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Case report

Extraosseous manifestation of Gaucher's disease type I: MR and histological appearance

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Abstract. Gaucher's disease type I is the most prevalent lysosomal storage disorder caused by an autosomal-recessive inherited deficiency of glucocerebrosidase activity with secondary accumulation of glucocerebrosides within the lysosomes of macrophages. The storage disorder produces a multisystem disease characterized by progressive visceral enlargement and gradual replacement of bone marrow with lipid-laden macrophages. Skeletal disease is a major source of disability in Gaucher's disease. Extraosseous extension of Gaucher cells is an extremely rare manifestation of skeletal Gaucher's disease. This is a report on the MRI and histopathological findings of an extraosseous Gaucher-cell extension into the midface in a patient with Gaucher's disease.

Key words: Gaucher's disease type I – Skeletal disease – Bone marrow imaging – MRI

Introduction

Gaucher's disease type I is the most common lysosomal storage disorder, caused by an autosomally inherited deficiency of glucocerebrosidase (acid β-Glucosidase). The undegraded glycosphingolipid accumulates specifically in cells of the monocyte–macrophage system producing hepatosplenomegaly and skeletal complications due to bone marrow infiltration [1, 2].

The clinical appearance of Gaucher's disease is manifested by progressive enlargement of the liver and spleen and gradual infiltration of the bone marrow by Gaucher cells. Anemia, thrombocytopenia, hepatosplenomegaly, and bone pain occur during the course of illness in most patients [3]. Bone involvement is a major complication of Gaucher's disease, affecting up to 80 % of patients [2].

Extraosseous extension of Gaucher cells is extremely rare [4]. To our knowledge, this is the first description of an extraosseous extension of Gaucher cells into the midface in a patient with Gaucher's disease type I. Magnetic resonance imaging and histopathological findings are presented.

Case report

A 47-year-old man was diagnosed with Gaucher's disease type I at the age of 20 years by liver and bone marrow biopsy. The genotype was L444P/L444P. Due to excessive splenomegaly, splenectomy had been performed in 1985. After removal of the spleen, the patient's condition deteriorated continuously with disabling bone pain and fatigue. Enzyme replacement therapy (ERT) was started in July 1995 after the diagnosis of severe skeletal involvement of the lower extremities was established through MRI. Imiglucerase (60 IU/kg b. w.) was administered intravenously every other week. During ERT fatigue resolved, bone pain improved dramatically, and the patient returned to work.

This patient presented with painful swelling of the right oral vestibulum und hypo-aesthesia of the right mental nerve. The patient was feverish (39.1 °C) and blood leukocytes were 11.5×10^3 cells/mm^3. Panoramic radiograph showed a generalized osteopenia of the mandible, cortical thinning, grossly widened marrow space, and frank radiolucency of the right mandible premolar–molar region. A submucosal dentogenic abscess was diagnosed. The lower right fourth, fifth, and seventh teeth were extracted and intraoral drainage was performed. Intraoperatively, gingival thickening and granulomatous tissue were observed in the right premolar–molar region. Postoperatively, penicillin G was given (5 million UI, three times per day). There was clini-

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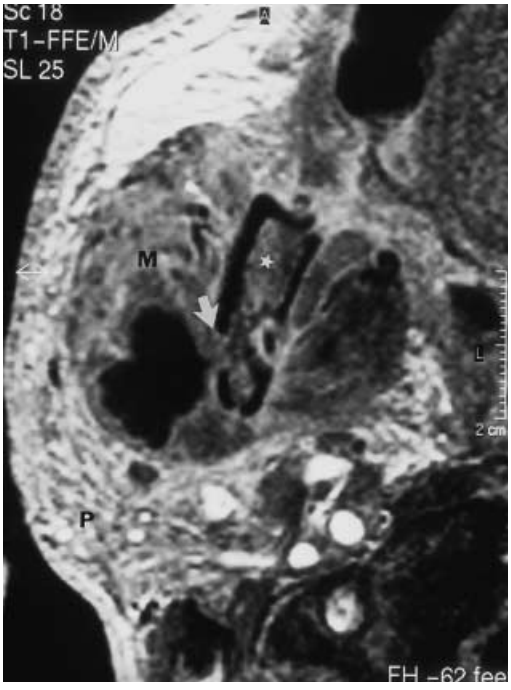

Fig. 1. Axial post-contrast T1-weighted 3D fast-field-echo image (slice thickness 0.5 mm) shows a hypointense tumor with a narrow neck of tissue *(arrow)* between the right mandible and the posterior part of the right masseter muscle. *M* masseter muscle; *P* parotid gland; *star* mandible; *L* left; *A* anterior

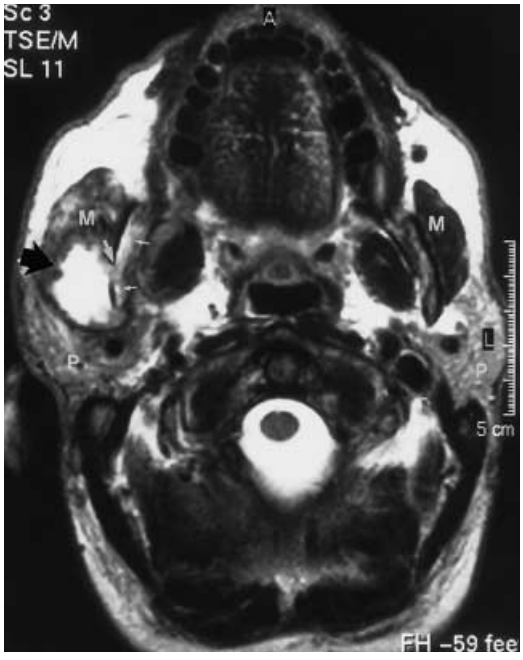

Fig. 2. Axial turbo spin-echo T2-weighted MR image of the midface shows the extraosseous extension of the mass within the right masseter muscle *(black arrow)*, appearing heterogeneous and hyperintense on T2-weighted images. The *white arrow* shows the destruction of the lateral cortical mandible. Note the hyperintense areas within the right mandibular cavity *(small white arrows)*. *M* masseter muscle; *P* parotid gland; *L* left; *A* anterior

cal, laboratory, and sonographic regression of infection and the patient was discharged after 14 days.

Five weeks later, the patient was referred again to the hospital for a right buccal soft tissue swelling. This time, panoramic radiograph revealed progressive radiolucencies of the right premolar–molar region.

Post-contrast T1-weighted images of the right midface showed a hypointense tumor within the posterior portion of the right masseter muscle. A narrow neck of tissue between mandible and masseter muscle was detected (Fig. 1). On T2-weighted images, the lateral area of the right mandible and the soft tissue tumor appeared heterogeneous and hyperintense (Fig. 2). Through a peroral incision, the liquid portion of the buccal tumor was drained. A biopsy of the right mandible and the soft tissue mass was performed. Histological examination revealed masses of Gaucher cells with lymphoid–plasmacellular infiltrations (Fig. 3). Swelling of the right buccal region resolved under i. v. antibiotics (amoxicilline 2.2 g three times per day) and the patient was discharged after 10 days with a mild residual soft tissue tumescence of the right masseter muscle.

Discussion

Skeletal involvement is a major source of disability in Gaucher's disease. Approximately 80% of patients have bone involvement, which results in serious complications in more than half of those affected [5, 6]. Clinical manifestations of skeletal bone disease include disabling bone pain, bone crises, bone deformities, and pathological fractures [2].

The MR appearance of bone marrow infiltration by Gaucher cells is characterized by an abnormal low signal intensity on T1- and T2-weighted images [7, 8] which reflects shortened T1 and markedly shortened T2 values in the replaced marrow [7]. It is well known from the literature that myelosclerosis, characterized by a decreased signal intensity on both T1- and T2-weighted images, can be secondary to Gaucher's disease [9].

Extraosseous extension of Gaucher cells is extremely rare. Hermann and co-workers reported on two Gaucher's disease patients with destruction of the femoral and tibial cortex, respectively, and extraosseous extension into soft tissue, mimicking malignancies [4]. In a study by Katz et al., 3 of 19 Gaucher patients with spinal involvement first diagnosed during childhood developed vertebral collapse with signs of root and cord compression as they grew [10]. Hermann et al. reported on three type-I Gaucher patients with epidural compression of the spinal cord [11].

Osseous lesions of the jaw are frequent in Gaucher's disease: A recent series described a prevalence of 89%, as evidenced by oral examination and panoramic radiographs. In that study the most prevalent findings were widening of the marrow cavity, frank radiolucencies, endosteal scalloping, cortical thinning, and root resorption [12].

In our patient panoramic radiograph showed progressive radiolucencies with cortical thinning and de-

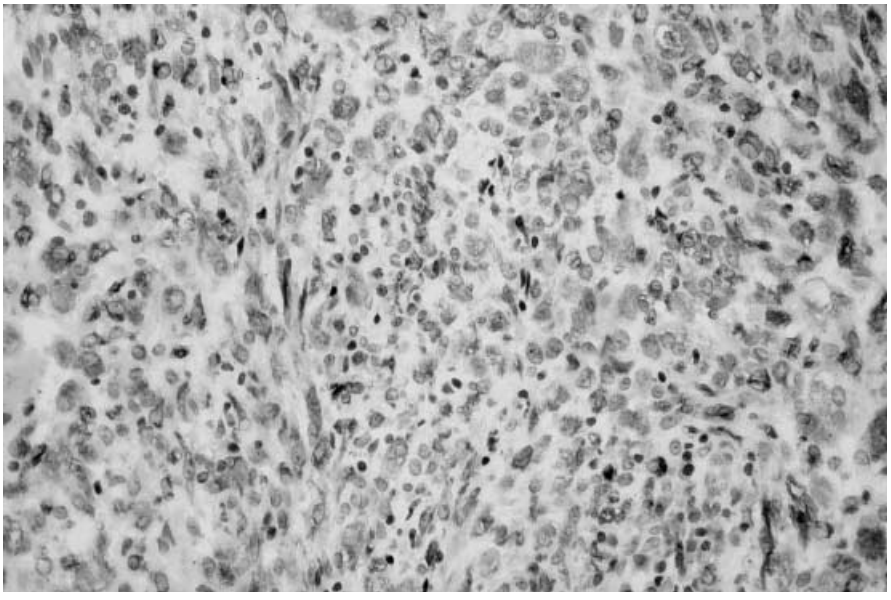

Fig. 3. Histological examination reveals numerous CD-68-positive Gaucher cells and lymphoid-plasmacellular infiltrations (original magnification, × 240)

struction, osteopenia, and a widened marrow space. Magnetic resonance imaging of the midface revealed an increase in signal intensity from T1- to T2-weighted images in the right mandible, indicating an active bone marrow process in Gaucher's disease [8]. The differential diagnosis of this signal appearance should reveal an osteomeylitis; thus, the biopsy and drainage did not reveal bacterial infection. Furthermore, hematological malignancies should be considered in the differential diagnosis since numerous case reports have documented the co-occurrence of Gaucher's disease and lymphoproliferative disorders including chronic lymphocytic leukemia, multiple myeloma, lymphoma, Hodgkin's disease and non-Hodgkin's lymphoma [13, 14, 15]. Shiran and co-workers demonstrated a 14.7-fold risk of hematological cancer and a 3.6-fold risk of cancer in 48 patients with Gaucher's disease as compared with 511 control subjects [16]. A case of extramedullary hematopoiesis, which might be a compensatory mechanism of secondary myelosclerosis [9], was described in a Gaucher patient, mimicking a paravertebral mass [17]. Kenan and co-workers described the unique case of an osteoblastoma of the humerus, simulating an extraosseous extension of Gaucher cells [18]. In our patient the presence of Gaucher cells within the marrow cavity probably weakened the cortex of the mandible. The original submucosal abscess and extraction of the teeth might have provoked cortical disruption, thereby alleviating extraosseous protrusion of bone marrow into the masseter muscle. Since 1990 an enzyme-replacement therapy (ERT) with modified placental glucocerebrosidase (Alglucerase, Ceredase®, Genzyme Corporation, Cambridge, Mass.) has been shown to arrest or reverse visceral, hematological, biochemical, and skeletal abnormalities, and to improve quality of life in patients with type-I Gaucher's disease [19, 20]. Recently, a modified recombinant glucocerebrosidase (Imiglucerase, Cerezyme®, Genzyme Corporation, Cambridge, Mass.) has been introduced.

In conclusion, MR imaging can be useful in evaluating the stage of skeletal involvement in Gaucher's disease and its complications, and provides a sensitive diagnostic method in monitoring the effects of ERT [7, 20, 21].

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