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Vanishing Bone Disease: A Review

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Vanishing bone disease, or Gorham disease, was first defined as a specific entity by Gorham and Stout[1] in 1955; it is a rare disorder characterized by proliferation of vascular channels, which results in destruction and resorption of osseous matrix. Only a few cases have been reported in the jaws. Vanishing bone disease or massive osteolysis of the lower jaw will initially affect the mandibular basal and alveolar bone, which subsequently involves the rami and the condyles. The etiology remains speculative, the prognosis is unpredictable, and effective therapy has still not been determined. The purposes of this review are to make our community aware of this rare entity and to discuss the etiopathology, clinical presentation, radiographic findings, differential diagnoses, and treatment modalities for patients with vanishing bone disease.

Numerous names have been used in the literature to describe this condition, such as phantom bone,[1] disappearing or vanishing bone disease,[2] acute spontaneous absorption of bone,[3] hemangiomatosis, lymphangiomatosis,[4] idiopathic osteolysis,[5] and Gorham disease. It is characterized by the spontaneous and progressive destruction of one or more of the skeletal bones. Idiopathic osteolysis was described first in 1838[6] and again in 1872[7] by Jackson, who reported a case of a "boneless arm." Romer[8] reported the first case in the jaws in 1924, in a 31-year-old woman. In 1954 Gorham et al[9] reported on 2 patients with massive osteolysis of the bone. One was a boy, aged 16 years, with right clavicle and scapula involvement. Chylothorax eventually developed, and the patient died. The other patient was a man, aged 44 years, who also had involvement of the right clavicle and scapula. In addition, these authors provided a brief review of 16 reported cases from the literature. In 1955 Gorham and Stout[1] provided a more comprehensive report on this subject. Gorham disease is usually associated with angiomatosis of blood vessels and sometimes of lymphatic vessels, which seemingly are responsible for it. The etiology of this disease remains unknown, although an initial trauma or modifications of local conditions, such as variation of pH and inflammation, are suspected.

Histologically, bone is replaced by an abundance of thin-walled capillary-sized vascular channels and, at a later stage, by fibrous connective tissue.[10] Any bone can be affected, although there is a predilection for the pelvis, humerus, axial skeleton, and mandible. In the lower jaw, the mandibular basal and alveolar bone is initially affected and the rami and the condyles are subsequently involved.

Etiopathology

To date, the exact etiology and nature of the disease process remain undetermined. The pathologic process is the replacement of normal bone by an aggressively expanding but non-neoplastic vascular tissue,[11,12] similar to a hemangioma or lymphangioma. Wildly proliferating neovascular tissue causes massive bone loss. In the early stage of the lesion, the bone undergoes resorption and is replaced by hypervascular fibrous connective tissue and angiomatous tissue. Histologically, involved bones show a nonmalignant proliferation of thin-walled vessels; the proliferative vessels may be capillary, sinusoidal, or cavernous. In late stages there is progressive dissolution of the bone leading to massive osteolysis, with the osseous tissue being replaced by fibrous tissue. The stimulus that generates this change in the bone is unknown.[12]

One main structural feature of the lesion is the presence of unusually wide capillary-like vessels, and therefore it is likely that the blood flow through these vessels is slow. It has been suggested that the slow circulation produces local hypoxia and lowering of the pH, favoring the activity of various hydrolytic enzymes.[13] There is strong activity of both acid phosphatase and leucine aminopeptidase in mononuclear perivascular cells that are in contact with remaining bone, perhaps indicating that these cells are important in the process of osseous resorption.[13]

Gorham and Stout[1] reported that active hyperemia, changes in local pH, and mechanical forces promote bone resorption. They hypothesized that trauma may trigger the process by stimulating the production of

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vascular granulation tissue and that "osteoclastosis" is not necessary. In contrast, Devlin et al[12] have suggested that bone resorption in patients with Gorham disease is due to enhanced osteoclast activity and that interleukin 6 may play a role in the increased resorption of bone. Moller et al[14] reported 6 cases of Gorham-Stout syndrome with histopathologic findings and presented evidence that osteolysis is due to an increased number of stimulated osteoclasts.

Hirayama et al[15] have reported on the cellular and humoral mechanisms of osteoclast formation and bone resorption in patients with Gorham-Stout syndrome. They suggested that the increase in osteoclast formation in Gorham-Stout syndrome is not due to an increase in the number of circulating osteoclast precursors but rather is due to an increase in the sensitivity of these precursors to humoral factors, which promote osteoclast formation and bone resorption. It has also been suggested that thyroid C cells and calcitonin may play an important role in the pathogenesis of Gorham disease.[16]

The disease can be monostotic or polyostotic, although multicentric involvement is exceptional. No ethnic or gender predilection has been noted.[17] The disease appears to be nonhereditary and is most common in children and young adults, but it has been described in patients aged up to 70 years or older. In 30% of cases maxillofacial involvement is seen with pain, malocclusion, and deformity.[18]

Clinical Features

Most cases occur in children or in adults aged less than 40 years. However, the disease has been described in patients aged as young as 1 month[19] to as old as 75 years.[20] Approximately 60% of all cases with vanishing bone disease occur in men.[21] The bones of the upper extremity and the maxillofacial region are the predominant osseous locations of the disease. More than 200 cases of vanishing bone disease have been reported in the literature. The process may affect the appendicular or axial skeleton. Cases have been reported in the skull (8 cases), maxillofacial region (42 cases), spine (18 cases), pelvis (18 cases), trunk (including clavicle and ribs) (35 cases), upper extremity (including scapula) (41 cases), and lower extremity (22 cases), in addition to multicentric involvement (11 cases).[22]

The mandible was affected alone by the osteolysis, partially or completely, in 23 cases, whereas the maxilla was never involved alone. Fourteen cases have been reported that involved multiple contiguous bones of the head, which represents a more advanced stage of the disease.[23]

Clinical manifestations vary and depend on the affected site. Some patients present with a relatively abrupt onset of pain and swelling in the affected area, whereas others present with a history of insidious onset of pain in the involved jaw. Pain is moderate, continuous in nature, and radiating to the left side of the face and neck. A history of swelling may or may not be present. The skin in the involved area could be clear without hemangiomas or edema and no sign of infection or pus discharge. The medical, personal, and family histories are usually noncontributory.

Although the degree of osseous deformity in patients with massive osteolysis may become severe, serious complications are infrequent. Paraplegia related to spinal cord involvement may occur in patients who have involvement of vertebrae.[24] Thoracic cage, pulmonary, or pleural involvement can lead to compromise of respiratory function, and death can ensue. Infection of bone and septic shock, though rare, have also been reported.[10]

Investigations

The standard laboratory blood tests are usually within normal limits and are not helpful to make a diagnosis of massive osteolysis. The serum alkaline phosphatase level may be slightly elevated.

Plain radiographs,[25,26] radioisotope bone scans,[27] computed tomography,[28] and magnetic resonance imaging (MRI)[29] have all been used.

Radiographic findings in patients with Gorham disease were described by Resnick.[30] During the initial stage of the lesion, radiolucent foci appear in the intramedullary or subcortical regions, resembling findings seen in patchy osteoporosis. Subsequently, slowly progressive atrophy, dissolution, fracture, fragmentation, and disappearance of a portion of the bone occur with tapering or "pointing" of the remaining osseous tissue and atrophy of soft tissues.

A panoramic radiograph can be advised. There will be resorption and decreased vertical height of the mandibular body with the resorption extended toward the basal bone.

Radioisotope bone scan may show increased vascularity on initial images and, subsequently, an area of decreased uptake corresponding to the site of diminished or absent osseous tissue. However, these results have been variable.[32] The reported MRI findings of Gorham osteolysis have also been variable. T1-weighted spin echo MRI shows uniformly low signal intensity in the involved bones, whereas an increased signal intensity generally is observed on T2-weighted spin echo images. Enhancement of the lesions is usually seen after intravenous administration of gadolinium (Figs 1–4).

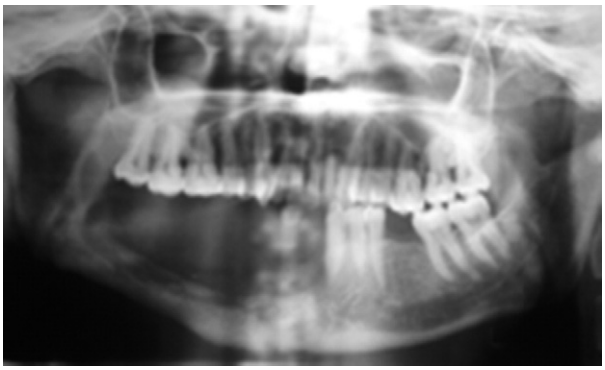

FIGURE 1. Panoramic radiograph showing missing teeth in right quadrant, resorption, and decreased vertical height of right mandibular body with bone resorption extending to mesial aspect of left canine.[31]

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Differential Diagnosis

After a thorough history and meticulous physical examination, appropriate blood investigations and radiographic studies are needed to rule out other common underlying causes of osteolysis, such as infection, cancer, and inflammatory or endocrine disorders. The diagnosis of Gorham-Stout syndrome should be suspected or made only after excluding these aforementioned conditions.[31] Aneurysmal bone cyst, extensive metastatic bone disease due to carcinoma of the breast, and osteosarcoma are some of the diseases that resemble vanishing bone disease and can be confirmed with a biopsy report.

Treatment

Given the rarity of this disease entity, there is no standard therapy available. The medical treatment for Gorham disease includes radiation therapy,[33] anti-osteoclastic medication (bisphosphonates), and alfa-2b

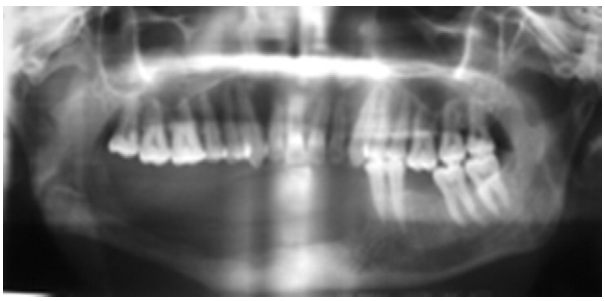

FIGURE 2. Panoramic radiograph taken 3 months after initial panoramic radiograph showing progressive resorption of right mandibular body and loss of bone, encroaching on mandibular canal space.[31]

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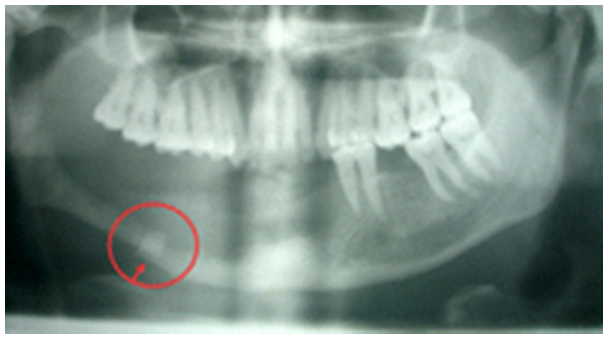

FIGURE 3. Panoramic radiograph taken 4 months after initial panoramic radiograph, with an *arrow* pointing toward fracture in right mandibular body with overriding fragments and osteolysis extending onto angle and ramus with resorption of coronoid process.[31]

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interferon.[34] The principal treatment modalities are surgery and radiation therapy. Surgical options include resection of the lesion and reconstruction by use of bone grafts and/or prostheses. Definitive radiation therapy in moderate doses (40-45 Gy in 2-Gy fractions) appears to result in a good clinical outcome with few long-term complications.[35] In children and adolescents who receive high-dose radiation therapy, the potential for secondary malignancy and growth restriction exists and should be considered before embarking on this mode of treatment. The prognosis for patients with Gorham disease is generally good unless vital structures are involved.

Discussion

The term used by Gorham and Stout[1] was "haemangiomatosis," implying a proliferative process. According to Gorham and Stout, the most characteristic histologic abnormality in massive osteolysis is the

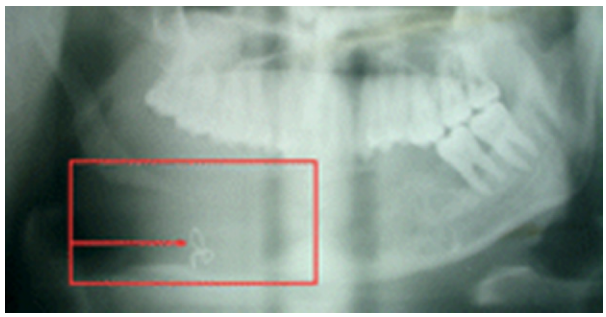

FIGURE 4. Panoramic radiograph taken 5 months after initial panoramic radiograph showing dramatic absence of bone from symphysis region to right condyle region, with *arrow* pointing to transosseous wiring seen floating in soft tissues and decrease in height of left mandibular body region.[31]

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change of bone into connective tissue. This connective tissue contains many thin-walled vessels, sometimes with red blood cells. In other areas, freely anastomosing vascular spaces lined by endothelial cells can be seen. The fatty marrow also contains some dilated blood vessels. Johnson and McClure[36] in 1958 reported on the relative frequency of massive osteolysis in different bones. The sequence is as follows: clavicle, scapula, proximal end of humerus, ribs, iliac bone, ischium, and sacrum. The disease has not been observed in the calvaria or in the distal bones of the extremities. The monostotic form occurs more frequently than the polyostotic form. In general, the patient is young, and both genders are equally affected. The process is painless: it starts suddenly, progress is rapid, and finally, the bone is replaced by a thin layer of fibrous tissue surrounding a cavity. Despite this, the function of the extremity is good. Laboratory findings are normal.[36]

Heffez et al[37] suggested 8 criteria for definitive diagnosis of massive osteolysis:

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, nonulcerative lesion
6. Absence of visceral involvement
7. Osteolytic radiographic pattern
8. Negative hereditary, metabolic, neoplastic, immunologic, and infectious etiology

Several therapeutic modalities have been used in the management of massive osteolysis. The nonoperative options include radiation therapy,[33] anti-osteoclastic medication (bisphosphonates), and interferon alfa-2b.[34] The operative options include surgical resection[33,35] and reconstruction by use of a bone graft[38] or prosthesis.[39,40] The success rate after the use of a bone graft is low. Most surgeons, based on their personal experience, have observed that the bone graft undergoes dissolution. In recent years, most patients have been treated with surgery and/or radiation therapy.[41]

Massive osteolysis is a rare, peculiar musculoskeletal disorder in which the affected bone virtually disintegrates and is replaced by vascular fibrous connective tissue. The etiology of massive osteolysis is still speculative. Its clinical presentation is variable, largely depending on the site of skeletal involvement. The history and prognosis of this disease are unpredictable, and no effective therapy is known. In recent years, most patients have been treated with surgery and/or radiation therapy.

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