CASE REPORT

Gorham's disease: a case report and literature review

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Abstract

Background: Gorham's disease is an extremely rare disorder of unknown aetiology. The disease is characterised by spontaneous and progressive osteolysis of one or more skeletal bones. Occurrence in the maxillofacial region is rare with fewer than 40 reported cases affecting the facial and jawbones.

Case report: A 4-year-old child was admitted to a district general hospital with a 7-day history of fever, sore throat, cough and pain in the left face and ear. Three months previously the patient had presented to a local dental hospital complaining of 'tooth pain'. There was tenderness on examination of the temporomandibular joints and cervical spine, and marked trismus. The teeth were very mobile with extensive gingivitis present. The child was referred to Great Ormond Street Hospital for Sick Children where he received cytotoxic therapy. The patient deteriorated and succumbed to the disease at 6 years of age.

Discussion: Prognosis of the disease is dependent on which structures are involved. Mandibular involvement is considered high-risk. The presentation of generalised tooth pain and mobility in a child should raise the suspicion of a systemic disorder affecting the jaws. Gorham's disease is one such condition to consider.

Clinical relevance

This case report demonstrates how a child with oral and facial symptoms combined with other systemic signs may present to an oral and maxillofacial surgery department. A systemic disease was not immediately suspected despite generalised tooth pain and mobility on presentation. It is intended that this case will highlight to oral surgeons, dentists and medical professionals alike that generalised tooth pain and mobility in a young child should raise the suspicion of a systemic disorder and that the disease described here is one such condition to consider.

Introduction

Gorham's disease or vanishing bone disease is an extremely rare disorder of unknown aetiology. The disease is characterised by spontaneous and progressive osteolysis of one or more skeletal bones. Progressive bony resorption occurs, being replaced with fibrovascular connective tissue.

Occurrence in the maxillofacial region is rare with fewer than 40 reported cases affecting the facial and jawbones. Disease of the jaws may manifest as pain, deformity, tooth mobility and malocclusion[1].

In this report, a case of Gorham's disease affecting several bones, including the mandible is presented.

Case report

A 4-year-old child was admitted to a district general hospital with regard to a 7-day history of fever, sore throat, cough and pain in the left face and ear. He also complained of neck pain and stiffness and had vomited once the day before. He had presented to his general

medical practitioner 2 weeks previously complaining of a cough. A 5-day course of a cephalosporin had not improved the symptoms.

His past medical history revealed that he had suffered from recurrent left-sided ear infections for 2 years. Grommets had been inserted 1 year previously. These had been removed 5 weeks before admission because of bleeding and discharge. Each anaesthetic was recorded as a difficult intubation because of severe neck stiffness. He had suffered from recurrent left-sided facial and neck pain for 2 years, each episode being accompanied by dysphagia and pain on chewing.

Three months previously the patient had presented to a local dental hospital complaining of 'tooth pain'. A dental panoramic tomogram was reported at that time as normal by the examining clinicians and the child was diagnosed as 'teething'.

The child was a normal delivery at 38 weeks. His height and weight were below the third percentile and his speech was delayed until his third year.

On examination, he exhibited micrognathia with asymmetry to the left. His ears were turned forwards. There were no skin lesions, hepatosplenomegaly or cervical lymphadenopathy. There was extreme tenderness on examination of the temporomandibular joints and cervical spine, and marked trismus. Oral examination showed that all deciduous teeth were present and caries free. However, the teeth were very mobile with extensive gingivitis present and oropharyngeal candidiasis was evident. There was a high arched palate with no clefting. His temperature on admission was 37.6°C.

Haematological investigation demonstrated the following:

A mild anaemia was reported. Platelets, white cells and neutrophils were elevated. C-reactive protein was significantly raised at 120.9 mg/L (normal = 0.08–8.0). Autoantibodies were negative. Other investigations were returned as normal (liver enzymes, urea and electrolytes, bone profile, hormonal assays and urine VMA).

Radiological investigations demonstrated multiple areas of rarefaction in the skull, pelvis, cervical spine, wrists, scapula and the mandible. A bone scan showed increased activity in the above areas. The dental panoramic tomogram radiograph (Fig. 1) revealed generalised osteolytic changes in the bone with a pencil-thin cortex and marked rarefaction in the posterior parts of the mandible.

A differential diagnosis included; histiocytosis X, Still's disease, fibrous dysplasia and Gorham's disease. Other differentials that may be considered are diseases of endocrine function (e.g. hyperparathyroidism),

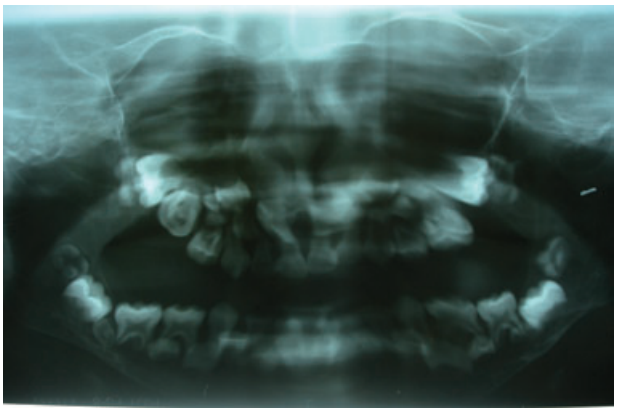

Figure 1 'Moth eaten' radiolucent appearance of the mandible.

infectious diseases (e.g. osteomyelitis) and inflammatory conditions (e.g. rheumatoid arthritis). A bone biopsy from the iliac crest showed macroscopically abnormal bone. A biopsy of the mandible was taken in this case. Histopathology was considered as consistent with the haemangiomatosis seen in Gorham's disease. The positive biopsy result combined with the osteolytic radiographic pattern, clinical signs, lack of involvement of other organs and the absence of other aetiological factors (neoplastic, immunological, metabolic, hereditary or infectious) helped confirm the diagnosis.

The child was referred to Great Ormond Street Hospital for Sick Children where he received cytotoxic therapy and morphine to reduce neck and general bone pain. Oral hygiene measures were introduced involving chlorhexidine 0.2%, but despite this, the tooth mobility worsened.

The patient was treated with six further cycles of cytotoxics over a 2-year period. During this time, the patient fell and fractured the left femur, which was treated successfully. The patient responded well to treatment initially and was on the 50th percentile growth chart and attended a normal school. Eventually, the patient died at 6 years of age following destruction of the cervical vertebrae and injury to the spinal cord.

Discussion

Gorham's disease has a number of synonyms including lymphangiomatosis, massive osteolysis, phantom bone disease and vanishing bone disease. The first case was reported by Jackson (1838) and described the spontaneous resorption of a humerus and led him to title his work '*A boneless arm*'[2]. Further cases continued to be reported until Gorham and Stout first described it as a

pathological entity in 1954; they identified the presence of lymphangiomatous vessel proliferation[3]. Since then, less than 160 cases have been reported in the literature. The prognosis of the disease is highly variable and unpredictable, causing anything from a minor disability to death which can occur in up to 16% of cases. It may affect single or less commonly multiple sites[4].

The disease can affect any part of the skeleton and thus far, there have been fewer than 40 reported cases affecting the maxillofacial bones, most often the mandible. Frederiksen *et al*.[5] found that all reported cases of the disease in the maxillofacial region initially involved the mandible, some of which later progressed to maxilla and skull. Of the other bones in the skeleton, the pelvis, humeral head and humeral shaft appear most commonly involved[6].

Although the aetiology of the disease is still unknown, it is thought that an increased osteoclast activity, coupled with proliferation of blood and lymphatic vessels, may play an important role in disease pathogenesis[7–9]. Gorham and Stout[3] proposed that proliferating capillaries from the haversian system caused an increased vascularity, which increased the surrounding oxygen tension, changed the pH of the tissue and resulted in lysis of the tissue. Increased bone resorption and osteoclast activity may be influenced by interleukin-6[10].

The osteolytic process is often painless allowing patients to continue with daily activities while bone destruction progresses, making the patient more susceptible to pathological fractures[11]. Onset of the disease is usually during childhood and early adulthood.

The disease is notoriously difficult to diagnose and is often diagnosed through a process of elimination of other osteolytic disorders. Heffez *et al*.[12] produced a set a diagnostic criteria to aid diagnosis:

1. a positive biopsy
2. absence of cellular atypia
3. minimal/no osteoblastic response and the absence of dystrophic calcification
4. evidence of local, progressive osseous resorption
5. non-expansile*, non ulcerative lesion
6. absence of visceral involvement
7. osteolytic radiographic pattern
8. negative hereditary, metabolic, neoplastic, immunologic or infectious aetiology.

*a number of cases presenting in the maxillofacial region present with an initial swelling.

In a review by Anavi *et al*.[13], the mean duration of symptoms before diagnosis was 6.4 years with the initial histopathologic diagnosis inaccurate in 45% of cases which highlights the difficulty faced by clinicians and pathologists when attempting to diagnose this condition. It is important to differentiate the disease from osteolysis caused by infection or inflammation (e.g. osteomyelitis or rheumatoid arthritis), endocrine disorders (e.g. hyperparathyroidism) and tumours (e.g. angiosarcoma, histiocytosis X)[14].

Radiographic features of Gorham's disease include a gradual coalescence of scattered radiolucencies over time, disappearance of lamina dura, porosis of trabecular structure and atrophy of bony contour[15,16]. However, radiographic presentation in the maxillofacial region, especially the teeth bearing regions of the mandible and maxilla, can strongly mimic the radiographic appearance of periodontal disease[17] despite adequate plaque control and a lack of gingival inflammation. Even though this presentation may occur in less than 25% of patients, it is an opportunity to diagnose the disease at an earlier stage, especially in the child patient in which periodontal pocket formation is very rare. Mandibular teeth mobility has been described as an early sign in the majority of patients with Gorham's disease of the jaws[5,6,17,18]. Radiographic evidence of bone loss, coupled with tooth mobility, may suggest a form of periodontal disease. However, the other clinical features of periodontal disease will not be present: oral hygiene will be satisfactory (with low plaque index scores), no signs of inflammation of the gingival tissues and no loss of attachment or presence of periodontal pockets[17]. Other symptoms may include pain, malocclusion, recurrent infection and involvement of the middle and inner ear.

Prognosis of the disease is dependent on which structures are involved. Lesions within the vertebral column and rib cage can potentially be fatal. Mandibular involvement is considered high-risk disease location as the disease can progress to involve the maxilla, skull and spine[17].

Currently, there is no recognised effective treatment for this disease. Surgical, radiation and medical therapies have been used with variable outcomes. Resection and bone grafting have always resulted in recurrences and failures[18]. Radiation therapy can be quite effective but its complications should be very carefully considered, especially in the child[19]. Several medical therapies have been tested often with poor outcomes. More recently, first generation biphosphonates have been reported to successfully arrest the course of osteolysis[14]. Zoledronic acid, a nitrogen-containing high-potency bisphosphonate, has been reported to be more potent and effective than the first generation bisphosphonates, and to have antiangiogenic properties in addition to osteoclast inhibition[20]. It has been proposed that this therapy could potentially be used in managing the active phase of the disease and could be offered as an

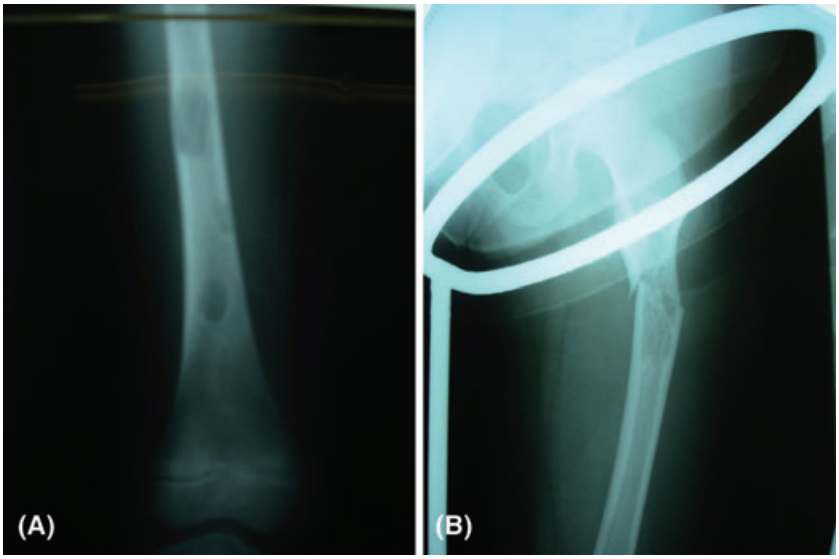

Figure 2 (A) Osteolytic changes in femur. (B) Pathogical fracture of femur.

alternative to radiotherapy. However, recently, it has been established that this mode of treatment is not without complications as bisphosphonates administered intravenously and orally have both been associated with osteonecrosis of the jaws[21].

Our case demonstrates how a patient with early signs of this rare condition may present to the dental surgeon. It also emphasises the difficulty of early diagnosis of the disease. The dental panoramic tomogram and lateral oblique views in our case show loss of dentoalveolar bone and a moth-eaten appearance to the supporting bone (Figs 1 & 2). Alveolar bone loss leads to generalised tooth mobility, which when coupled with signs of periodontal disease in a child should raise suspicions of systemic disease affecting the tooth supporting structures. Undoubtedly, this is easier to see in hindsight with the diagnosis known. Nevertheless, the overall clinical picture would not support a common dental disorder such as periodontal disease.

The presentation of generalised tooth pain and mobility in a child should raise the suspicion of a systemic disorder affecting the jaws. Gorham's disease is one such condition to consider.

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