

## Case Report

# Oral Aspects of Gaucher's Disease: A Literature Review and Case Report

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**Background:** Gaucher's disease (GD) is a lysosomal storage disease with a high incidence in Ashkenazi Jews. The disease is caused by an autosomally recessive inherited deficiency of the lysosomal enzyme glucocerebrosidase, leading to the accumulation of glucocerebroside in macrophages. The lipid-laden macrophages, called Gaucher cells, can be detected in liver, spleen, and bone marrow tissues.

**Methods:** A case report of periodontal treatment of a 47-year-old female patient with GD with recurrent gingival hemorrhage and toothache is presented. Periapical radiographs revealed cyst-like lesions in the mandibular premolar-molar regions accompanied by severe apical root resorption, enlargement of the periodontal ligament and bone-marrow spaces, and loss of trabecular structure and radiopaque appearance of bone. An abnormally narrow and sharp coronoid process and effacement of the cortical borders of the mandibular canal were noted.

**Results:** The patient was diagnosed as having generalized severe chronic periodontitis. Treatment included oral hygiene motivation and instructions, scaling, root planing, and access flap therapy, resulting in resolution of periodontal signs and symptoms and a marked improvement in the patient's feeling of well being.

**Conclusions:** Periodontal treatment can be effective in patients with GD. Oral findings may lead to early detection of GD, especially in the absence of clinical symptoms. Dentists should be aware of possible oral and radiographic manifestations of the disease and the role of periodontal treatment in improving patient's oral health and quality of life. J Periodontol 2007;78:783-788.

### KEY WORDS

Gaucher disease; gingival hemorrhage; oral manifestations; periodontal diseases.

Gaucher's disease (GD) is the most common entity among lysosomal storage diseases,<sup>1</sup> named after Philippe Ernst Gaucher, a medical student who in 1882 first described this disease as a clinical syndrome in a 32-year-old woman whose spleen and liver were enlarged.<sup>2</sup> The disease is an autosomal recessive trait characterized by a defect in acid  $\beta$ -glucocerebrosidase, an enzyme that cleaves glucocerebroside into glucose and ceramide. The defect is located in the long arm of chromosome 1, with >100 mutations identified related to the disease.<sup>3</sup> The defect causes glycolipid material to accumulate in macrophages termed Gaucher cells. The lipid-laden Gaucher cells can be detected in the liver, spleen, and bone marrow tissues.<sup>4</sup> Global prevalence of the disease is 1:50,000; however, among the Jewish population of Ashkenazi origin, prevalence is 1:400 to 1:865, ~50 times greater than the general population.<sup>5</sup> These figures may be underestimated, because some patients may be misdiagnosed or undiagnosed because of lack of symptoms.<sup>5</sup>

Three forms of GD are recognized by the existence and severity of the neural involvement: type 1 (chronic non-neuronopathic form), the most common type, showing a high prevalence in Ashkenazi Jews; type 2 (acute neuronopathic form), a lethal disease expressed first in infancy where death usually occurs by 2 years of age; and type 3 (subacute neuronopathic form), having a variable course in which death occurs in the second or third decade.<sup>6</sup>

Patients with GD present unique laboratory findings. Thrombocytopenia is common and may cause spontaneous bleeding and hemorrhaging.<sup>7</sup> Some patients, most commonly of Ashkenazi origin, show low levels of factor 11.<sup>8,9</sup> Most patients have anemia and neutropenia, exposing them to infections.<sup>10</sup> Among the clinical symptoms, splenomegaly is the most prevalent initial finding. Hepatomegaly is also a frequent finding.<sup>10</sup> The skeletal involvement is characterized by bone marrow infiltration of Gaucher cells and defective bone remodeling, leading to osteopenia, osteonecrosis, and avascular infarction. Pathologic fractures,

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avascular necrosis of the femoral head, and instability of the spine with consequent vertebral compression and spinal cord involvement can result in severe mobility impairment.<sup>11</sup> Pulmonary failure can result from both infiltration of the lung by Gaucher cells and vertebral collapse caused by compression.<sup>11</sup> The most common radiographic findings in long bones are osteopenia, loss of trabecular structure, cortical thinning, and radiolucent lesions.<sup>11</sup>

In the past, treatment of GD was only symptomatic. This included splenectomy to treat pressure on adjacent organs and analgesics for bone crises.<sup>12</sup> Today, enzyme supplement therapy is the treatment of choice given to most patients. Clinical trials show a dramatic response to intravenous administration, which include improvements in well-being and quality of life.<sup>12,13</sup>

Jaw involvement is often asymptomatic and can be detected as an incidental finding on routine dental radiographs.<sup>14</sup> Several radiographic findings in the jaw have been described: generalized osteopenia, loss of trabecular structure, effacement of lamina dura, displacement of the mandibular canal, pseudocystic radiolucent lesions, and apical root resorption of teeth adjacent to the lesions, all of which mostly appear in the mandible.<sup>15</sup>

Involvement of the maxillary sinus was reported in the literature only in a few cases.<sup>16,17</sup> Table 1 summarizes the common radiologic findings in patients with GD.

Oral findings include yellow pigmentation of the oral mucosa and patchiae.<sup>18</sup> Delayed eruption of permanent teeth was found in 56% of young patients <20 years of age and represented a difference between chronologic and dental ages.<sup>19</sup> In a survey conducted among patients and carriers of Jewish Ashkenazi ori-

gin, a correlation between gingival and decayed, missing, and filled surfaces (DMFS) indices and the clinical signs of GD could not be established.<sup>20</sup> Table 2 summarizes published articles depicting the oral aspects of GD, most of which are case reports.

### CASE DESCRIPTION

A 47-year-old Jewish woman of Ashkenazi origin was sent by her hematologist to the Unit of Periodontology, Rambam Health Care Campus. She complained of gingival hemorrhage and toothache, leading to avoidance of toothbrushing, dental phobia, and a severe gag reflex. The patient was diagnosed 20 years previously with type 1 GD. Additional diagnoses included factor 11 deficiency and essential hypertension. Treatment included daily oral beta blocker<sup>†</sup> and bi-weekly intravenous enzyme replacement therapy.<sup>§</sup> Hematologic laboratory tests at admission (partial thromboplastin time [PTT], prothrombin time [PT], bleeding time, and blood count) were within normal range except for a low platelet count (Table 3).

The clinical examination revealed patchiae in the mucosa of the right cheek (Fig. 1). There were large deposits of plaque and calculus, acute generalized gingival inflammation, spontaneous bleeding, and swollen, cauliflower-like papillae (Fig. 2). All teeth presented increased mobility and moderate to deep probing depths (5 to 10 mm). Missing teeth #1, #17, #18, #19, #29, and #32 were extracted in the past because of deep caries. Teeth #2, #15, and #16 were overerupted and in contact with the opposing edentulous ridge and presented poor plaque control.

Periapical radiographs showed advanced loss of alveolar bone and radiographically visible calculus deposits. Cyst-like lesions in the premolar-molar regions of the mandible accompanied by severe apical root resorption were identified (Fig. 3). Those teeth were vital. Enlargement of the periodontal ligament and bone marrow spaces, loss of trabecular structure, and radiopaque appearance of bone were also common findings (Fig. 4). An orthopantomograph revealed an abnormally narrow and sharp coronoid process and effacement of the cortical borders of the mandibular canal (Fig. 5). Also, deep carious lesions were identified in teeth #3 and #13.

The patient was diagnosed with generalized severe chronic periodontitis (differential diagnosis was periodontitis as a manifestation of systemic disease associated with a genetic disorder), caries, partial edentulism, and overeruption.

### TREATMENT COURSE

The initial cause-related therapy included oral hygiene instructions, scaling, and root planing. Carious

**Table 1.**

### Maxillofacial Radiologic Findings in Patients With GD\*

| Findings                                      | Percent of Total Sample<br>(28 patients) |
|---|--|
| Mandible involved                             | 84                                       |
| Maxilla and mandible involved                 | 16                                       |
| Generalized osteopenia                        | 20                                       |
| Enlargement of marrow spaces                  | 84                                       |
| Radiolucent lesions                           | 24                                       |
| Cortical thinning                             | 8  |
| External root resorption                      | 16                                       |
| Inferior displacement of the mandibular canal | 20                                       |

\* Adapted from Carter et al.<sup>19</sup>

† Atenolol, Teva Pharmaceutical Industries, Petach-Tikva, Israel.

§ Cerezyme Genzyme Therapeutics, Cambridge, MA.

**Table 2.**  
**Summary of Published Articles**

| Reference                        | Year | Report Type | Study Population  | Findings   |
|----------------------------------|------|-------------|---|--|
| Michanowicz et al. <sup>23</sup> | 1967 | CR          | 21-year-old Jewish patient with GD                            | Carious lesions, radiolucent lesions at the apices of mandibular molar roots, and generalized osteoporosis. Endodontic treatment and extractions performed without any complications.  |
| Weigler et al. <sup>22</sup>     | 1967 | CR          | 28-year-old Jewish patient with GD                            | Fractured lower molar tooth. Periapical radiograph revealed a large radiolucent lesion between lower left molars. Extraction performed without any complications.  |
| Bildman et al. <sup>14</sup>     | 1972 | CR          | 16-year-old black girl  | Orthopantomograph showed bilateral diffuse radiolucent areas in the mandible leading to the diagnosis of GD. A biopsy taken at the time of extraction of carious teeth confirmed the suspicion of GD.  |
| Sela et al. <sup>24</sup>        | 1972 | CR          | 67-year-old Jewish patient with GD                            | Autopsy findings showed involvement of the mandible expressed by histologic infiltration with Gaucher cells.   |
| Browne <sup>18</sup>             | 1977 | CR          | 39-year-old Jewish patient with GD                            | Poor oral hygiene. Yellow pigmentation of oral mucosa. Radiographic generalized loss of trabecular appearance and root resorption in the apices of mandibular molars. Periodontal therapy and extractions were performed without complications.                      |
| Regenye et al. <sup>21</sup>     | 1992 | CR          | 23-year-old patient with GD                                   | Involved in a motor vehicle accident. Presented with fractures of the mandible. Postoperative infection treated successfully with clindamycin. No excessive bleeding was noted during surgical procedures.   |
| Bender et al. <sup>15</sup>      | 1996 | R+CR        | 20- and 29-year-old patients with GD (one of whom was Jewish) | No hemorrhagic complications after extractions and periodontal scaling.<br><br>Improvement in the radiologic appearance of the mandible showed reconstruction of trabeculae and reduction of radiolucent lesions after several years of hormone replacement therapy. |
| Carter et al. <sup>19</sup>      | 1998 | CS          | 28 patients with GD   | Twenty-five of 28 patients showed radiographic evidence of jaw involvement.<br>Prevalent findings: widening of bone marrow spaces, cyst-like lesions, cortical thinning, root resorption, displacement of mandibular canal, and delayed eruption of permanent teeth. |
| Fischman et al. <sup>20</sup>    | 2003 | CS          | 87 patients and 31 carriers                                   | Despite prevalence of thrombocytopenia, gingival bleeding was not noted.<br>Although there was radiologic evidence of bone involvement, no greater incidence of tooth loss or mobility was found.  |

CR = case report; CS = case series; R = review.

lesions were restored with plastic restorations, root canal fillings, and provisional crowns. At reevaluation, there was considerable improvement in the patient's plaque control (Fig. 6). After initial preparation, a marked resolution of the inflammatory lesions was noted, with no residual gingival overgrowth. However, residual pockets of 5 to 7 mm and subgingival calculus deposits were recorded. Teeth #2, #15, and #16 still presented increased mobility and buccal and distal furcation involvement.

Access flap surgery was indicated to treat residual pockets and calculus deposits combined with extractions of teeth #2, #15, and #16.

Replacement of extracted and missing teeth was discussed with the patient before surgery. The option of dental implants was not recommended because of the quality of bone and lack of information on the predictability of implant therapy in patients with GD. A removable partial denture was rejected by the patient because of a severe gag

**Table 3.**  
**Case Presentation: Laboratory Test Results**

|  | At Admission | Before Surgery | Reference Range |
|--|--------------|----------------|-----------------|
| Red blood cell count ( $\times 10^3/\mu\text{l}$ )   | 6.00         | 6.66           | 4.8 to 10.8     |
| White blood cell count ( $\times 10^6/\mu\text{l}$ ) | 5.22         | 5.51           | 3.8 to 5.0      |
| Platelet count ( $\times 10^3/\mu\text{l}$ )         | 118          | 113            | 130 to 400      |
| PT (seconds)   | 11.0         | 10.6           | 8.5 to 12.5     |
| INR  | 1.12         | 1.06           | 0.75 to 1.3     |
| PTT (seconds)  | 40.8         | 40.4           | 30.0 to 42.0    |
| Bleeding time (minutes)                              | 3.2          | 3.5            | 1.00 to 4.50    |

INR = international normalized ratio.



**Figure 1.**  
Pathetchiae on the right cheek mucosa.



**Figure 2.**  
Acute generalized gingival inflammation, spontaneous bleeding, and swollen, cauliflower-like papillae. Note the multiple plaque and calculus deposits.



**Figure 3.**  
Radiolucent cyst-like lesions surrounded by a cortical envelope between the apices of lower premolar teeth. Note the external root resorption of first premolar. The teeth were vital.



**Figure 4.**  
Widening of the periodontal ligament (distal root of molar tooth), loss of trabecular appearance, and a radiopaque area in the periapical region. Note the multiple subgingival calculus deposits.



**Figure 5.**  
Abnormal coronoid process (narrow and sharp), unclear borders of the mandibular canal, radiolucent areas in the mandible, and loss of trabecular structure.

**Figure 6.**

After initial cause-related therapy, there was a major improvement in plaque control and shrinkage of gingival tissues.

**Figure 7.**

Clinical appearance 3 months after surgery.

reflex. Consequently, the short arch option was chosen.

The patient's hematologist was consulted before the surgical procedure and advised no preoperative hematologic preparation. Surgery was carried out under deep sedation. Flaps were raised in the areas of deep residual pockets, and debridement was carried out. In the course of surgery, there was increased bleeding from the sockets of the extracted teeth. Hemostasis was achieved by local application of oxidized, regenerated cellulose hemostat<sup>||</sup> into the sockets and mattress suturing. The patient was monitored for 24 hours before discharging from the hospital. Healing was normal without further complications. Porcelain metal crowns were fabricated and delivered for teeth #3 and #13 ~8 weeks after surgery. Three months after surgery, the patient presented with very good plaque control and residual pockets of 1 to 3 mm. Figure 7 shows the clinical appearance 3 months after surgery.

## DISCUSSION

The main potential surgical complication in GD, especially non-splenectomized patients, is excessive hemorrhaging caused by thrombocytopenia.<sup>15,18,21</sup> However, in most of the cases reported in the literature,<sup>14,15,18,21-23</sup> abnormal hemorrhaging was not reported, and healing was normal. In the present case, increased bleeding was indeed noted during extractions but was locally controlled, with no postoperative complications, similar to previous reports. However, it is recommended that the patient's physician be consulted before performing invasive procedures in patients with GD and that a complete blood count, including PT, PTT, bleeding time, and platelet count, be carried out as part of the initial examination and data collection.<sup>7,20</sup>

The present case presented a unique oral radiologic appearance in the mandible, which included bilateral cyst-like lesions in the lower molar-premolar

regions, accompanied by severe apical root resorption of adjacent teeth. The cyst-like lesions represent the pathognomonic enlargement of bone marrow spaces, probably caused by accumulation of Gaucher cells.<sup>18,19,25</sup> As in other reports, the patient presented with widening of the lamina dura and loss of trabecular structure. However, involvement of the maxillary sinus and displacement of the mandibular canal were not seen. Evidence of bone regeneration and a return to normal trabecular appearance after extractions was seen in our patient, corroborating previous reports.<sup>15,23</sup> A diffuse sclerotic radiopaque appearance as seen in the patient may resemble Paget's disease or fibrous dysplasia. The radiographic appearance may sometimes resemble plasma cell myeloma or cancerous spread, especially when accompanied with acute bone pain.<sup>15</sup> Autopsy findings in one of the reports<sup>24</sup> described replacement of bone marrow of the long bones and mandible with masses of Gaucher cells, a finding similar to the appearance of a neoplasm. Dental radiographs may lead to early detection of the disease, especially in the absence of clinical symptoms. Bildman et al.<sup>14</sup> described a case in which the disease was accidentally discovered in a 16-year-old girl who attended an oral surgery clinic for removal of multiple carious teeth. Bilateral diffuse radiolucent areas in the mandible were evident in a routine orthopantomograph and a biopsy taken from the extraction site confirmed the diagnosis of GD.

As a final note, the patient presented here reported improved well-being after active treatment. This subjective sign is a significant postoperative result, particularly in patients experiencing systemic disorders that severely affect their quality of life, such as GD.

## CONCLUSION

Oral findings may lead to early detection of GD, especially in the absence of clinical symptoms; therefore,

<sup>||</sup> Surgicel, Johnson & Johnson, Brunswick, NJ.

dentists should be aware of possible oral and radiographic manifestations of the disease.

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