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## Case Report

# Gorham disease involving the maxillofacial bones: A perplexing entity

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## ABSTRACT

Gorham disease is a rare disorder with progressive osteolysis which leads to the vanishing of bones. Its etiology and ideal management strategy are still an enigma. A case of Gorham disease involving the maxillofacial region in a 25-year-old male with an emphasis on etiology and diagnosis is discussed.

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## Introduction

Gorham disease is a rare musculoskeletal disorder with spontaneous progressive massive osteolysis of bone. This disease diversely affects the axial and appendicular skeletons, with the shoulder, pelvic girdle, and skull being the common sites. In

the maxillofacial region, the mandible is mostly involved. The disease is usually associated with angiomatosis of blood vessels and rarely with the proliferation of thin-walled endothelium-lined lymphatic vessels.

J.B.S. Jackson was the first person to describe a case of the vanishing bone disease in 1838 [1]. However, the first person to report a case in the jaws was Romer in 1924, whereas Thoma

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**Table 1 – Synonyms of Gorham disease.**

- Gorham disease
- Phantom bone disease
- Vanishing bone disease
- Massive osteolysis
- Idiopathic massive osteolysis
- Gorham-Stout syndrome
- Progressive osteolysis
- Morbus Gorham-Stout disease
- Massive Gorham osteolysis

in 1933 reported the first complete osteolysis in the mandible [2]. Lemuel Whittington Gorham and Arthur Purdy Stout in 1955 presented a case series of patients with vanishing bone disease [3].

Various synonyms of Gorham disease in common parlance are listed in Table 1. Only 50 cases of Gorham disease with maxillofacial involvement are reported in the literature to date [4], and its mysterious etiology and ideal management strategy are still an enigma. Here we report a case of Gorham disease involving the maxillofacial skeleton in a 25-year-old male with an emphasis on etiology and diagnosis.

### Case report

A 25-year-old male reported to our outpatient department in January 2016 with a complaint of pain and swelling of the left lower back gum region over the past 1 month. The swelling was initially small in size which gradually increased to its present size. The quality of life of the patient was compromised due to dull pain, difficulty in mastication, and phonation. The patient also reported occasional bleeding from the swelling. There was no history of fever, weight loss, or paresthesia. According to his medical history, 15 years back, he had been diagnosed with astrocytoma and had been treated with a combination of surgery and radiotherapy. A thyroidectomy had been done 8 years ago to remove nodular goiter. His eruption milestones were normal with well-formed teeth. Family history was non-contributory. The vital signs were within normal limits, and no other sensory or motor neurologic deficits were detected.

There was a marked asymmetry on the right side of the face with a linear scar on the midline of the forehead (Fig. 1). The right ramus and the body of the mandible were thin compared with those on the left. Intraoral examination revealed a solitary well-defined, raspberry-like multilobular, pedunculated exophytic gingival growth on the left alveolar mucosa extending anteroposteriorly from the distal of the lower left mandibular second premolar to the mesial aspect of the left third molar. The size of the lesion was approximately 5 × 6 cm, pink in color with multiple pinpoint erythematous areas. The left lower second molar was buccally displaced (Fig. 2). On palpation, the lesion was tender and had a soft-to-firm consistency, with a tendency to bleed on probing, with no pus discharge. The lesion was compressible, non-reducible, and nonpulsatile. Provisional diagnosis of hemifacial atrophy on the right side of face and a fibrosed pyogenic granuloma between lower left mandibular second premolar and third molar was considered.

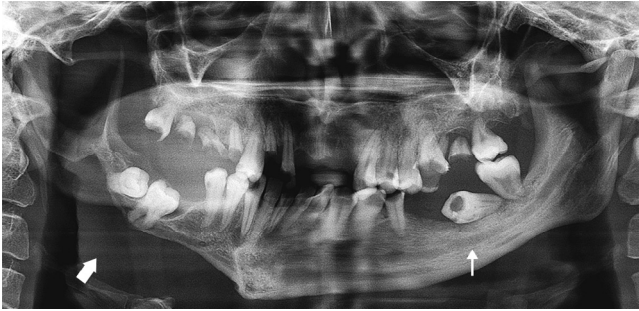


**Fig. 1 – Frontal view: Facial asymmetry on the right side of face when compared with that of left (black arrow) and a sharp linear scar noticed on the midline of the forehead (white arrow).**

Panoramic imaging revealed a well-defined massive osteolytic lesion on the right side of the body of the mandible which extended from the lower border of the mandible inferior to the right mandibular canine, involving the right ramus, coronoid,



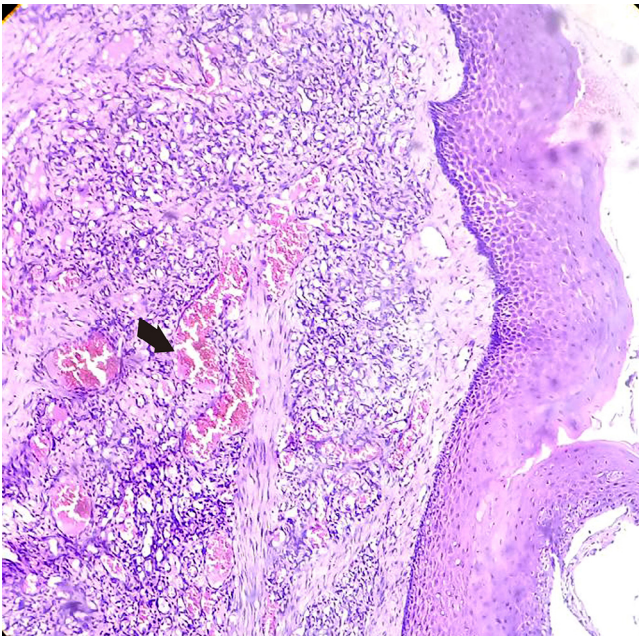
**Fig. 2 – Intraoral examination revealed a multilobular, pedunculated exophytic gingival overgrowth on the left alveolar mucosa between 35 and 38, displacing 37 buccally (displaced tooth is denoted using a black arrow), 36 is missing.**



**Fig. 3** – A panoramic image showing a well-defined massive osteolytic lesion in the right body of mandible (white thick arrow) extending to the right ramus, coronoid, and condylar process. Also noticed is a widening of the left inferior alveolar canal (white thin arrow).

and condylar process with a widening of the left inferior alveolar canal (Fig. 3). Plain and contrast computed tomography scans revealed osteolysis of the right body of the mandible, the ramus, and the right medial and lateral pterygoid plates.

This case had a multifocal unilateral osseous involvement resembling hemifacial atrophy. The sharp linear scar on the midline of the forehead resembled en coup de sabre, but on history it was found to be a surgical scar. Normal facial skin and tissues, normally functioning cranial nerves, and properly mineralized teeth with normal eruption status excluded the chance of hemifacial atrophy. History of radiotherapy through the suprasellar region may induce hypoplasia, but there was evidence of osteolysis even before radiotherapy and



**Fig. 4** – Histopathologic examination of biopsy specimen from gingival overgrowth revealed fibrovascular connective tissue with numerous thin-walled vascular spaces (black arrow) and chronic inflammatory cell infiltrate without cellular atypia suggestive of angiomatous lesion in the left alveolar mucosa between 35 and 38.

**Table 2** – Diagnostic criteria for massive osteolysis by Heffez et al. (Gorham disease).

1. Minimal or no osteoblastic response and absence of dystrophic calcification
2. Positive biopsy for angiomatous tissue
3. Absence of tumor or cellular atypia
4. Evidence of local progressive osseous resorption
5. Non-expansile, nonulcerative lesion
6. Absence of visceral involvement
7. Osteolytic radiographic pattern
8. Negative hereditary, metabolic, neoplastic, immunologic, or infectious etiology

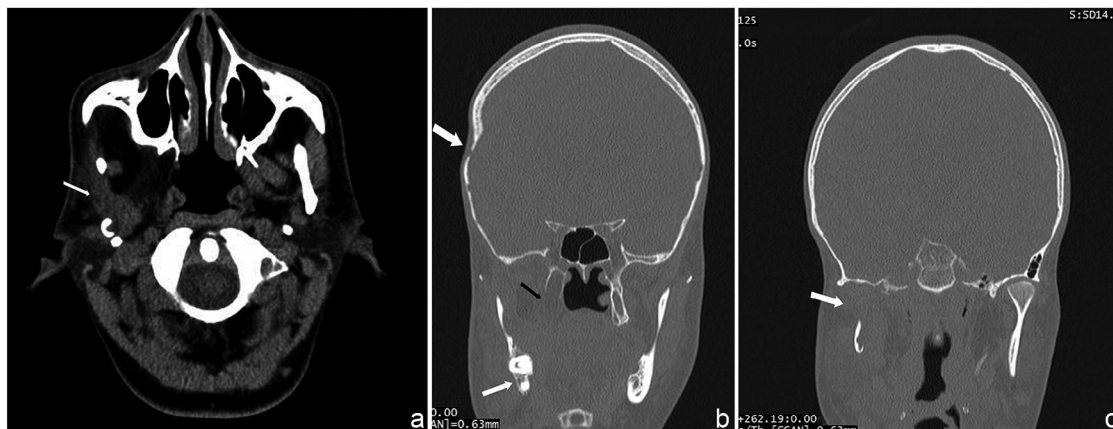
well-mineralized third molars in the affected site helped in ruling out radiation-induced hypoplasia. A slowly-progressing lesion, absence of weight loss, paresthesia and loose teeth, and an absence of dysplastic changes helped in ruling out the possibility of bone malignancies. Hematologic investigation revealed serum levels that showed calcium, phosphorous, alkaline phosphatase, T3, T4, and thyroid-stimulating hormone to be within the normal limits, which helped in ruling out any metabolic diseases.

Excisional biopsy of the gingival growth was performed and histopathologic evaluation revealed fibrovascular connective tissue with numerous thin-walled vascular spaces and chronic inflammatory cell infiltrate without cellular atypia (Fig. 4), which was suggestive of an angiomatous lesion.

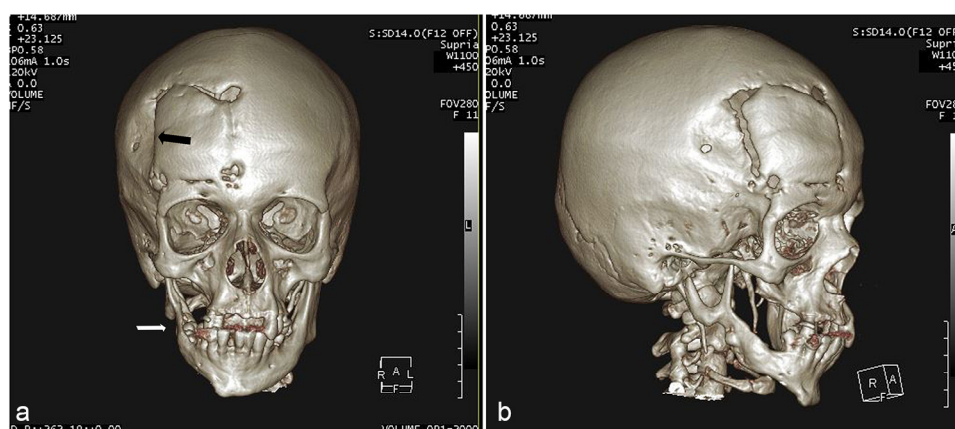
Based on this history of the patient, clinical behavior, radiographic features, and the histopathologic findings, a diagnosis of Gorham disease was made as per the criteria of Heffez et al. (Table 2). A panoramic image taken after 14 months revealed progressive osteolysis below the right mandibular second molar and widening of the left inferior alveolar canal (Fig. 5). Follow-up computed tomography and 3-dimensional reconstruction images revealed massive osteolysis of the right mandible and the pterygoid plates and evidence of right frontal craniotomy (Figs. 6 and 7). As part of the treatment, the patient was advised to take Tab. alendronate 70 mg once every week for a duration of 6 months, and a periodic review was advised. A written informed consent for the publication of this case report and the accompanying images was obtained from the patient.



**Fig. 5** – Follow-up panoramic image after 14 months revealing progressive osteolysis below 47 (white thick arrow) and increase in widening of the left inferior alveolar canal (white thin arrows) when compared with that of the previous panoramic image.



**Fig. 6 – (A) Follow-up CT axial section image revealing osteolysis of the right ramus of the mandible (white arrow). (B) Follow-up CT coronal section image revealing osteolysis of the right medial and lateral pterygoid plates (thin black arrow) and the right body of mandible (white thin arrow). Also noticed is evidence of right frontal craniotomy (white thick arrow). (C) Follow-up CT coronal section image revealing osteolysis of the right ramus and the condylar process (white arrow). CT, computed tomography.**



**Fig. 7 – (A) Three-dimensional CT reconstruction image showing massive osteolysis of the right body of mandible extending to the right ramus (white arrow) and the evidence of right frontal craniotomy noticed (black arrow). (B) Three-dimensional CT reconstruction image showing massive osteolysis of the right body of mandible extending to the right ramus and the right coronoid process. Evidence of right frontal craniotomy noticed. CT, computed tomography.**

## Discussion

Gorham disease is a rare phenomenon characterized by progressive destruction of 1 or more bones, which is replaced with an aggressively expanding non-neoplastic vascular tissue and later replaced with a dense fibrous tissue without bone regeneration [5]. There is no genetic transmission reported.

According to Gorham and Stout, the trauma may induce excessive production of vascular granulation tissue which may lead to massive osteolysis [1,3]. During bone healing, initially a neovascularization of the blood clot between the bone fragments is usually noticed, and any error in this process may act as a trigger for this osteolytic sequence [3,6]. In the case being analyzed, no traumatic component was noticed. It must be stressed that surgical intervention for astrocytoma and

thyroid disease were done at sites distant from the lesion. The presence of wide vessels in the affected areas leads to slow blood flow rate, resulting in local hypoxia and lowering of pH [7], which in turn activates hydrolytic enzymes, leading to osseous resorption [8,9].

Devlin et al. suggested that the bone resorption occurs due to increased osteoclastic activity mediated by interleukin-6 [5,10]. Hirayama et al. suggested that the increase in osteoclasts happens due to increase in sensitivity of osteoclastic precursors to humoral factors, which promote osteoclast formation [11]. According to Korsic et al., agenesis or dysfunction of thyroid C cells may also promote massive osteolysis in Gorham disease [12]. Thyroid C cells secrete calcitonin which inhibits the activity of osteoclasts and decreases the calcium level in blood. Our patient had a history of thyroidectomy done 8 years ago, but presently his hematologic investigation reports are within normal limits.

There is no sex or racial predilection, and this disease is mostly seen below the age of 40 years [7]. When massive osteolysis involves the mandible, mobile teeth, malocclusion, deviation of the mandible, and facial deformity are often observed. Spontaneous pathologic fractures are common in these patients. In some cases of massive osteolysis, spontaneous arrest of the lesion is noticed.

Radiographically, the initial lesion appears as a radiolucent focus in the intramedullary or subcortical regions, which later slowly progresses to the cortical bone, causing dissolution and eventual disappearance of the bone, with tapering or pointing of the remaining osseous tissue (sucked candy appearance) [6]. Loss of lamina dura and thinning of the cortical plates often precede the development of radiolucency. Radioisotope bone scans show diminished or absent osseous tissue in an area of decreased uptake. Histopathologically, lesions exhibit nonspecific vascular proliferation intermixed with fibrous connective tissue and chronic inflammatory cells which were also noticed in this case. Diagnosis of Gorham disease can be done based on the criteria put forth by Heffez et al. (Table 2) [13].

Anti-osteoclastic medication bisphosphonates, alfa-2b interferon 3 million units daily [14], calcium, fluoride, vitamin D, estrogen, actinomycin D, combination of cisplatin 75 mg/m<sup>2</sup> and 5 fluorouracil 1000 mg/m<sup>2</sup> are some of the medications used for the treatment of Gorham disease [11,15] but with limited success. Alfa-2b interferon has succeeded in disorders with vessel proliferation and anti-angiogenic properties. Low-dose radiotherapy has been suggested to arrest the course of osteolysis in Gorham disease. Radiation therapy in moderate doses (40-45 Gy in 2 Gy fractions) has also been proven to be effective. Surgical intervention with bone grafts or prostheses are also done widely but with limited success. Current clinical trials are evaluating the efficacy of rapamycin [6].

## Conclusion

Gorham disease is an extremely rare disease with a perplexing multifactorial etiology. Diagnosis is mainly based on the diagnostic criteria of Heffez et al., that is, using clinical presentation, radiologic imaging data, and biochemical and histologic data. We should also eliminate the possibilities of neoplastic, inflammatory, neuropathic, and metabolic disorders. Even though there are a plethora of treatment modalities, ideal management strategy is still an enigma.

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