trauma 10 months back for which she was placed on U slab. Patient showed worsening of pain and swelling and gradual progression of osteolysis on follow up radiological examination. After histopathological confirmation of diagnosis, we started patient on radiotherapy in doses of 35 Gy given in 16 fractions over the period of 3 weeks which helped in arresting disease progression and to some extent improving radiological outcome evident on 1 year follow up.

Keywords: Gorham's, massive osteolysis, radiotherapy

1. Introduction

Though medical science has advanced to a level where it can solve many complex genetic issues, some mysteries are still unsolved. The Vanishing bone disease which is also known as Gorham - stout disease or massive osteolysis disease is one of the rare bone diseases characterized by massive resorption of osseous matrix with proliferation of vascular channels. It was first described by Gorham and colleagues in 1954 which was presented later in detail by Gorham and stout [1, 2]. The mechanism for aetio pathogenesis is still unclear despite lapse of more than 50 years.

To date, Various hypothesis has been postulated to describe aetiopathogenesis. Gorham and stout hypothesized that trauma may trigger the process of stimulating the production of vascular granulation tissue and bone resorption may be due to local hyperaemia and change in local pH [2]. Devlin and colleagues has postulated that increase in osteoclastic activity is responsible for bone resorption [3]. Moller and associates supported the findings of Devlin [4]. Heyden and colleagues observed strong activity of acid phosphatase and leucine aminopeptidase in mononuclear perivascular cells which is responsible for bone resorption [5]. Hirayama and colleagues reported that bone resorption is not due to increase in osteoclast precursor but due to their increase sensitivity to humoral factors that promote osteoclast formation [6].

This syndrome is considered as the type IV of osteolysis, according to Hardegger *et al* [7], among five types:

Type I is hereditary multicentric osteolysis with dominant transmission

Type II is hereditary multicentric osteolysis with recessive transmission.

Type III is nonhereditary multicentric osteolysis with nephropathy and

Type V is Winchester syndrome, defined as a monocentric disease of autosomal recessive inheritance [7].

GSD may affect one or more, often contiguous, bones with predominant sites of manifestation including the pelvis, shoulder girdle, spine, ribs, and skull. Diagnosis is based on clinical, laboratory, radiological, and histopathological findings.

2. Case Presentation

A case of 17 year old female presented with complaint of pain and swelling over right arm following a fall 10 months back. Consequently she sustained a closed shaft humerus fracture and was kept in U slab with limb immobilization for 2 months. On examination, there were no scars or sinuses over affected limb. There was diffuse swelling involving whole right arm. On palpation, tenderness was present over right arm and forearm without rise of local temperature. Range of motion was painful at shoulder and elbow joint. She also had wrist drop with loss of sensation in radial nerve distribution. Her past medical history was unremarkable.

Plain radiographs revealed progressive massive osteolysis involving whole of right humerus extending upto right elbow joint (Fig.1 & 2). Proximal right radius and ulna also showed patchy bone destruction sparing articular surfaces (Fig. 3).

MRI shows sign of Muscle isointense signal showing proliferation of fibrous tissue at the bony defect. The normal high intensity marrow signal is seen only in the proximal and distal remnants of humerus (Fig. 4). Histology of open true cut biopsy shows Benign vascular proliferation with fatty bonemarrow and thinning of bony trabeculae which is replaced by abundant proliferating vascular channels (Fig. 5)

Haematological investigations and biochemical profile including serum alkaline phosphatase levels were all normal. As the patient had generalised swelling of right upper limb, a duplex scan was performed in order to exclude a vascular cause for oedema. It revealed multiple abnormal hypoechoic vascular channels which displayed flow in the power doppler mode only. This was followed by CT angiography which revealed normal deep arterial and venous systems.

Based on clinical, radiological and histological findings, diagnosis of Gorhams-Stout disease was made. Patient was started on radiotherapy in doses of 35 Gy in 14 fractions over 3 weeks. Pain and swelling subsided gradually and there was evidence of increase in cortical density of bone on 1year follow up. (Fig.6)

3. Discussion

Though GSD had been mentioned of benign character, its prognosis is unpredictable [8]. GSD can affect any age group and there isn't any epidemiological correlation between race, gender and geography. While GSD has been reported throughout the body, commonly involved sites include the mandible (15%), ribs (12%), scapula (10%), humerus (8%), pelvis (10%), and femur (11%) [9], recently Hu *et al* [10] reported femur as a predominant affected bone. The clinical presentation of a patient mainly shows pain, swelling and functional impairment of affected region. Due to destructive nature of disease, complications are usually fatal.

Radiographically, Gorham's disease progresses through four stages. The disease initially presents as radiolucent foci resembling patchy osteoporosis. Next, bony deformity increases with further loss of bone mass. The cortex is then disrupted with endothelial invasion into adjacent soft tissues and/or across joints. Finally, there is shrinkage of the ends of affected bones producing a "sucked candy" appearance [11].

The disease is confirmed by the histopathological analysis of the lesions. Heffez *et al* [12] suggested the following 8 diagnostic criteria of Gorham-Stout syndrome: (1) positive biopsy findings in terms of angiomatous tissue presence; (2) absence of cellular atypia; (3) minimal or no osteoclastic response and absence of dystrophic calcifications; (4) evidence of local bone progressive resorption; (5) non-expansive, non-ulcerative lesion; (6) absence of visceral involvement; (7)

osteolytic radiographic pattern; and (8) negative hereditary, metabolic, neoplastic, immunologic and infectious aetiology.

As the pathogenesis of GSD is unclear, none of the treatment modality is fully reliable [10]. Till date, both medical as well as surgical line of management is under evaluation. Bisphosphonate has shown positive results [13, 16] along with alpha 2 interferon treatment [14, 15, 16]. The effectiveness of anti-angiogenic drugs like bevacizumab has also been tried earlier with good success rate [17]. Surgical resection of diseased tissue with or without bone grafts along with radiation therapy [18] is getting positive feedbacks. Treatment is mainly directed towards specific symptoms. There has been reported cases of spontaneous resolution of disease [9, 19].

In our patient, we started radiotherapy in doses of 35 Gy given in 16 fractions over the period of 3 weeks which helped in arresting disease progression evident on 1 year follow up. There was marked subsidence in pain and swelling. Early use of radiation therapy may arrest endothelial cell proliferation, and thereby limit the spread of disease and allow the patient to avoid relatively complicated surgery with its inherent risks [18, 20] Radiation therapy may also be used successfully in patients who are poor surgical candidates or patients who have failed surgical treatments. Dunbar and colleagues concluded that doses of 40–45 Gy at 1.8 Gy to 2 Gy per fraction produce a good outcome in a high proportion of patients with minimal long-term complications [18]. Choma *et al.* in 1987 identified 18 cases of Gorham's disease treated with radiotherapy, 11 of whom showed arrest or improvement of their disease and 5 with demonstrated regrowth of bone [9]. The major disadvantage to using radiation therapy for Gorham's disease is the possibility for acute and long-term side effects that vary by treatment, the potential for secondary malignancy and growth restriction should be considered before administering high-dose radiation therapy to children, who represent a significant proportion of Gorham's disease patients.

4. Conclusion

Gorham's disease although rare, yet should be considered in differential diagnosis of osteolytic metastasis or primary lesion, osteomyelitis, multiple myeloma. Though many modalities of treatment have been described historically including megaprosthesis, yet radiotherapy can prove to be beneficial in subsidence of symptoms and improving radiological outcome.

Figure Legends



Fig 1: Image of right humerus 5 months after trauma.



Fig 2: Image of right humerus 10 months after trauma.



Fig 3: Image of right radius-ulna 10 months after trauma.

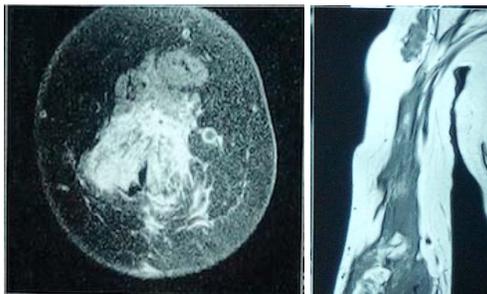


Fig 4: MRI picture of Right humerus

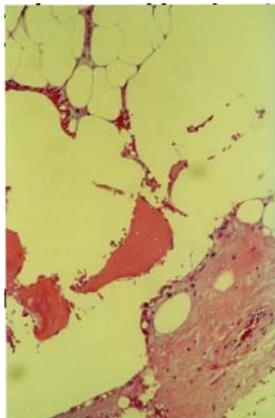


Fig 5: Histopathological examination finding.



Fig 6: Image of right humerus 1 year after radiotherapy.

There is no conflict of interest.

5. References

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