Gorham's: Vanishing bone disease of arm

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ABSTRACT

Vanishing bone disease is a rare disorder of the musculoskeletal system reported first in 1938 by Jackson and later described by Gorham and Stout. Since then, about 200 cases of this disorder have been reported. Much research has been done regarding etiopathogenesis, yet no conclusive evidence exists regarding the single best treatment modality. We present the case of a 55-year-old female with complaints of pain and swelling of the left arm and a history of trauma 1 year ago, for which she underwent open reduction and internal fixation. The pain and swelling persisted on follow-up. She had progressive osteolysis as well as the absence of osteoblastic reaction on imaging. After histopathological diagnosis, the patient started bisphosphonate, calcium, and Vitamin D3, but in view of severe pain and high proliferative index, she was treated with radiotherapy to the left arm. The case is being reported for its rarity and scarcity in the literature for defined treatment.

Key words: *Gorham-Stout disease, Radiotherapy, Vanishing bone disease*

Vanishing bone disease (VBD) is a very rare disorder characterized by the uncontrolled proliferation of vascular or lymphatic capillaries within the bone and surrounding soft tissue [1]. While VBD has been reported throughout the body, commonly involved sites include the mandible (15%), ribs (12%), scapula (10%), humerus (8%), pelvis (10%), and femur (11%) [2]. The patient chiefly presents with pain, swelling, and functional impairment of the affected region. Due to the destructive nature of the disease, complications are usually fatal. The etiopathogenesis is still unclear despite the lapse of more than 50 years since the first report in 1938.

About 200 cases have been described till date and various hypotheses have been postulated for etiopathogenesis. 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 hyperemia and change in local pH [3]. This report proves to be an addition to the already sparse literature available for Gorham-Stout disease which might help in the establishment of standard clinical practices for the management of VBD.

CASE REPORT

A 55-year-old woman presented with complaints of pain and swelling over the left arm following the history of trauma 1 year ago sustaining a fracture of the left humerus, for which she underwent open reduction and internal fixation.

At the presentation to the radiation oncology department, the patient's pulse was 104/min at the left radial artery (all peripheral pulses and left axillary pulse were palpable), blood pressure was 136/90 mmHg at the right brachial artery, and the jugular venous pressure was not raised. The patient was afebrile with a respiratory rate of 16/min. On general examination, there were no pallor, icterus, cyanosis (central/peripheral), clubbing, or lymphadenopathy.

The patient was conscious, well-oriented to time place and person, higher functions were intact. Bilateral chest air entry was clear with no added respiratory sounds; S1 and S2 were heard with no murmur. Abdomen was soft, non-tender with no palpable mass or organomegaly. On local examination, an old healed surgical scar of approximately 8–9 cm was seen on the middle third of the left arm. On palpation, tenderness was present over the lateral aspect of the middle third of the left humerus without a rise of local temperature. The range of motion at the shoulder was painfully restricted.

Hematological investigation and biochemical profile including serum alkaline phosphatase and parathyroid hormone level were normal. The radiological examination (Fig. 1) of the left arm revealed a healed fracture of the shaft of the humerus with multiple progressive osteolysis as well as the absence of osteoblastic reaction and new bone formation in the shaft of the humerus. X-rays and pelvis showed no abnormality. Bone scintigraphy with technetium 99m displayed increased tracer perfusion in the middle portion of the shaft of the left humerus. Tc-99m methoxyisobutylisonitrile tumor imaging revealed increased uptake. The consistency of this tissue was gritty and vascular.

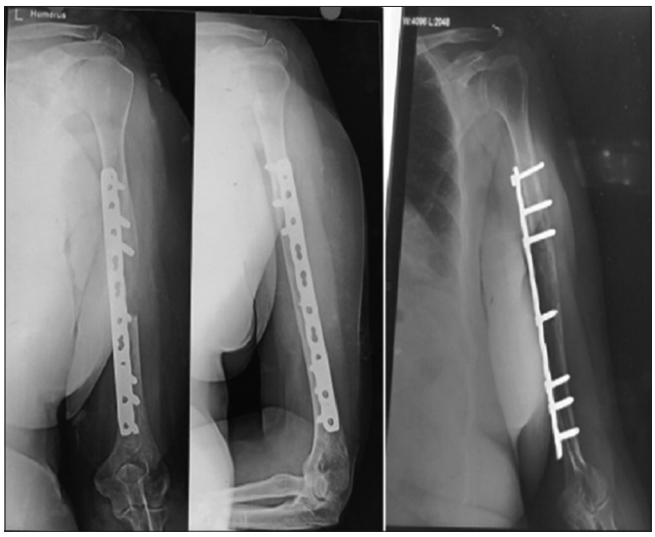

Figure 1: Radiographs showing pathological fracture of the left humerus and fixation done for the same

The histopathological examination (Fig. 2) of the left humerus biopsy revealed fibroblastic hyperproliferation admixed with a few large atypical cells with the absence of cellular atypia. Mitotic figures were 6–7/10 high-power field. On immunohistochemical staining, CD 31 and D2-40 were positive and Ki67 was 60%. Findings were consistent with the VBD.

After histopathological diagnosis, we started on bisphosphonate, calcium, and Vitamin D3. There was paucity in the literature for definitive treatment; hence, the tumor board decided for external beam radiotherapy (EBRT) in view of severe pain and high proliferative index. She was treated with external beam radiation of 50 Gy in 25 fractions at 2 Gy per fraction over a period of 5 weeks. Pain and swelling were relieved till the last follow-up about 12 months following the radiotherapy. There has been no progression in lesions so far.

DISCUSSION

VBD is a rare benign musculoskeletal disorder with an unpredictable prognosis [1]. Its diagnosis is usually delayed and often missed. In 1838, Jackson first described the case of a patient with a "boneless arm" [4]. In 1955, Gorham and Stout described the clinical, anatomical, and pathological features of the Gorham and Stout disease. They described the invasion of the bone by lymphangiomatous tissue, leading to progressive massive osteolysis [5].

Gorham-Stout syndrome can affect any age group and there is not any epidemiological correlation between race, gender, and geography. Although the etiology of VBD is unknown, there are many hypotheses such as post-traumatic hyperemia, changes in blood pH, hypoxia, unrestricted growth of granulation tissue, and endothelial cell-mediated absorption of the bone matrix [6]. Hu *et al*. conducted a study on six cases of Gorham-Stout syndrome with histopathological examination findings suggested that osteolysis is due to an increased number of stimulated osteoclasts [7]. In our case report, trauma may have acted as a triggering factor in the development of VBD. The usual presentation of VBD includes pain, swelling, and functional impairment of the affected regions which can also be seen in our case.

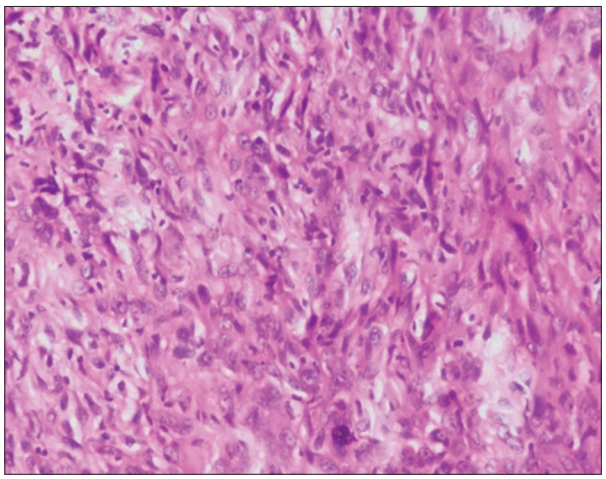

Figure 2: H and E stained section revealed fibroblastic hyperproliferation admixed with a few large atypical cells (×200)

VBD is a poorly understood disorder of abnormal lymphovascular proliferation resulting in a localized bone loss, usually painless unless complicated by a pathological fracture and usually involving the femur, proximal humerus, shoulder girdle, pelvis, skull, and mandible [8]. In our case, the patient had developed a pathological fracture that had to be fixed.

Diagnosis is based on radiological, biochemical, and histopathological investigations. Hammer *et al*. suggested the following eight diagnostic criteria of VBD: (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 etiology [9].

Various modalities have been employed for the treatment of VBD. Bisphosphonate has shown positive results [10] along with alpha-2 interferon treatment [11]. Surgical resection of the diseased tissue with or without bone grafts along with radiotherapy is getting positive feedback. Radiation therapy either in an adjuvant setting or as a sole modality is suggested by many authors. Early use of radiotherapy may arrest endothelial cell proliferation and thereby limit the spread of disease and allow the patient to avoid complicated surgery with its inherent risks [12]. Due to the limited availability of the literature regarding the entity, treatment has not been established. Some authors have advocated excision with strut grafting/prosthesis; others advocate medical management in the form of antiresorptive therapy such as bisphosphonate and radiation therapy.

For patients with VBD, radiation therapy can be used successfully in patients who are poor surgical candidates or those who have failed in surgical treatment [13,5]. Escalating doses of radiation therapy to treat Gorham's disease help in the eradication of radiosensitive proliferating endothelial cells. Clones derived

from remaining viable cells are spaced too irregularly to form an occlusive vessel. Moderate doses of 25–45 Gy have been reported as effective [14]. Dunbar *et al*. reviewed 22 published cases of Gorham's disease treated with radiotherapy before 1993 and concluded that doses of 40–45 Gy at 1.8 Gy–2 Gy per fraction produced a good outcome with minimal long-term complications in a large proportion of patients. Radiation therapy was successful in 14 of the 22 patients (64%) described in their review.

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 five with demonstrated regrowth of bone [2]. Radiation doses of 30–45 Gy fractionated into 2 Gy or less can stop disease progression, especially if delivered in early stages, and provide for pain relief [13]. The mechanism of the action of radiation is probably the death of the active proliferating endothelial cells that lead to the arrest of bone replacement and relief of the lymphatic obstruction [14]. Our patient was treated with external beam radiation of 50 Gy in 25 fractions at 2 Gy per fraction over a period of 5 weeks. She is on regular follow-up and currently progressive free at 12 months after EBRT.

CONCLUSION

In a patient presenting with progressive massive osteolysis, Gorham's-Stout disease, although rare, should be considered as a differential diagnosis of osteolytic metastasis, osteomyelitis, and multiple myeloma. Apart from surgical and medical management, EBRT has shown benefit in controlling symptoms and delaying progression.

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