Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology 28 (2016) 147–151

Contents lists available at ScienceDirect

Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology

journal homepage: www.elsevier.com/locate/jomsmp

Case Report

Gorham-Stout disease: Progressive massive osteolysis of the mandible

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ARTICLE INFO

Article history:
Received 4 September 2014
Received in revised form 4 September 2015
Accepted 24 September 2015
Available online 1 November 2015

Keywords:
Massive osteolysis
Lymphangioma
Gorham-Stout disease

ABSTRACT

Gorham-Stout disease (GSD) is an extremely rare massive osteolytic bone disease, and the pathogenesis and etiology are unknown. It is characterized by the uncontrolled proliferation of distended, thin-walled vascular and lymphatic channels within bone, which leads to resorption and replacement of the bone with angiomas and/or fibrosis.

A 35-year-old man had complained of masticatory disturbance caused by mandibular teeth mobility and mandibular swelling for several years. He suffered from an eating disorder because of the severe mobility of his mandibular teeth, and he presented at our hospital for consultation. He had swelling and grade III mobility without pain; his skin was normal in color with a 70 mm × 50 mm lesion of elastic and firm texture at the submental region. The ill-defined mandibular bone destruction was seen radiographically. Magnetic resonance imaging (MRI) showed that the lesion occupied the submental region and inside the mandibular bone, and these lesions were isolated. The biopsy results suggested a diagnosis of lymphangioma. The patient received radical surgery, and histological examination suggested lymphangioma. We diagnosed GSD because massive osteolysis of the mandible associated with lymphangioma was seen in the lesion. The postoperative course was uneventful, with no local recurrence 36 months after surgery. Given the rarity of this disease entity, there is no standard therapy. The details of this case are presented, and diagnostic and management considerations are described.

1. Introduction

Lymphangiomas are benign tumors that grow proportionally with patients' body growth by the proliferation of lymphatic vessels. The incidence of lymphangioma is estimated to amount to 6% of all benign tumors in children, but lymphangioma in adults is very rare. In the head and neck region, lymphangioma appears most commonly on the tongue, buccal mucosa, lips, and neck [1].

Mandibular osteolysis is usually the result of a well-defined pathogenic process. Usually the destruction is associated with some underlying disease, such as periodontal or periapical infection, osteomyelitis, or odontogenic cyst, or tumor.

Gorham-Stout disease (GSD) is an extremely rare massive osteolytic bone disease, but the pathogenesis and etiology are unknown. The lesion typically occurs in the shoulder, skull, pelvic girdle, jaw, ribs, or spine. It is characterized by the uncontrolled proliferation of distended, thin-walled vascular and lymphatic vessels within bone, which leads to resorption and replacement of the bone with angiomas and/or fibrosis. Treatment of the massive osteolysis is, for the most part, palliative and limited to symptom management [2–4].

Here, we describe a case of a massive osteolysis in the mandible and severely mobile teeth with lymphangioma. We performed radical surgery for this lesion. The lesion was finally diagnosed as GSD. The etiology, diagnosis, and management considerations of GSD are described in this literature.

☆ Asian AOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

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http://dx.doi.org/10.1016/j.ajoms.2015.09.007

2. Case report

A 35-year-old man presented at our department with masticatory disturbance caused by mandibular teeth mobility and mandibular swelling for several years. He had been injured in a motorbike accident with laceration at the mental region, and he underwent debridement and suture treatment 15 years ago. Extraoral examination revealed swelling at the submental region, which was 70 mm × 50 mm in diameter, painless, non-tender, elastic, and non-mobile (Fig. 1A). The lesion contained serous liquid, and blood oozed from part of the left lower molar when the mass was compressed. Intraoral examination revealed significant periodontal bleeding, increased probing depth, remarkable teeth mobility, and gingival crevicular fluid (Fig. 1B).

Panoramic radiography revealed horizontal alveolar bone loss at the mandible (Fig. 2). Magnetic resonance imaging (MRI) showed that the lesion occupied the submental region and inside the mandibular bone, and these lesions were isolated. Contrast-enhanced MRI of the mandibular alveolar bone region showed multiple high signals in the lesion (Fig. 3A), and the submental region showed swelling deep in the platysma muscle and an unclear accumulation image (Fig. 3B). 99mTc scintigraphy showed accumulation in the right mandibular bone, the right mandibular condyle, and the left temporal bone (Fig. 4), but gallium scintigraphy did not show accumulation. There were no abnormal findings in any other regions.

A needle biopsy was performed, and the specimen was taken from the submental lesion. Histopathological diagnosis suggested lymphangioma. We performed a radical surgery for the submental lesion and alveolar lesion that includes extraction of all lower teeth under general anesthesia. The submental lesion was resected with submental approach, and the alveolar lesion was resected with intra-oral approach. Intraoperative findings showed that the tumor

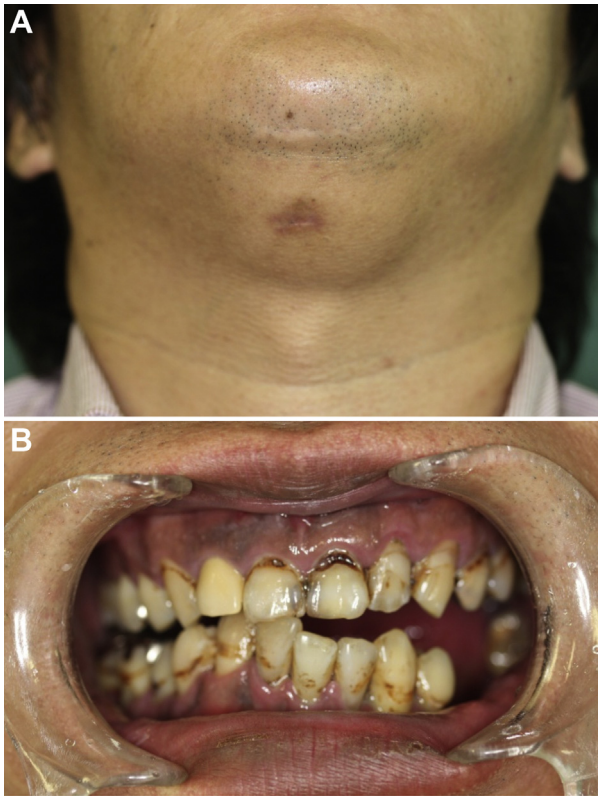

Fig. 1. (A) Extraoral examination revealed swelling of the submental region. (B) Intraoral examination revealed significant periodontal bleeding, increased probing depth, remarkable teeth mobility, and gingival crevicular fluid.

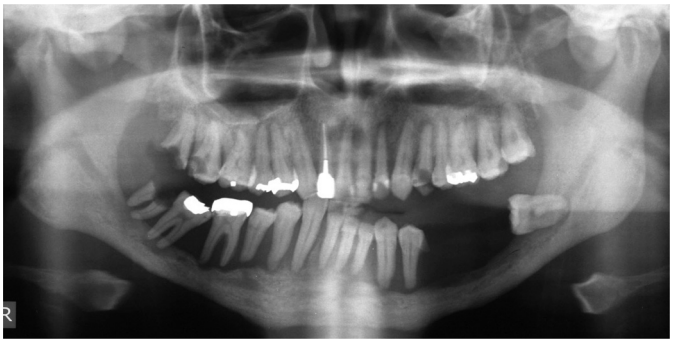

Fig. 2. Panoramic radiography shows resorption and decreased vertical height of the mandibular body with resorption extending toward the basal bone.

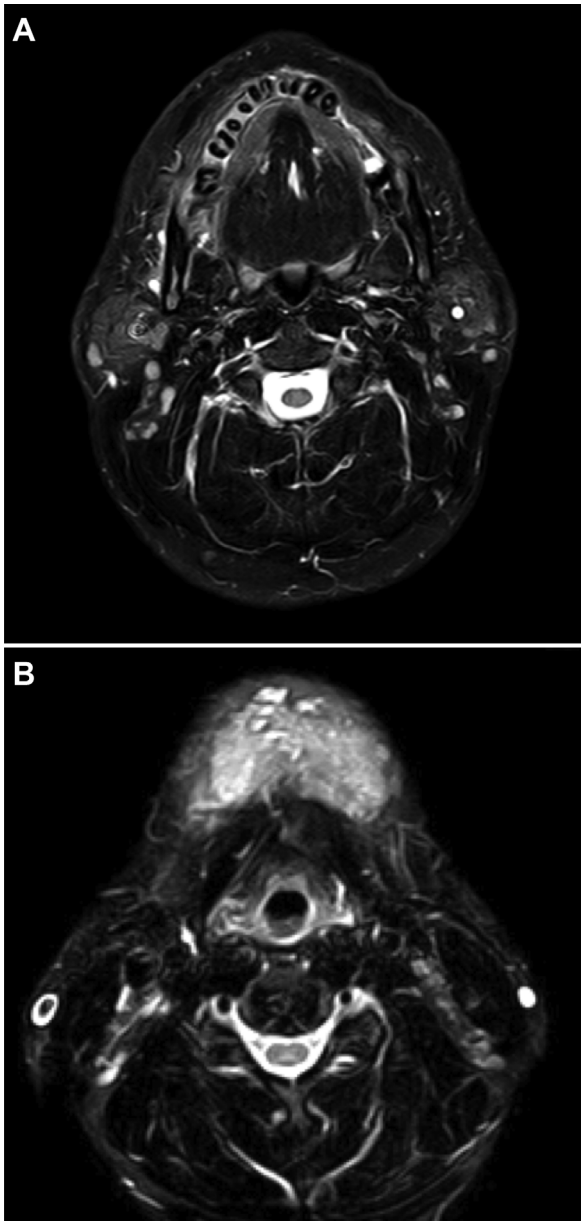

Fig. 3. Magnetic resonance imaging (MRI). (A) Mandibular alveolar region showed multiple high signals in the lesion. (B) Submental region showed multiple high signals in the lesion; its border was indistinct under the mentum.

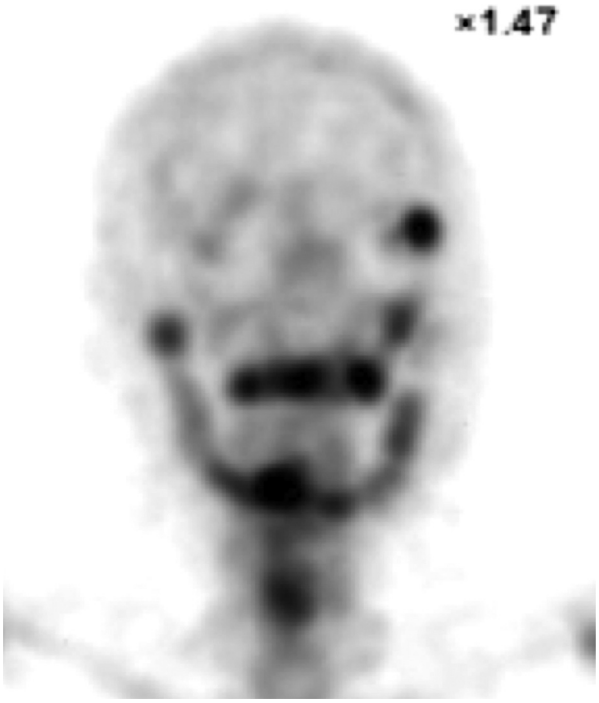

Fig. 4. 99mTc scintigraphy showed accumulation in the mandibular right cuspid, first premolar, the right mandibular condyle, and the left temporal bone domain.

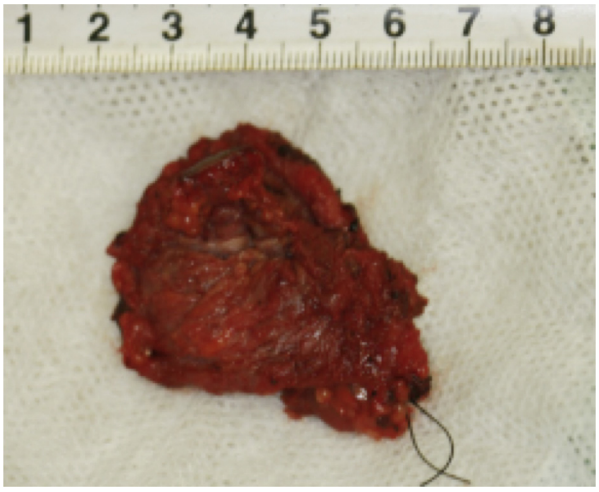

Fig. 5. The surgical specimen was 45 mm × 30 mm in diameter.

was well encapsulated and non-infiltrative, and the extirpation was easy from this site. The submental specimen was similar to a fluid-filled cyst and measured 45 mm × 30 mm in diameter (Fig. 5).

Histopathogical examination of the surgical specimen at cuspid and first premolar of the right mandible revealed the mass to be composed of a proliferation of variably dilated and thin-walled lymphatic vessels that were occasionally accompanied by lymphocytic aggregates, admixed with muscle-coated small blood vessels, and embedded in a fibrosclerotic storm among the skeletal muscle and adipose tissue. Immunohistochemically, the endothelial cells of the vessels were positive for D2-40. These findings suggested lymphangioma (Fig. 6A and B). There was no difference between the mandibular bone lesion and the submental lesion. The tumor was diagnosed as cystic lymphangioma.

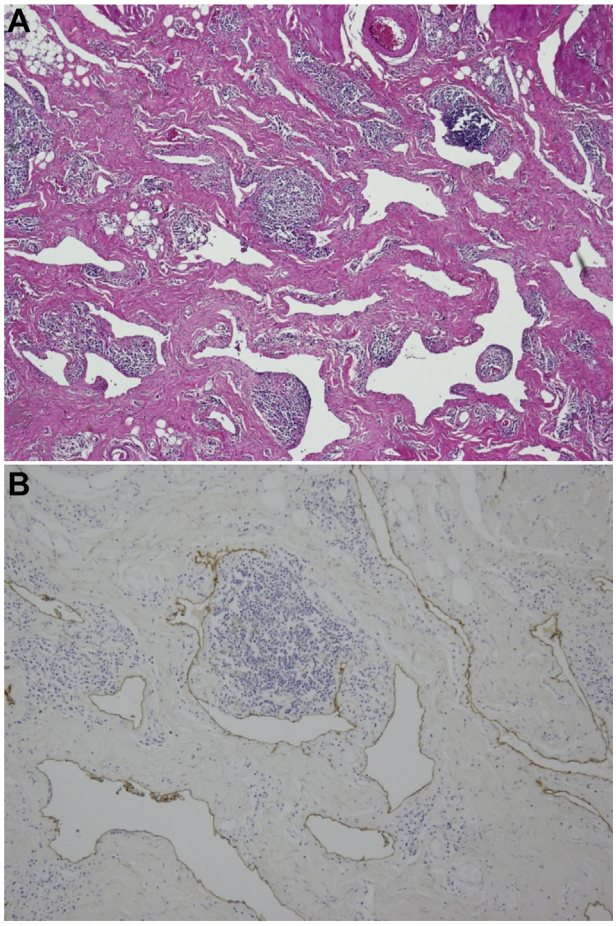

Fig. 6. (A) Histopathological findings revealed that the tumor was composed of a proliferation of variably dilated and thin-walled lymphatic channels, which were occasionally accompanied by lymphocytic aggregates. (B) Immunohistochemically, the endothelial cells of the channels were positive for D2-40.

One year after surgery, radiographic examination showed that only the inferior border of the mandible remained, and both sides of the condyle were partially resorbed (Fig. 7). 99mTc scintigraphy showed persistent accumulation in the right mandibular condyle and the left temporal bone, similar to one year earlier (Fig. 8). These results suggesting hyperostosis remained at these lesions. The patient's mastication disorder was improved with dentures. His postoperative course was uneventful, with no local recurrence or metastasis 36 months after the operation.

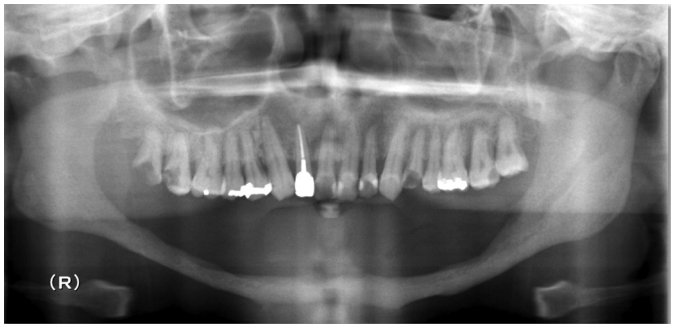

Fig. 7. Panoramic radiography 1 year after surgery showed that only the inferior border of the mandible remained and both sides of the condyle were partially resorbed.

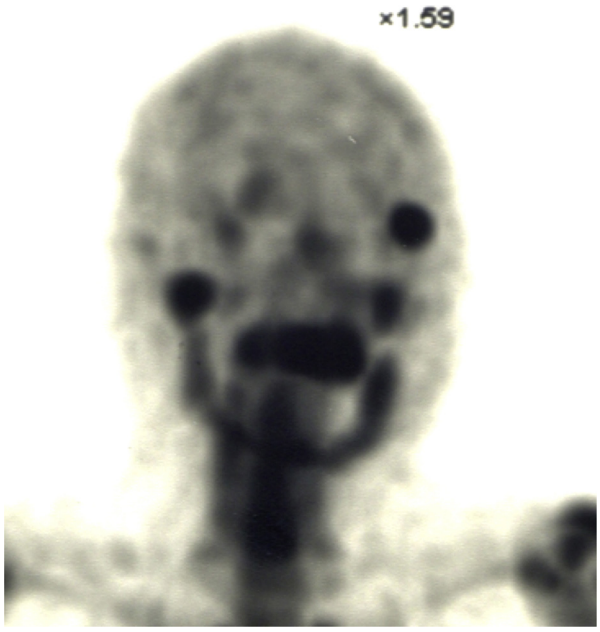

Fig. 8. 99mTc scintigraphy showed persistent accumulation in the right mandibular condyle and the left temporal bone.

3. Discussion

In 1838, Jackson [5] described the clinical and anatomic findings of a case of GSD in a patient with a disappearing humerus. Heffez and colleagues established the eight histopathological and clinical criteria of GSD as follows: (1) a positive biopsy for angiomatous tissue; (2) the absence of cellular atypia; (3) minimal or no osteoblastic response and absence of dystrophic calcification; (4) evidence of local, progressive osseous resorption; (5) a non-expansible, non-ulcerative lesion; (6) the absence of visceral involvement; (7) an osteolytic radiographic pattern; and (8) negative hereditary, metabolic, neoplastic, immunologic, or infectious etiology [6]. In our case, only the submental lesion was expansible, except this issue, satisfied all of these criteria, and the lesion was therefore considered to be GSD.

Many reports have discussed the etiology of Gorham disease. Gorham and Stout first suggested that hyperemia may disturb the cellular balance between osteoclasts and osteoblasts [7]. Devlin et al. reported that bone resorption in Gorham disease patients is due to enhanced osteoclast activity, and that IL-6 may play a role in this resorption [8]. Young et al. suggested that this condition might be one of a large spectrum of disorders caused by basic underlying endothelial dysplasia and that the lymphatic system, vascular system, or both may be involved [9]. Wiggs and Sismanis reported that this proliferation occurs in older patients because of an instigating stimulus, such as infection or trauma [10]. Aneeshkumar et al. reported injury to be an inducing cause of adult lymphangioma [11], while Knoch suggested that activation of a silent hematoma after minor trauma might lead to resorption of bone [12]. In our case, the patient had a motorbike accident 15 years ago, during which the patient injured the submental region. This may be the triggering episode of the pathogenesis of the lymphangioma.

Histologically, lymphangioma consists of lymphatic vessels that are remarkably expanded so that their interiors are covered with one layer of endothelial cells in the lamina propria. Despite osteoclast being found in the tissue of the lesion, GSD is not caused by increased osteoclastic activity [13]. In our case, the tumor appeared to differ from normal lymphangioma based on the histological findings, which showed an accumulation of lymphocytes around the hyperplastic lymphatic vessels.

In the panoramic radiography, our case mimicked periodontal disease. Mignogna et al. also reported a case of GSD mimicking periodontal disease, and they recommended differential diagnoses, such as inflammatory disease, endocrine disease, intraosseous malignancies or metastasis, lymphoma, histiocytosis X, eosinophilic granuloma, infective processes, and odontogenic tumors [14]. On Tc-99m bone scintigraphy in GSD, lesions may demonstrate an increased uptake of the radiopharmaceutical agents on the initial images, and may subsequently show an area of decreased uptake corresponding to the diminished bone region [15]. Our case demonstrated that remarkable uptake of the lesion was seen on the follow-up bone scintigraphy; however, the reason of this issue is still unclear. Clinically, there are two phases of the disease: active bone destruction and lysis with pain and swelling are followed by a quiescent phase. The fibrovascular tissue with multiple thin-walled vessels is progressively replaced by fibrous tissue [16]. Gorham and Stout suggested that proliferating capillaries arising from the Haversian system may cause increased vascularity, which increases the local oxygen tension, changes the pH of the tissue, and results in tissue lysis [7]. In the early stages of the lesion, the bone undergoes resorption and is replaced by hypervascular fibrous connective tissue and angiomatous tissue [13].

Given the rarity of this disease entity, there is no standard treatment for GSD. Treatment for GSD includes surgery and radiation therapy, as well as pharmacotherapy, such as bisphosphonates, α-2b interferon, estrogen, calcium glycerophosphates, calcitonin, vitamin D supplements, and sodium fluorides [16]. Surgical options include excision of the lesion [13,17]. Radiation therapy has shown benefits as the endothelial cells of proliferating capillaries are considered to be radiosensitive. Definitive radiation therapy used in moderate doses from 40 to 45 Gy in 2-Gy fractions appears to result in good clinical outcomes with few long-term complications [18]. In high-dose radiation therapy for children and adolescents, the potential for secondary malignancy and growth restriction should be considered before the treatment [13]. In our case, the patient received only surgical resection and no recurrence after 36 month of surgery.

There is no consensus on the standard therapy for massive osteolysis of GSD, and therefore, it is often necessary to combine various protocols. It is necessary to carry out progress observation carefully in the future.

Conflict of interest

The authors declare that there is no conflict of interest.

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