Alternative Pharmacologic Therapy for Aggressive Central Giant Cell Granuloma: Denosumab

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In the search for new pharmacologic therapies for central giant cell granuloma (CGCG), proteins that are essential to osteoclastogenesis are intriguing potential targets. In the present case report, we describe a 25-year-old patient with an aggressive CGCG of the maxilla, who was successfully treated with the antiresorptive agent denosumab, after other pharmacologic treatment had failed to achieve regression or stabilization of the tumor. Denosumab could be a promising alternative to potentially mutilating surgery for CGCG. However, more research is needed before definite conclusions can be drawn about the potential role of this agent in the treatment of CGCG.

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Central giant cell granuloma (CGCG) is a rare benign osteolytic lesion of the jawbone. A 5-year population-based study estimated its incidence at 0.00011%.[1] It was first described by Jaffe[2] as a reactive-reparative process. However, it is now considered to be a true neoplasm.[3]

The most common treatment has been surgical curettage. However, recurrence rates of 11 to 72% have been reported in published studies, especially for the so-called aggressive lesions.[4] In the past 2 decades, a number of pharmacologic therapies have been described.[4] Pharmacologic treatment offers the advantage of preventing, or at least minimizing, extensive and mutilating surgical procedures, which have been characterized by detrimental functional outcomes, an inevitable loss of teeth and nerve function, and altered facial contours. Until now, the most common and successfully applied pharmacologic agents have been intralesional corticosteroid injections and systemic treatment with calcitonin or interferon alfa-2a.[5-7]

The proteins that play a role in osteoclastogenesis have been hypothesized to be a possible target in the systemic treatment of CGCG.[4] The discovery and subsequent understanding of the essential role of the receptor activator of nuclear factor kappa-B (RANK)/receptor activator of nuclear factor kappa-B ligand (RANKL)/osteoprotegerin (OPG) pathway in bone biology has opened the door to new potential therapeutic targets.

Denosumab is a monoclonal antibody against RANKL and was developed as a treatment for osteoporosis. It is an effective antiresorptive agent and could be useful in the treatment of other skeletal diseases with excessive osteoclast activity, such as CGCG. In the present report, we describe a patient with an aggressive CGCG. She was treated with denosumab after other pharmacologic

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treatments had failed to achieve regression or stabilization of the tumor.

Case Report

A 25-year-old woman with a history of type I diabetes was referred because of a progressive swelling of her anterior maxilla. Histopathologic examination of a biopsy specimen confirmed the diagnosis of CGCG (Fig 1A). Hyperparathyroidism was excluded by the results from laboratory investigations.

The clinical examination showed severe protrusion of the upper lip and flattening of the nasolabial folds (Fig 2A). On intraoral examination, a firm swelling

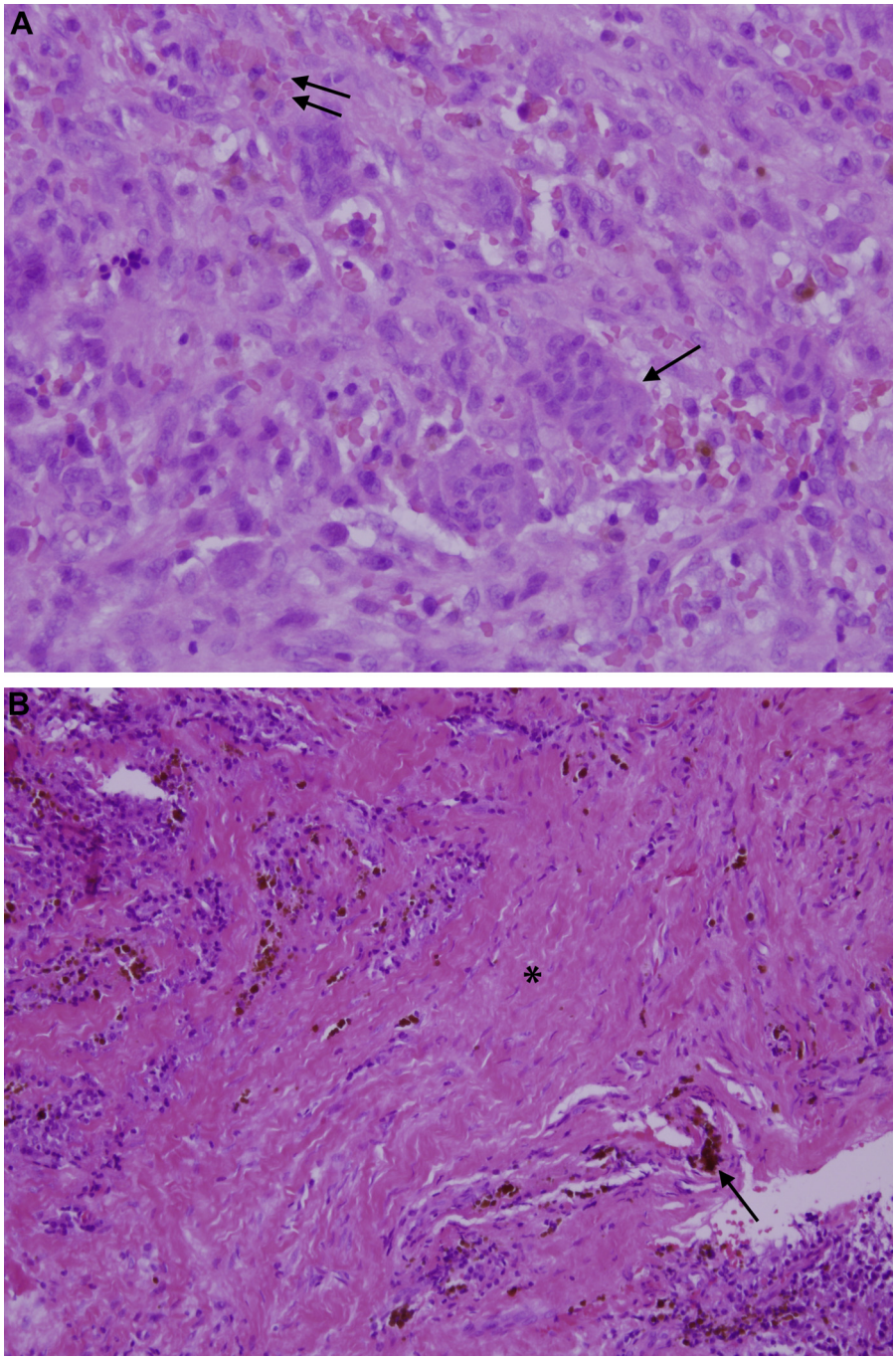

FIGURE 1. *A,* Histopathologic appearance before treatment. Hematoxylin-eosin–stained section demonstrating a highly cellular lesion with mononuclear macrophage-like cells and spindle-shaped fibroblastic cells. Multinuclear osteoclast-like giant cells are dispersed throughout the lesion (*arrow*). Extravasated erythrocytes (*double arrow*) were present, with areas of hemosiderin deposits (not shown). *B,* Histopathologic appearance after treatment. Hematoxylin-eosin–stained section demonstrating fibrotic tissue (*asterisk*) with signs of mild chronic infection and old hemorrhage (hemosiderin deposits; *arrow*). No signs were seen of the earlier diagnosed central giant cell granuloma.

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