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Gorham's disease of the mandible mimicking periodontal disease on radiograph

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Abstract

Background: Gorham's disease is a rare disorder characterized by spontaneous and progressive osteolysis of one or more skeletal bones. The radiographic findings associated with Gorham's disease are particularly dramatic, as in some cases a complete resorption of the involved bone can occur, leading to the definition of phantom bone, vanishing bone, or disappearing bone disease.

Material and methods: A 24-year-old female patient with a previous diagnosis of periodontal disease and progressive mandibular alveolar bone loss was referred to our Oral Medicine section. The initial radiographic picture showed infrabony defects and horizontal bone loss.

Results: After further extensive local and systemic evaluation, including histopathological, laboratory and imagine techniques investigations, the patient was diagnosed to be affected by Gorham's diease. Meanwhile the progression of the osteolytic process had caused the loosening of all the left mandibular teeth and a pathologic fracture. Appropriate medical therapy was successful in stabilizating the resorptive process, with no evidence of further progressive disease.

Conclusions: When Gorham's disease involves the mandible, the role of the periodontologist is extremely important in diagnosing promptly the disorder and preventing the functional and aesthetic consequences of advanced and extensive bone loss. Gorham's disease should be included among the pathologic entities mimicking periodontal disease on radiograph, such as inflammatory disease (e.g. osteomyelitis), endocrine disease (e.g. hyperparathyroidism), intra-osseous malignancies or metastases, lymphoma, histiocytosis X, mainly eosinophilic granuloma, infective process (e.g. tuberculosis and actinomycosis), odontogenic tumours.

Key words: bone resorption; Gorham's disease; Lymphangiomatosis; mandible; periodontal disease

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Gorham's disease, also called massive osteolysis, is a rare disorder characterized by spontaneous and progressive osteolysis of one or more skeletal bones (Gorham & Stout 1955, Choma et al. 1981). The radiographic findings associated with Gorham's disease are particularly dramatic, as in some cases a complete resorption of the involved bone can occur (Choma et al. 1981), leading to the definition of phantom bone, vanishing bone, or disappearing bone disease (Gorham & Stout 1955, Tsang et al. 2004). The mechanism of osteolysis, as well as its etiological factors, are largely unknown. Currently it is believed that increased osteoclast activity (Devlin et al. 1996, Hirayma et al. 2001) together with a proliferation of blood and lymphatic vessels (Gorham & Stout 1955, Choma et al. 1981, Aviv et al. 2001) may play a pivotal role in Gorham's disease pathogenesis, leading to bone resorption and invasion of adjacent soft tissues, respectively. The prognosis of Gorham's disease is highly variable and unpredictable, ranging from minimal disability to death, because of the involvement of vital structures (Choma et al. 1981). Among about 150 cases reported in the literature (Lee et al. 2003), fewer than 40 have been found to affect bones of the maxillo-facial region (Schiel & Prein 1993, Benhalima et al. 2001).

In this report, an additional case of Gorham's disease affecting the mandible and mimicking periodontal disease on radiographs is described.

Case report

A 24-year-old female was referred to our Oral Medicine Division complaining of mild pain over the left side of the mandible. She stated that more than 1 year earlier she was diagnosed to be affected by periodontal disease and treated accordingly with non-surgical periodontal therapy and teeth splinting. Afterwards, as subsequent orthopantomograms showed a progressive worsening of alveolar bone loss, she was suggested to contact an Oral Medicine clinic for further evaluation.

Intra-oral clinical examination showed absence of gingivitis, and a slight mobility of the left mandibular teeth, from the first molar to central incisors, although from the left pre-molar zone to the right canine region the teeth were splinted. Periodontal probing failed to show loss of attachment and periodontal pockets (Fig. 1). Teeth vitality was assessed and confirmed through thermal test. Extraoral palpation demonstrated a longitudinal parasymphyseal depression of the lower margin of the left hemi-mandible. An in-depth evaluation of current and previous orthopantomograms led us to recognize the presence of a progressive ostolytic process which was initially localized to a small region of the alveolar bone of the mandible (pre-molar and incisive areas), then extended to the surrounding bone involving almost all the left mandibular teeth over about 1 year (Fig. 2). The radiographic picture was very similar to that of periodontal disease, with earlier orthpantomograms showing infrabony defects and horizontal bone loss.

Another osteolytic process, not in continuity with but at the same level of the previous one, was visible; it involved the lower margin of the left hemi-mandible, seemed to be absent in the first orthopantomogram, and was progressive.

In accordance with the above reported findings, the previous diagnosis of periodontal disease was considered erroneous, and a comprehensive work-up was initiated in order to investigate all the possible local and systemic causes of mandibular osteolysis not related to periodontitis.

A biopsy of the alveolar osteolytic region was performed, and ^{99m}Tc scintigraphy, radiographic skeletal survey, and laboratory investigations were required. The latter included thyroid and parathyroid hormones, calcitonin, red blood cell examination, white blood cell count and differential, platelet count, erythrocyte sedimentation rate, levels of serum electrolytes, creatinine, alkaline phosphatase, urine analysis, and tumour markers (CA 15-3, CA 125, CEA, α-FP), which resulted in normal limits. Only calcium levels were found to be slightly higher than normal. No pathologic features were evident on chest radiograph.

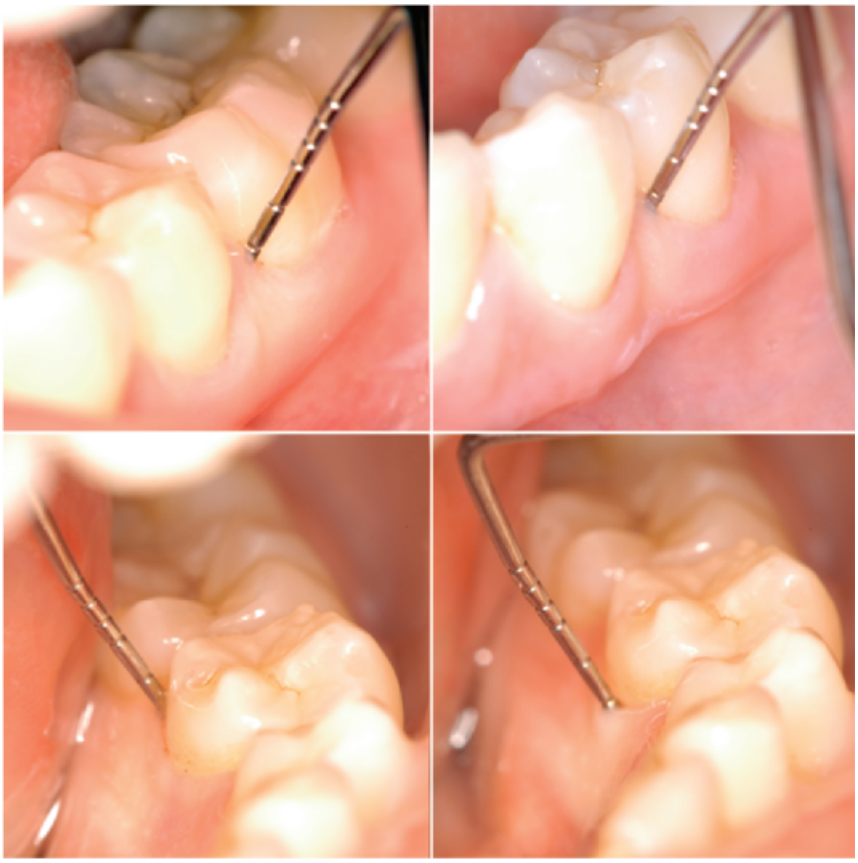

Fig. 1. On periodontal probing no loss of attachment and periodontal depths were found.

^{99m}Tc scintigraphy showed increased uptake in the left hemi-mandible, without evidence of other skeletal lesions. The results of radiographic skeletal survey confirmed the presence of a monostotic osteolytic process localized at the mandible. During this extensive work-up, a new orthopantomogram showed a rapidly progressive course of the disease, with an extension of the osteolytic process and severe mandibular bone resorption, which involved all the teeth and the lower margin of the left hemi-mandible which appeared extremely tapered in the pre-molar/canine region. An initial involvement of the symphisis as well as the lower margin of the right parasymphyseal region was also evident. Clinically, the teeth were extremely mobile and the left parasymphyseal depression was more evident extraorally. Accordingly, the involved teeth were extracted and additional specimens of the remaining fibrous tissue were submitted for histopathological evaluation. During extraction, the teeth looked to be attached only to marginal gingiva, which, together with alveolar gingiva, appeared very mobile because of underlying alveolar and basal bone loss.

In order to better evaluate the extension of the resorptive process, an axial computed tomography (CT) scan of the mandible together with a three-dimensional CT scan was required. Microscopically, the analysis of the specimens removed from the osteolytic defect consisted of a non-specific fibrous tissue containing lymphocytes and plasma cells together with vascular proliferation. CT examination revealed an almost complete loss of the whole alveolar bone of the left hemi-mandible, with a full-height bone resorption in the parasymphyseal region, where a pathological fracture was evident. The distal fragment (segment) appeared to be dislocated upwards and medially (Figs 3 and 4).

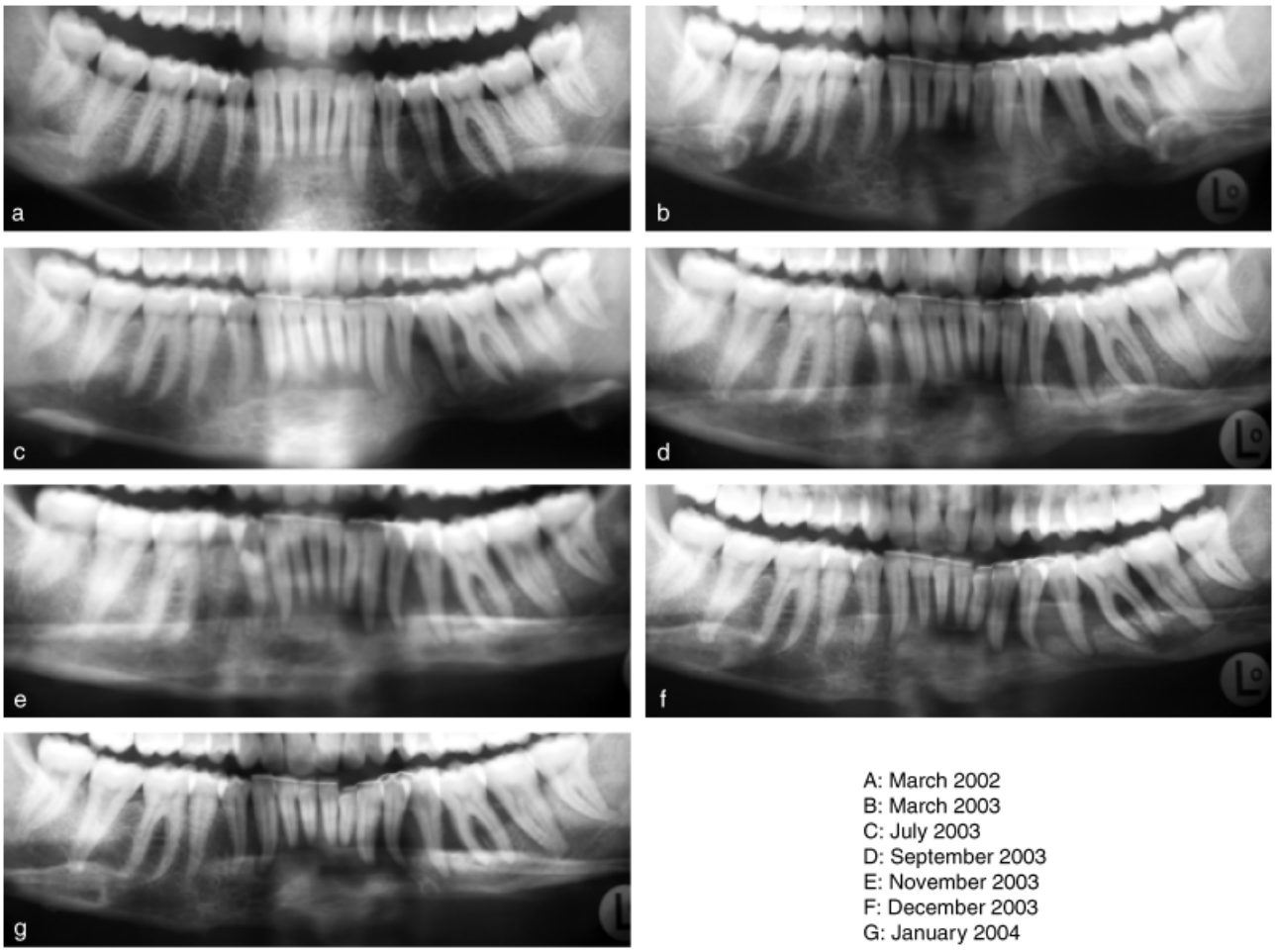

Fig. 2. Consecutive orthopantomograms show the initial presence of infrabony defects and horizontal bone loss which progressively extended to the bone surrounding almost all the left mandibular teeth over about 1 year. At the lower margin of the left hemymandible and symphisis are evident other progressive osteolytic processes.

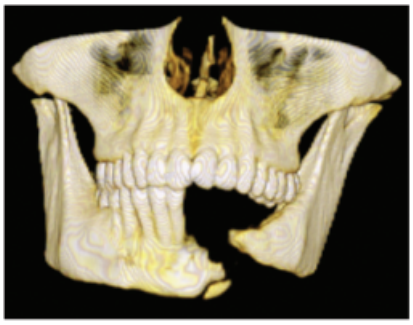

Fig. 3. Computed tomography shows a marked alveolar bone loss of the left emimandible and full-height bone resorption in the parasymphyseal region, where a pathological fracture was evident.

In conclusion, the clinical, histopathological and radiographic features were compatible with a diagnosis of Gorham's disease of the mandible, without any other skeletal involvement.

In addition, the total body dual energy X-ray absortiometry (DEXA scanning) showed no other areas of lower bone density, thus confirming the monostotic nature of the disease.

The patient was immediately scheduled for radiotherapy, which has been reported to result in good outcomes. Nevertheless, she refused radiation because of potential facial aesthetic side-effects. As a consequence, because biphosphonates have been reported to be effective in some patients with Gorham's disease (Motamedi et al. 2003, Tsang et al 2004), we started therapy with e.v. zoledronic acid (4 mg every 28 days) and oral calcium carbonate (1500 mg/die). A three-dimensional CT scan of the mandible, as well as creatinine and serum calcium levels, were performed monthly to follow-up the evolution of the disease, the effectiveness, and potential side-effects of the therapy. Fortunately, the therapy has been successful in stopping the progression of the disease, and the patient has remained stable without further bone resorption for more than 6 months. She is scheduled to continue zoledronic acid monthly for another 6 months, until month 12 of therapy, when, in case of disease stability, a surgical reconstruction of the mandible will be planned.

Discussion

In 1838, J. B. S. Jackson reported the first case of massive osteolysis, describing a young man with spontaneous resorption of the humerus (Jackson 1838). The clinical features were so impressive to lead the author to describe the case as the ''boneless arm'' (Jackson 1838). Afterwards, the disease was observed by other authors until the half of the 20th century, when Gorham & Stout (1955), reviewing the previous

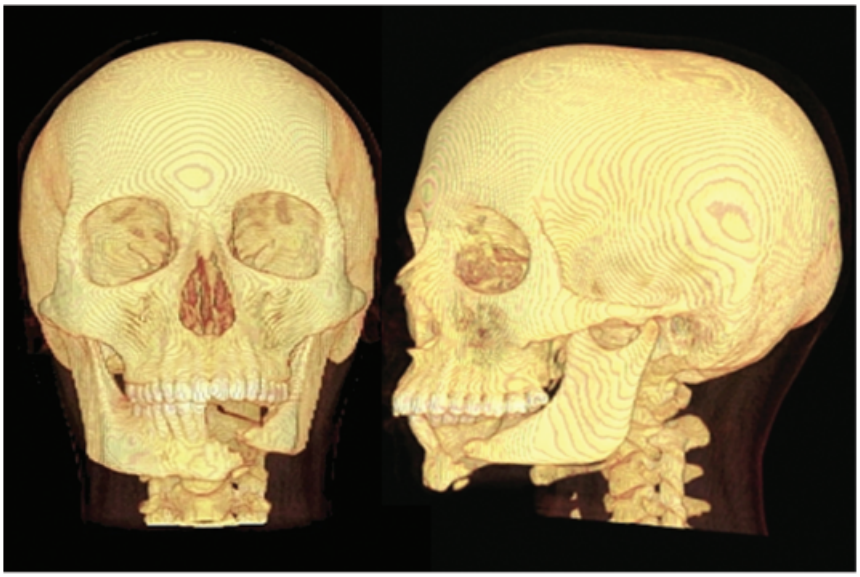

Fig. 4. Computed tomography of the cranium shows mandibular bone resorption, fracture and dislocation of the distal fragment.

cases, defined it as a specific pathologic entity and underlined the presence of lymphangiomatous vessel proliferation. Since then, about 150 cases of Gorham's disease have been reported in the literature, and more knowledge about it is now available. With regard to prognosis, the complications of Gorham's disease vary from minimal disability to death (Choma et al. 1981). Even if the osteolytic process often arrests spontaneously, the involvement of vital structures, such as the vertebral column and rib cage, is able to cause death. The course of the disease is particularly insidious, as the osteolytic process is typically painless, allowing normal patient activity to continue while bone destruction occurs, making the patients susceptible to pathologic fractures (Ricalde et al. 2003).

It is also the case of the patient we described, who developed a fracture of the mandible during our work-up.

However, the involvement of the maxillo-facial region should lead to diagnose the disease earlier, because of the subsequent frequent occurrence of teeth mobility, the evaluation of dental radiographs required to approach such a mobility, and the presence of cosmetic facial disturbances.

Mandibular teeth mobility has been described as an early sign in the majority of patient with Gorham's disease of the jaws (Frederiksen et al. 1983, Bouloux et al. 1999, Holroyd et al. 2000, Motamedi et al. 2003), and is typically associated with radiographic evidence of alveolar bone loss.

Patients with these features are usually referred for evaluation to the periodontist, who has the role to analyse the pathologic process and differentiate it from several conditions able to cause osteolysis localized to the periodontal region.

In our case, the radiographic features strongly mimicked periodontal disease, thus probably leading to the previous diagnosis of periodontal disease. However, at our observation the clinical features were not consistent with such a diagnosis, as the diagnostic criteria of periodontal disease were not present: oral hygiene was satisfactory (full-mouth plaque index $<10\%$), the gingival tissues did not show signs of inflammation (full-mouth bleeding score was 15%) and periodontal probing failed to show loss of attachment and periodontal pockets. Also Bouloux et al. (1999) reported a case of Gorham's disease of the mandible where teeth mobility were not associated with loss of periodontal attachment and increased probing depths, whereas the majority of the other reports did not adequately evaluate the periodontal status. With regard to this, it should be pointed out that, as our patient was previously treated with periodontal therapy, the results of periodontal examination are clearly not reliable. Nevertheless, as the osteolytic process is thought to start at the subcortical level (Motamedi et al. 2003), it is likely that in early phases of Gorham's disease the resorption of alveolar bone might cause teeth mobility without increased probing depths.

The observation of these clinical features might lead the periodontist to further evaluate the other possible causes of alveolar osteolysis mimicking periodontal disease on radiograph, including inflammatory disease (e.g. osteomyelitis), endocrine disease (e.g. hyperparathyroidism), intra-osseous malignancies (To et al. 1991) or metastases (Ogutcen-Toller et al. 2002), lymphoma (Nittayananta et al. 1998), histiocytosis X, mainly eosinophilic granuloma (Artzi et al. 1989, Nicopoulou-Karayianni et al. 1989, Unlu et al. 1997) infective process (e.g. tuberculosis and actinomycosis) (Nagler et al. 2000), odontogenic tumours (Haghighat et al. 2002).

Therefore, a biopsy from the involved area, laboratory investigations, as well as imaging techniques should be performed to find a potential cause of the osteolytic process. Accordingly, definitive diagnosis of Gorham's disease is a diagnosis of exclusion, after having failed in detecting serum biochemical abnormalities, and with microscopic findings showing a non-specific vascular fibrous connective tissue containing foci of lymphocytes, plasma cells and active fibroblasts.

It is our intention to underline that, when Gorham's disease involves the jaws, the role of the periodontologist is extremely important in diagnosing promptly the disorder and preventing the functional and aesthetic consequences of advanced and extensive bone loss. Furthermore, mandibular involvement is considered a potential high-risk disease location, as severe progression from mandible to maxilla, skull, and spine has been reported (Jackson 1838), thus leading to poor prognosis. Accordingly, an early diagnosis of Gorham's disease of the maxillofacial regions is crucial to prevent patient's morbidity and mortality, and seems to be feasible because of the presence of early signs such as teeth mobility and periodontitis-like alveolar bone loss.

In conclusion, we stress that the periodontist should include also Gorham's disease among the pathologic entities mimicking periodontal disease, causing teeth mobility, and without loss of attachment and increase in probing depths.

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