Massive osteolysis of the skull and upper cervical spine

Case report and review of the literature

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Massive osteolysis is a type of idiopathic osteolysis in which there is spontaneous onset of bone resorption. Almost any bone in the body can be affected. The authors present the case of a 62-year-old man diagnosed with massive osteolysis of the occipital bone and the upper two cervical vertebrae. Despite extensive pneumocephalus, no neurological sign or spinal instability was evident. In this case 4000 cGy of radiation in 200-cGy fractions was administered to the diseased area while the patient was kept in a Miami-J collar. At the 2-year follow-up examination, arrest of the disease process and new bone formation was evident on radiographic studies.

KEY WORDS • massive osteolysis • Gorham’s disease • lytic bone lesion

JACKSON reported the first case of massive spontaneous absorption of bone in a patient with a boneless arm. This form of osteolysis, which is characterized by spontaneous onset of rapid destruction and resorption of bone with no known cause, appeared to be different from the other types of osteolytic processes known at the time. In 1955 after reviewing the literature, Gorham and Stout established this type of osteolysis as a distinct clinical, radiological, and pathological entity. Subsequently, it became known as Gorham’s massive osteolysis or “Gorham’s disease.” However, examples of this entity have been published in which various other descriptive terms have been used: vanishing bone disease, disappearing bone, phantom bone, lymphangioma of bone, hemangioma of bone, cryptogenic osteolysis, spontaneous resorption of bone, essential osteolysis, acute spontaneous absorption of bone, progressive atrophy of bone, hemangiomatosis, and lymphangiectasis.

More than 100 cases of Gorham’s disease have been reported in the literature. These include eight cases involving only the calvaria, five cases involving the cervical spine, and four cases involving the skull base and upper cervical spine. One of the cases involving the skull base and cervical spine was related to a history of trauma. In this paper we describe a second case of Gorham’s disease involving the skull base and cervical spine that was related to a history of trauma. Classification of idiopathic osteolysis and the role of conservative management of Gorham’s disease in the area of craniovertebral junction are also discussed.

Case Report

History and Examination. This otherwise healthy 62-year-old retired steel worker was evaluated for mild head trauma in February 1994 and was found, on lateral skull x-ray films, to have an extensive lytic lesion involving the occipital bone (Fig. 1). The patient had sustained previous blunt trauma to the occiput 4 months earlier. Two months after the injury, he developed persistent occipital headaches. He had no other neurological or systemic signs or symptoms. Subsequently, a biopsy specimen of the lytic skull lesion was obtained. The pathological findings were consistent with benign fibrous tissue, having areas of prominent blood vessels. No definitive diagnosis was made, and the patient was referred to our institution for further evaluation.

Laboratory and Radiographic Findings. The results of laboratory studies including serum calcium, phosphate, and alkaline phosphatase were normal. Results of serum and urine electrophoresis and bone marrow biopsy were also normal. Nonenhanced axial computerized tomography (CT) scanning of the head and upper cervical spine with three-dimensional reconstruction showed a focal, infiltrative lytic lesion involving the occipital bone and
C1–2 (Fig. 2). Cranial magnetic resonance (MR) imaging revealed mildly enhancing epidural soft tissue (Fig. 3). Skeletal scintigraphy did not show any abnormal uptake of radionuclide.

Operation. The patient underwent an additional open suboccipital skull biopsy in April 1994. The skull was friable and soft with involvement of all three tables. Granulation tissue and scarring were present in the epidural space.

Pathological Findings. Hematoxylin and eosin–stained sections revealed fragments of sparsely cellular, fibrous tissue with prominent thin-walled small blood vessels, suggestive of hemangioma interspersed with fragments of mature and reactive bone. There was no inflammatory infiltration or evidence of malignancy (Fig. 4).

Diagnosis, Treatment, and Outcome. Based on the clinical presentation and pathological findings, the patient was believed to have Gorham’s disease. Over a 4.5-week period he received a total of 4000 cGy of radiation in 200-cGy fractions to the occipital bone and C1–2, during which time he wore a Miami-J collar. After radiation therapy, the patient’s headaches resolved, although he had difficulty tilting or rotating his head. At the 2-year follow-up evaluation, cranial CT scanning showed reversal of the disease process with new bone formation (Fig. 5) and resolution of the pneumocephalus.

Discussion

Classification of the Disease and Diagnostic Criteria

Massive osteolysis used to be considered to consist of two types:12,40 Gorham’s disease and angiomatosis (hemangiomatosis or lymphangiomatosis) with massive osteolysis. Current opinion holds that angiomatosis with massive osteolysis is not a primary bone disease but rather a separate entity in which vascular proliferation is the cause of the osteolysis; bone hemangiomas and systemic lymphangectasis are examples. Angiomatosis with massive osteolysis stands in contrast to the idiopathic form of mas-
ies. In 1983, Heffez, et al.\textsuperscript{23} presented eight diagnostic criteria for the diagnosis of Gorham’s disease: 1) a biopsy specimen consistent with angiomatous (hemangiomatous or lymphangiomatous) tissue; 2) absence of cellular atypia; 3) minimal or no osteoblastic response and absence of dystrophic calcification; 4) evidence of local progressive osseous resorption; 5) nonexpansive, nonulcerated lesion; 6) absence of visceral involvement; 7) osteolytic radiographic pattern; and 8) no history of hereditary, metabolic, neoplastic, immunological, or infectious etiology. Thus the diagnosis is primarily a diagnosis of exclusion.

We used these criteria and the classification by Hardegger and colleagues\textsuperscript{22} for idiopathic osteolysis in extracting cases from the English literature of Gorham’s disease or Gorham’s massive osteolysis involving single lesions of the calvaria, the cervical spine, and the skull base in conjunction with the upper cervical spine.

**Pathogenesis of the Disease**

The patient age at the onset of this disease has been reported to be from 18 months to 71 years, with a peak in the second and third decades. Males may be more often affected. There is no predilection for a particular race or ethnic group. Any bone in the body can be affected, although the clavicle, scapula, humerus, rib, and pelvis are most commonly involved. The skull is rarely involved, the first case being reported by Iyer and colleagues\textsuperscript{29} in 1975. These authors also reported the first case of skull involvement with cerebrospinal fluid (CSF) rhinorrhea.\textsuperscript{28}

The disease is almost always focal, either confined to a single bone or, more frequently, extending by direct spread to a number of contiguous bones. If skin and/or soft-tissue involvement is present, it is adjacent to the bony lesion.\textsuperscript{17,20,43} In the early stages of the disease, there may be soft-tissue swelling overlying the involved bone. In the later stages, there will be lack of bone. The bone erosion itself is a painless process, but bone pain can arise from pathological fractures. The course of this disease is rapid progression and, in a majority of cases, results in complete resorption of the involved bone(s). Although the disease can arrest spontaneously, it is unpredictable and the stimulus that is responsible for its arrest is not known. New bone formation with ossification typically does not occur after arrest.\textsuperscript{20}

On gross examination, the affected bone appears osteoporotic with a soft, spongy texture. Some authors have described a milky or clear fluid oozing from the bone at the time of biopsy or excision.\textsuperscript{14,20,39} Histological investigation has shown no prominence of osteoclastic or osteoblastic activity. Inflammatory cell infiltration is also absent within the bone. The lesion is associated with non-neoplastic proliferation of thin-walled endothelium-lined capillaries or sinusoidal vascular channels. According to Johnson and McClure\textsuperscript{31} capillary proliferation is seen only in the early stages and fibrosis occurs in the latter stages of the disease. In the calvaria, all three tables can be involved.\textsuperscript{26,29} In the majority of cases, the dura is not invaded and remains intact. There may be reactive inflammatory changes on the surface of the dura in addition to a buildup of dense epidural connective tissue.

The cause of Gorham’s disease is unclear. Hornig and Beatty\textsuperscript{26} reported the first two cases in which Gorham’s massive osteolysis in the skull was thought to be the result of trauma. Leriche\textsuperscript{24} proposed posttraumatic hyperemia as the mechanism leading to an excessive and overshooting type of Sudeck’s atrophy. Although half of all patients
have a history of trauma, it is not clear if trauma is the cause.

The mechanism of bone resorption in Gorham’s disease still needs to be determined. Hambach and colleagues have suggested that there is an underlying inborn metabolic defect, a notion supported by Chai, et al., who observed the occurrence of the disease in a young patient. Halliday, et al., have postulated that, because some patients have synchronous skin hemangiomas, there must be an underlying congenital vascular defect. Gorham and coworkers have postulated that an angioma might act as a shunt, increasing local oxygen tension, which leads to bone resorption. Of the many mechanisms identified to be involved in bone resorption, one proposed chemical pathway is through release of organic acids together with enhanced biosynthesis and release of many lysosomal enzymes. Heyden, et al., and Dominguez and Washowich noted strong acid phosphatase and leucine aminopeptidase activity in perivascular mononuclear cells, suggesting that these cells may participate in the resorptive process. Dickson, et al., presented histochemical findings that showed mononuclear phagocytes, osteoclasts, and endothelial cells to have acid phosphatase activity in slices of tissue removed from a patient. Naranjo and coworkers found alkaline phosphatase in the serum and hydroxyproline in the urine of Gorham’s patients, suggesting progressive bone destruction and an underlying metabolic disorder affecting bone replacement. At a cellular level, factors such as collagen degradation products activate osteoclasts that mediate bone resorption. Choma, et al., reported an increase in osteoclasts at the interface between vascular channels and cortical bone. Hornig and Beatty suggested that minor trauma can precipitate an osteolytic lesion by triggering a nonspecific inflammatory reaction involving the periosteum. Thompson and Schurman proposed that the disease was caused by unrestricted growth of granulation tissue, which exerts pressure and atrophy.

Radiographic Studies

Four stages of radiographic findings have been described for Gorham’s disease: 1) early changes in intramedullary and subcortical radiolucent foci resembling nondescript patchy osteoporosis; 2) concentric shrinkage of bones creating an appearance that resembles a “licked stick of candy”; 3) complete resorption of involved structures unless there is spontaneous arrest; and 4) progression of the osteolysis to nearby bones, without sclerosing or osteoblastic reaction. Computerized tomography scanning is useful in defining the degree of osteolysis, and contrast enhancement does not show uptake. Magnetic resonance imaging of Gorham’s disease was first reported by Dominguez and Washowich in 1994. According to these authors, conventional spin-echo MR imaging sequences reveal the disappearance of bone and delineate the extension of the soft tissue. Areas of altered signal intensity on T₁- and T₂-weighted images may represent areas of hem-

![Fig. 4. Photomicrograph revealing thin-walled small vessels (arrows) among new and reactive bone and sparse fibrous tissue. H & E, original magnification × 400.](image-url)
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Fig. 5. Upper: Nonenhanced axial CT (bone algorithm) scan showing a focal bone defect with evidence of new bone formation within the occipital bone. Lower: Three-dimensionally reconstructed CT scan (bone view) depicting significant resolution of the previously identified lytic process within the occipital bone.

orrhage at different stages. Heavily T₁-weighted images may demonstrate tiny cystic cavities within the osteolytic areas.¹⁵ Technetium bone scans can demonstrate increased uptake.²⁵,²⁶ On angiography, although there may be an irregular collection of veins in the late venous phase, there are no abnormalities seen in the arterial phase.¹¹

Patient Prognosis

The majority of patients survive, but the impact of the disease ranges from minimal disability to death. Disabilities arise from minor or severe skeletal deformities caused by bone resorption and loss of tissue support. Vertebral involvement can lead to spinal cord compression and paraplegia.²⁵,²³,¹⁶ Erosion of the skull can lead to CSF rhinorrhea, whereas erosion of the chest wall can cause thoracic duct occlusion with chylothorax.²⁵,²⁸,¹²,⁶ Choma, et al.,⁷ reported 15 deaths (16%) in 97 cases. Ten deaths were attributed to respiratory complications from involvement of the thoracic cavity, three deaths were from spinal cord transection, two were from sepsis, and one was from asphyxia and aspiration.

Eight patients with lesions confined to the calvaria have been reported, five of these in detail. Treatment in four patients included debridement and cranioplasty. The disease was arrested after treatment in two of the four patients (Table 1). Of five patients with cervical spine involvement, three underwent multiple autologous bone fusions and two received radiation therapy. All fusion attempts failed because of resorption of the grafts. The disease was arrested for 6 years in the patient treated with radiation therapy, although bone resorption then recurred. Three patients died of causes other than neurological complications, including the one who received radiation therapy (Table 1). Radiation therapy achieved arrest of the disease in five patients with involvement of the skull base and upper cervical spine (Table 1).

Treatment of the Disease

Several types of treatment have been attempted with generally inconclusive results. In 1988 Branco and Da Silva⁴ tried hormones; compounds of magnesium, calcium, and aluminum; ultraviolet radiation; various vitamins; and transfusion of placental blood as well as blood from growing children—all of which failed. Most recently, treatment has focused on removal of the affected bone, bone grafting or replacement by inorganic material, and radiation therapy. Excision of the affected regions, with or without fusion or replacement by inorganic material, has been successful in preserving some degree of functionality in some cases.⁵,¹⁰,¹¹,¹⁶,²⁶ Bone grafting has failed in the majority of cases because of progression of the pathological process and resorption of the graft.⁵,⁷,¹⁴,¹⁷,⁲⁴ In our review it seems as though surgical debridement and prosthetic replacement with an inorganic material has a better chance of success than autologous bone fusion (Table 1). This may be an effective treatment for lesions in the calvaria. However, in the cervical spine, where debridement would increase the risk of instability, fusion is necessary because instrumentation alone will not suffice.

Radiation therapy, advocated particularly by Halliday and associates,⁷ has been seen to arrest the progression of the disease.⁷ The success of radiation therapy has been linked to the extreme radiosensitivity of the proliferating endothelial cells. Radiation causes sclerosis, thereby inhibiting further growth of the lesion.¹³ The therapeutic success of radiation therapy has been questioned because there are many cases of spontaneous arrest in patients not receiving treatment.¹⁰,¹⁴,²³,²⁸ However, more recent publications support the beneficial effects of radiation therapy. Dunbar, et al.,¹¹ reviewed the literature and reported a total of 22 patients with Gorham’s disease, including four of their own, who were treated with radiation therapy. In 14 of the patients, treatment was successful in arresting the disease. These authors also noted that doses less than 20 Gy were generally ineffective, whereas doses between 25 and 40 Gy resulted in arrest of the osteolytic process. They therefore recommended doses of 40 to 45 Gy in fractions of 1.8 to 2.0 Gy. Some authors have reported regrowth of bone after radiation therapy.⁷,¹⁴,²⁴,²⁵,³¹ however, others have not observed this, even with arrest of the disease.¹¹

In our case, despite the presence of pneumocephalus, there was no obvious CSF leak or meningitis. Although there was extensive destruction of the upper bony cervical spine, there was no evidence of instability, presumably because of intact ligamentous structures. Because there was no immediate life-threatening process, neurological symptoms, or spinal instability, our patient was not treated surgically. Despite evidence that surgical excision of
TABLE 1

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Age at Presentation (yrs)</th>
<th>Duration (yrs)</th>
<th>Signs &amp; Symptoms</th>
<th>Location of Lesion</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fine &amp; Gonski, 1976</td>
<td>14</td>
<td>42</td>
<td>growing skull defect</td>
<td>lt parietal</td>
<td>?</td>
<td>none</td>
</tr>
<tr>
<td>Iyer, 1979</td>
<td>45</td>
<td>58</td>
<td>CSF rhinorrhea &amp; frontal meningitis</td>
<td>antibiotics</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Chai, et al., 1984</td>
<td>30</td>
<td>38</td>
<td>growing skull defect</td>
<td>rt frontoparietal</td>
<td>none</td>
<td>debridement &amp; removal of margin of normal bone</td>
</tr>
<tr>
<td>?</td>
<td>6</td>
<td>growing skull defect</td>
<td>?</td>
<td>none</td>
<td>6 mos spontaneous arrest of disease</td>
<td>?</td>
</tr>
<tr>
<td>Castleman &amp; McNeely, 1964</td>
<td>21</td>
<td>24</td>
<td>posttraumatic neck pain</td>
<td>C4–6</td>
<td>heman</td>
<td>post autologous bone fusion</td>
</tr>
<tr>
<td>?</td>
<td>?</td>
<td>posttraumatic neck pain</td>
<td>?</td>
<td>multiple surgeries w/ RT</td>
<td>16 yrs</td>
<td>progression of disease; death secondary to respiratory arrest</td>
</tr>
<tr>
<td>?</td>
<td>8</td>
<td>neck pain &amp; spastic quadriparesis</td>
<td>C2–4</td>
<td>RT</td>
<td>8 yrs</td>
<td>arrest of disease &amp; resolution of quadriparesis for 6 yrs; repeated onset of bone resorption after 6 yrs; death secondary to respiratory arrest at age 16 yrs</td>
</tr>
<tr>
<td>Foult, et al., 1995</td>
<td>?</td>
<td>32</td>
<td>posttraumatic neck pain &amp; lymphangiomatosis</td>
<td>C2–T1</td>
<td>mixed heman</td>
<td>multiple anterior &amp; posterior autologous bone fusions</td>
</tr>
<tr>
<td>Hoffman, et al., 1980</td>
<td>7</td>
<td>9</td>
<td>recurrent CSF leak, lt petrous, post cli- meningitis, noid, sphenoid bone, &amp; torticollis bone, &amp; C1–2</td>
<td>heman</td>
<td>RT</td>
<td>2 yrs arrest of disease</td>
</tr>
<tr>
<td>Kurczynski &amp; Horwitz, 1981</td>
<td>14</td>
<td>32</td>
<td>occipital headaches, lt sphenoid bone,</td>
<td>heman</td>
<td>RT</td>
<td>3 yrs arrest of disease</td>
</tr>
<tr>
<td>?</td>
<td>?</td>
<td>neck stiffness, lt occipital bone &amp; mastoid pain</td>
<td>C1–2</td>
<td>?</td>
<td>7 yrs arrest of disease</td>
<td></td>
</tr>
<tr>
<td>Khosrovi, et al. (present study)</td>
<td>62</td>
<td>62</td>
<td>posttraumatic occipital bone &amp; headaches</td>
<td>C1–2</td>
<td>heman</td>
<td>RT</td>
</tr>
</tbody>
</table>

* Ant = anterior; heman = hemangiomatosis; lymphan = lymphangiomatosis; mid = middle; post = posterior; RT = radiation therapy; ? = unknown.
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the involved bone would arrest the pathological process, the evidence of failure of any type of instrumentation and bone fusion argued against immediate surgical intervention. Any surgical debridement of the craniovertebral junction and upper cervical spine would have made this patient’s spine unstable. The decision to use radiation therapy was supported by the evidence that this treatment modality is effective in the skull base and upper cervical spine (Table 1). Radiographic studies after radiation therapy confirmed the arrest of the pathological process and evidence of new bone formation in our patient. The pneumocephalus resolved completely, and at no time during the course of therapy did this patient develop meningitis. Therefore radiation therapy in the absence of spinal instability or neurological impairment seems effective. One could postulate that, even in the presence of instability, a rigid brace such as a halo and radiation therapy should be used before selecting fusion.

Conclusions

Gorham’s disease is a primary form of osteolysis with an unknown cause; the disease is rapidly progressive but has a variable and unpredictable course. There are no diagnostic laboratory studies. Radiographic studies show an osteolytic process with no particular characteristic feature that by itself would provide a clue to the clinician as to the diagnosis of this entity. Three-dimensionally reconstructed CT scanning is useful in evaluating the extent of the disease. Magnetic resonance imaging assists in the characterization of the soft-tissue component of the lesion. Angiomatosis of the vascular or lymphatic type does not negate the diagnosis of Gorham’s disease if all other diagnostic criteria are met. Until further understanding of the cause and mechanism of this disease is achieved, the best existing diagnostic criteria are those introduced by Heffez, et al. Although the disease may spontaneously arrest, the stimulus for its arrest is not known; this makes it impossible to predict how much bone and functional loss will result. Surgery is not necessarily the first treatment of choice for involvement of the craniovertebral junction and upper cervical spine. The best treatment appears to be radiation therapy. Once the disease has been arrested, bone grafting with bone and/or use of inorganic material, if needed, have a better chance of success.

References


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