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Locally Advanced Giant Cell Tumor of the Sphenoid Bone in an Adolescent: Spectacular Response to Denosumab Enabling Conservative Management

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Abstract **Case Report**

Giant cell tumor of bone (GCTB) is a locally aggressive neoplasm that rarely involves the skull base. We report the case of a 15-year-old girl with a primary sphenoid GCTB presenting with progressive visual impairment, diplopia, and strabismus. Imaging revealed an extensive locally aggressive sphenoid lesion involving critical skull base structures. After initially non-contributory biopsies, a repeat sphenoid biopsy established the diagnosis of GCTB based on morphological and immunohistochemical findings. Given the challenging location and the high morbidity associated with surgical resection, treatment with denosumab was initiated. The patient experienced rapid improvement in visual function after the first injection, followed by sustained clinical improvement and a favorable radiological response with tumor regression and calcification. Multidisciplinary reassessment ultimately supported continuation of medical therapy without surgery. This case highlights the potential of denosumab as an effective, function-preserving therapeutic strategy for selected patients with locally advanced sphenoid GCTB, allowing sustained disease control while avoiding high-risk surgery.

Keywords: giant cell tumor of bone, sphenoid bone, skull base, denosumab, adolescent, visual recovery.

INTRODUCTION

Giant cell tumor of bone (GCTB) is a usually benign but locally aggressive osteoclastogenic stromal tumor, accounting for approximately 3–5% of primary bone tumors and classically arising in the epiphyseal regions of long bones in young adults [1,2]. Skull involvement is exceptional, representing less than 1% of GCTB; when present, the sphenoid and temporal bones are favored sites [3,4]. Sphenoid GCTB may produce diplopia, visual impairment, headache, and cranial nerve palsies because of its close relationship with the cavernous sinuses, optic pathways, sella, and skull base [3]. Surgery remains the preferred treatment when complete resection can be achieved safely, but radical surgery may carry substantial neurological and functional morbidity. Denosumab, a monoclonal antibody targeting RANKL, provides an important option for unresectable disease or when surgery would cause major morbidity [1,5]. We describe an adolescent with an extensive sphenoid GCTB and severe neuro-ophthalmological manifestations who experienced rapid visual recovery and sustained radiological control with denosumab, allowing conservative management.

CASE REPORT

A 15-year-old girl with no significant medical history developed right-sided strabismus in August 2024. Progressive visual impairment and diplopia prompted cerebral MRI on August 28, 2024, which demonstrated an aggressive 50 × 34 × 30 mm soft-tissue lesion centered on the sphenoid sinus. The lesion caused sphenoid wall destruction and involved the sella turcica and bilateral cavernous sinuses, with extension to the posterior-superior nasopharynx. The initial radiological differential diagnosis included a locally advanced nasopharyngeal malignancy.

A first nasopharyngeal biopsy in September 2024 showed only nonspecific subacute inflammatory changes. Because symptoms continued to worsen, additional biopsies were performed. A sphenoid sinus biopsy obtained in December 2024 demonstrated a tumor composed of diffuse sheets of mononuclear cells admixed with numerous large multinucleated giant cells. The nuclei of both components were cytologically similar, with fine chromatin and no significant atypia; no tumor necrosis was identified. Immunohistochemistry

showed positivity for CD68 and p63 and absence of CKAE1/AE3 expression. Central pathology review confirmed a giant cell tumor.

By late December 2024, the patient had bilateral strabismus, progressive loss of visual acuity, diplopia, left nasal congestion, and impaired abduction of the left eye suggestive of sixth cranial nerve palsy. Repeat MRI on December 25 showed a large, lobulated, locally aggressive sphenoid lesion extending to the right orbit, sellar floor, cavernous sinuses, temporal fossae, and posterior cranial fossa, with marked mass effect on adjacent structures.

The case was reviewed multidisciplinary. Radiotherapy was not retained, and the patient was referred for systemic treatment because local surgery was considered difficult and potentially morbid. Denosumab was started in February 2025 at 120 mg subcutaneously on day 1 with loading doses on days 8 and 15, then every 28 days. Dental evaluation and calcium/vitamin D supplementation were incorporated into treatment monitoring. Strikingly, visual function began to recover after the first injection and continued to improve during subsequent cycles.

The patient remained clinically well on monthly denosumab. MRI performed on September 29, 2025 showed reduction of the sphenoid lesion from 47 × 49 mm to 40 × 45 mm (approximately 14%). Subsequent multidisciplinary neurosurgical review noted important tumor reduction and treatment-associated calcification, interpreted as favorable response. Given the marked clinical improvement and radiological control, surgery was no longer considered indicated and conservative medical management was continued. At the latest documented follow-up 2026, the patient was clinically well and continued denosumab 120 mg monthly and showed a very favourable clinical response.

Discussion

Sphenoid GCTB is exceptionally rare. A recent systematic review identified only 79 previously reported sphenoid cases, with most patients presenting in the second or third decade and with symptoms caused by local mass effect, particularly diplopia, ophthalmoplegia, cranial nerve III or VI palsy, and decreased vision [3]. The present case is notable for the patient's young age, extensive skull-base involvement, diagnostic delay after initially negative biopsies, and rapid functional response to systemic therapy.

Histologically, GCTB consists of neoplastic mononuclear stromal cells accompanied by mononuclear histiocytic cells and osteoclast-like multinucleated giant cells. H3F3A/H3.3 G34 alterations are highly characteristic and can aid difficult diagnoses [3]. Molecular testing was not available in our patient; therefore, the diagnosis rested on morphology, immunophenotype, radiological features, and expert pathology review. This limitation should be acknowledged, particularly because giant-cell-rich lesions of the skull base have a broad differential diagnosis.

Complete resection is generally preferred for accessible disease, but sphenoid tumors frequently surround critical neurovascular structures. In the 2026 systematic review, most reported patients underwent surgery, often subtotal, while denosumab was used only in a small number of cases [3]. Denosumab blocks RANKL-dependent osteoclast formation and activity. Large phase II studies in adults and skeletally mature adolescents have demonstrated durable disease control and avoidance or reduction of morbid surgery in many patients with advanced GCTB [1,5]. A published sphenoid GCTB case also demonstrated tumor shrinkage and peripheral calcification after short-term denosumab [4].

Our patient's response was clinically more striking than suggested by dimensional change alone: visual recovery began after the first dose, while later imaging showed modest size reduction and calcification. This illustrates an important feature of denosumab-treated GCTB: therapeutic benefit may include ossification, reduced osteolysis, and functional improvement without dramatic RECIST shrinkage [4,6]. The treatment is not without risk. Long-term series report hypophosphatemia, osteonecrosis of the jaw, atypical femoral fracture, and hypercalcemia after discontinuation, supporting careful dental, calcium/phosphate, vitamin D, and long-term clinical monitoring [1]. In a young patient, treatment duration and eventual discontinuation require individualized multidisciplinary assessment.

Conclusion

Locally advanced sphenoid GCTB can threaten vision and neurological function while being poorly suited to radical surgery. In this adolescent, denosumab produced very rapid visual improvement, sustained disease control, tumor shrinkage, and calcification, ultimately allowing a nonoperative strategy. Denosumab can therefore be a valuable function-preserving option for carefully selected sphenoid GCTB when surgery is unresectable or expected to cause major morbidity. Long-term surveillance remains essential.

Patient Consent

Informed consent for publication of this case and any accompanying anonymized clinical images was obtained from the patient's legal guardian.

Ethical Statement

This report describes routine clinical care. Institutional ethics committee approval was not required

for a single anonymized case report according to local policy.

Conflict of Interest: The authors declare no conflicts of interest.

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