

# Giant Cell Tumor of the Lateral Skull Base: Diagnostic and Management Options

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## Abstract

### Keywords

- ▶ giant cell tumor of bone
- ▶ lateral skull base tumor
- ▶ neurosurgery
- ▶ osteoclastoma
- ▶ radiotherapy

Giant cell tumor of bone (GCTB) is a rare, benign, osteolytic neoplasm that most commonly occurs in early adulthood and often involves the long bones of the body. Although GCTB largely affects the epiphyses of long bones, several reports of GCTB involvement of the cranial and facial bones exist in the literature. In addition to reviewing other reported cases of GCTBs of the lateral skull base in the literature, the authors report here on the clinical presentation, radiographic findings, and neurosurgical management of a patient found to have a GCTB of the middle and infratemporal fossae, which was treated by aggressive en bloc resection of the lateral skull base.

## Introduction

Giant cell tumor of bone (GCTB; or osteoclastoma) is an uncommon, benign, osteolytic neoplasm. GCTB comprises 3 to 5% of all primary bone tumors and occurs predominantly in early adulthood (peak incidence ages, 20–40 years) with a slight female predominance (3:2).<sup>1–3</sup> These tumors are thought to originate from neoplastic nonosteogenic stromal cells of the bone marrow and are characterized histologically by numerous multinucleated osteoclastic giant cells diffusely distributed among a background of mononuclear stromal and macrophage lineage cells.<sup>1,4–6</sup> GCTB most commonly affects the epiphyses of long bones, particularly of the distal femur and proximal tibia.<sup>6</sup> Patients classically present with a combination of pain, swelling, or pathologic fracture at the tumor origin.<sup>7</sup> Although regarded as benign, GCTB can recur locally following en bloc surgical resection.<sup>8,9</sup> In 2 to 3% of cases, GCTBs can hematogenously metastasize to the lungs, resulting

in benign pulmonary implants with rare malignant transformation.<sup>9,10</sup> Despite an improved understanding of the molecular and cellular biology underlying the GCTB pathogenesis, the behavior of this tumor is often heterogeneous and can be difficult to predict on the basis of clinical, radiographic, or histologic features.

Although involvement of the appendicular skeleton is more typical for GCTB, axial skeleton involvement, especially of the cranial and facial bones, has also been reported and is becoming increasingly appreciated in the literature. Approximately 2% of GCTBs involve the head and neck.<sup>11–13</sup> Involvement of the axial skeleton is often associated with increased morbidity because of local infiltration of critical structures and the associated difficulty of complete tumor resection, particularly compared with resection of GCTBs of the appendicular skeleton.<sup>8,14</sup> GCTB of the skull has also been reported to behave in a locally aggressive fashion.<sup>15</sup> Nevertheless, surgery remains the treatment of choice for GCTBs, including those in the skull,

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with en bloc or wide local excision portending the lowest risk of recurrence and best clinical outcomes in patients.<sup>4,16</sup> Although much research has focused on GCTBs involving the long bones, numerous studies have also reported on GCTBs involving the lateral skull base. Here, we review other reported cases of GCTBs involving the lateral skull base and report on the clinical presentation, radiographic findings, neurosurgical management, and outcome of a patient with a GCTB of the middle and infratemporal fossae.

## Methods

A literature search was performed using the PubMed/Medline database for cases of GCTB of the lateral skull base. The literature search spanned articles published between 1970 and June 2017. The keywords utilized in the search included: "giant cell tumor of bone," "GCTB," "GCT," "osteoclastoma," "lateral skull base," and "skull base tumor." The list of publications was reviewed for articles with relevance to our study (i.e., reports of GCTB of the lateral skull base). Full-text articles in the English language were reviewed and chosen based on whether they included a reported case of a patient with a GCTB involving the lateral skull base.

## Case Report

### History and Examination

A 22-year-old man presented to the neurosurgical service after sustaining a traumatic brain injury when he was hit by a vehicle while riding his bike without a helmet. The patient experienced a brief loss of consciousness at the scene and reported a nonfluctuating headache. He was taken to an outside hospital, where a noncontrast head computed tomography (CT) scan demonstrated a left temporal intraparenchymal hemorrhage, left temporal bone fractures, multiple

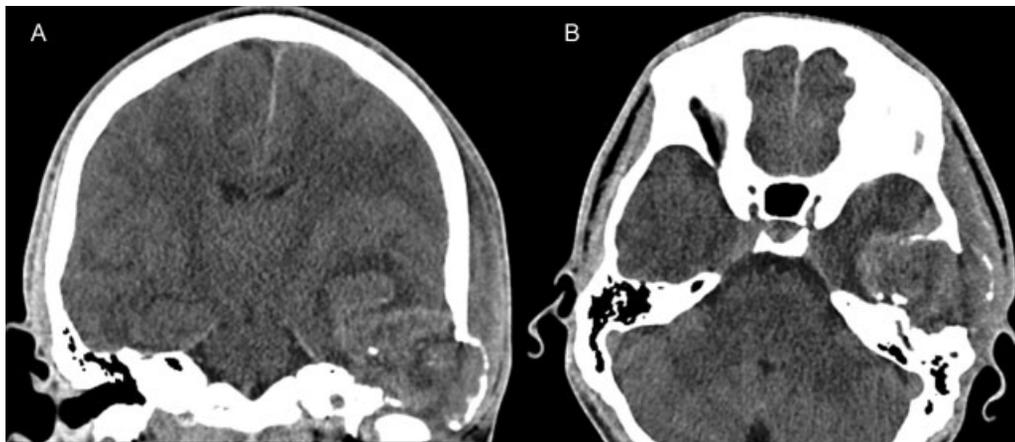
facial bone fractures, and an incidental lytic bone mass of the left lateral skull base (►Fig. 1). The patient was transferred to our institution for further evaluation.

Upon additional history gathering, the patient reported decreased hearing in the left ear over several months, as well as a recent slight bulging of his left face. On examination, the patient was awake, alert, and oriented to person and place. Cranial nerves were grossly intact, except for diminished sensorineural hearing in his left ear. Motor and sensory examinations were grossly intact throughout. He underwent diagnostic magnetic resonance imaging (MRI), which revealed a large tumor extending from the middle cranial fossa into the infratemporal fossa, with an associated intraparenchymal hemorrhage involving the left temporal lobe (►Fig. 2). Given this finding, the patient was taken to the operative theater for tumor resection.

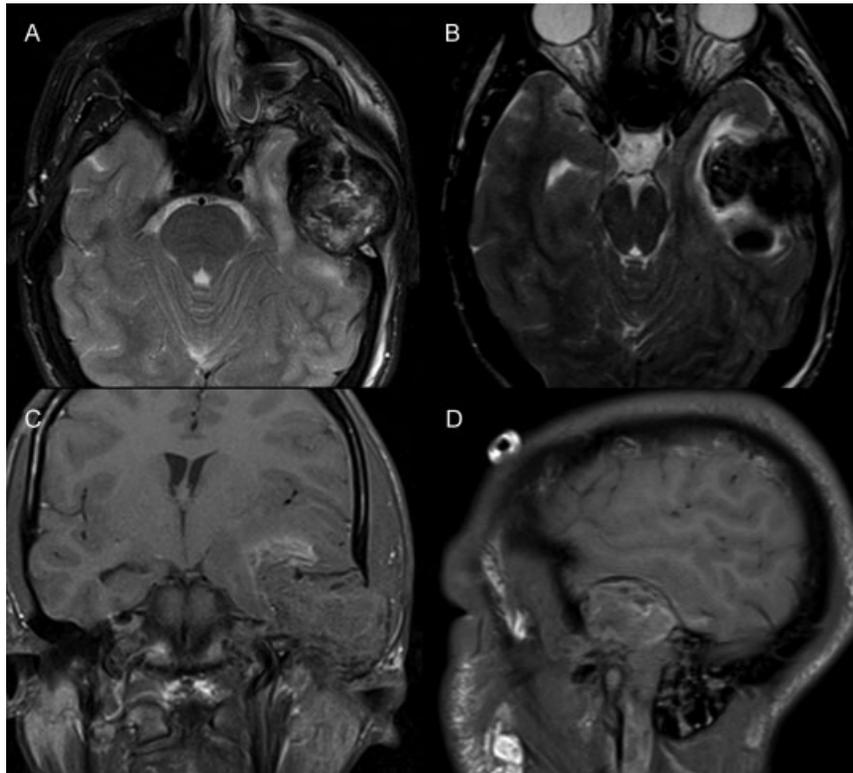
### Operative and Postoperative Course

The patient was positioned supine and secured in a Mayfield frame for microsurgical resection of the lesion. Given the infratemporal extension of the tumor, a Fisch-type approach was utilized, with a preauricular incision providing access to the infratemporal and intracranial components of this neoplasm. After elevation of the temporalis muscle, the tumor was found to be intimately involved with the bony structures. Frozen and eventual final pathology samples were consistent with a giant cell tumor without malignant features (►Fig. 3). Accordingly, a gross total resection of the tumor with negative margins was performed.

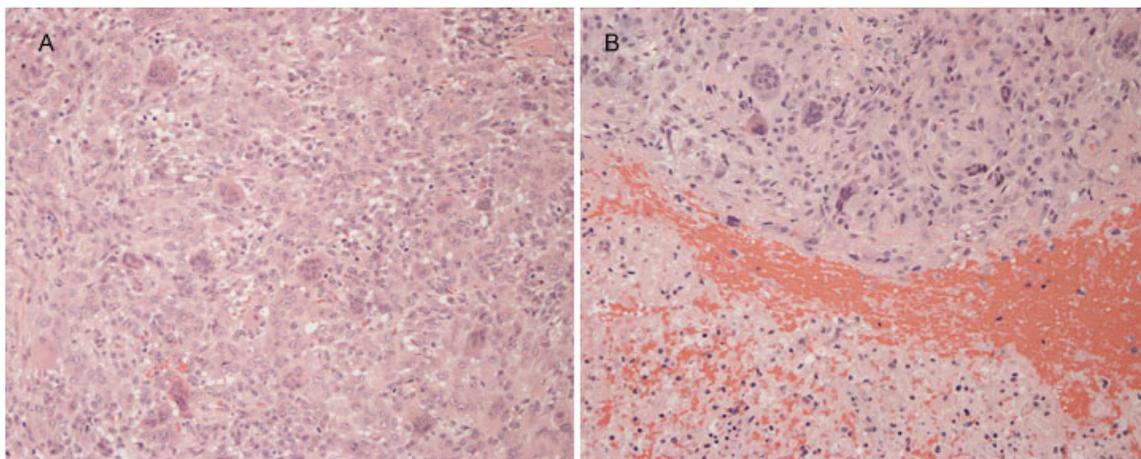
The temporal bone was drilled thoroughly with sacrifice of the left vestibulocochlear nerve to attain adequate margins. The left facial nerve was identified and skeletonized to protect and preserve function. Tumor-infiltrated temporal, frontal, and zygomatic bones were removed. Tumor feeding vessels arising from the superficial and deep temporal



**Fig. 1** Preoperative head computed tomography (CT) showing giant cell tumor of bone (GCTB) arising from the left lateral skull base. (A) Coronal head CT without contrast demonstrating a lytic mass of the left squamous part of the temporal bone with extension into the left sphenoid bone, mastoid air cells, and middle ear cavity. Imaging demonstrates destruction of the left lateral wall of the middle cranial fossa with bony fragment displacement laterally, medially, and inferiorly. The mass is also associated with intracranial hemorrhage and air within the hematoma that extends into the left temporal lobe. Moderate mass effect is present with left-to-right shift. (B) Axial head CT without contrast showing a lytic mass originating from the squamous part of the temporal bone. Imaging also reveals comminuted left orbital fractures, left maxillary sinus fractures, and a left zygomatic arch fracture.



**Fig. 2** Preoperative magnetic resonance imaging (MRI) of giant cell tumor of bone (GCTB) arising from the left lateral skull base. (A) Axial T2-weighted MRI demonstrating destructive heterogeneous, hypointense, peripherally enhancing lesion centered in the left squamous part of the temporal bone that measures  $4.5 \times 4.0 \times 4.9$  cm. (B) Axial T2-weighted MRI demonstrating hypointense mass with extension anteriorly into the left sphenoid bone. Imaging is notable for intracranial extension, mass effect on the left temporal lobe, and surrounding vasogenic edema. Midline shift of  $\sim 5$  mm is present with early left uncus herniation, effacement of the left ambient cistern, and compression of the midbrain. (C) Coronal T1-weighted MRI demonstrating a mass arising from the squamous part of the temporal bone and extending into the left temporal lobe. (D) Sagittal T1-weighted MRI demonstrating anteroposterior and craniocaudal extension of the tumor.

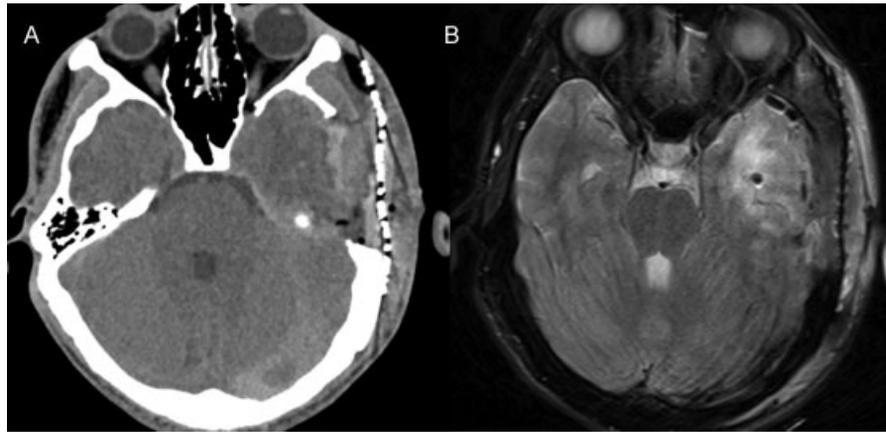


**Fig. 3** Photomicrograph of hematoxylin and eosin (H&E)-stained histopathologic specimens from a patient with giant cell tumor of bone (GCTB) of the infratemporal fossa. (A) H&E stained specimen ( $100 \times$ ) demonstrating numerous multinucleated osteoclastic giant cells distributed diffusely among a background of neoplastic mononuclear stromal cells and mononuclear macrophage lineage cells. (B) H&E stained specimen ( $100 \times$ ) demonstrating tumor necrosis with nearby multinucleated osteoclastic giant cells and mononuclear stroma cells.

arteries were coagulated to devascularize the tumor. Normal bony margins were obtained. With respect to the intracranial compartment, tumor involving the dura was resected. In addition, upon reflection of the dura, the tumor was found to involve the left lateral temporal lobe, causing hemorrhage

and mass effect. The left temporal lobe involved by the tumor was surgically resected.

At the completion of the procedure, the facial nerve was stimulated to ensure its integrity, and meticulous hemostasis was obtained. To repair the skull base defect, mesh



**Fig. 4** Postoperative computed tomography (CT) and magnetic resonance imaging (MRI) demonstrating gross total resection of giant cell tumor of bone (GCTB) of the left lateral skull base with mesh cranioplasty. (A) Axial head CT without contrast demonstrating postsurgical changes. Comminuted left orbital and maxillary sinus fractures are present. (B) Axial T2-weighted MRI demonstrating postsurgical changes from left temporal bone craniectomy, tumor resection, and mesh cranioplasty. Imaging shows no signs of residual disease. Complete surgical resection with resultant decompression and normalization of midline shift is apparent on postoperative imaging.

cranioplasty with polymethyl methacrylate was fashioned to a normal cranial contour. A small amount of superficial fat was placed into the site of the defect. MRI demonstrated complete removal of the tumor in this patient (► Fig. 4). Postoperatively, the patient had nonserviceable hearing in the left ear, but was otherwise neurologically intact, including preservation of the facial nerve function, and was discharged home on postoperative day 5. No adjuvant radiation was planned. At the 3-month follow-up, the patient was neurologically intact but did require cerebrospinal fluid diversion for a hygroma.

## Results

► **Table 1** summarizes the cases of tumors involving the lateral skull base identified in our review of the English language literature. Including our case, a total of 94 patients with GCTBs of the lateral skull base were identified through our review. As an aggregate, 56% of patients were male (53/94), while 44% were female (41/94). The mean age at presentation was 36.8 years (range: 0.17–79 years). Clinical presentations were variable and included headache (33%, 29/88), hearing loss (31%, 27/88), facial/preauricular swelling (22%, 19/88), facial/preauricular pain (17%, 15/88), tinnitus (15%, 13/88), aural fullness (10%, 9/88), diplopia (10%, 9/88), vision loss (10%, 9/88), ear pain (8%, 7/88), facial nerve palsy (8%, 7/88), proptosis (5%, 4/88), and dizziness (5%, 4/88). GCTB origin, in order of frequency, was temporal bones (62%, 58/94), sphenoid bones (32%, 30/94), occipital bones (5%, 5/94), and frontal bones (1%, 1/94).

Treatment data were reported for 91 patients. Of these patients, 52% (47/91) received gross total resections, 46% (42/91) subtotal resections, and 2% (2/91) did not receive treatment. Of 90 patients with clear documentation, 37% (33/90) received adjuvant radiotherapy following surgical treatment.

Of patients with reported follow-up, 14% (12/86) had local disease recurrence. In addition, of those patients with recurrence, 50% (6/12) had received subtotal resections alone, 25% (3/12) received subtotal resections with adjuvant radiother-

apy, and 25% (3/12) received gross total resections alone. Of note, no patients receiving gross total resections with adjuvant radiotherapy developed recurrence ( $n = 4$ ).

## Discussion

GCTB is considered a benign, but locally aggressive, neoplasm of bone. These tumors are thought to originate from nonosteogenic neoplastic stromal cells of the bone marrow admixed with multinucleated osteoclastic giant cells.<sup>1,6</sup> GCTBs most commonly affect the epiphyses of long bones, but have also been appreciated in the cranial and facial bones, including the skull base.<sup>6</sup> Although considered a benign lesion, GCTB has a variable natural history, with the risk of local recurrence or distant metastasis being highly unpredictable. Unlike other types of cancer, metastatic spread of GCTB does not carry similar prognostic implications.<sup>17</sup> Despite improved understanding of the underlying cellular and molecular biology underpinning GCTB pathogenesis, our knowledge regarding this tumor's behavioral heterogeneity remains incomplete.

GCTBs of the cranial and facial bones most commonly affect the temporal and sphenoid bones.<sup>14,15,18–20</sup> GCTBs of the lateral skull base are often locally aggressive and can invade nearby critical structures.<sup>18,21</sup> It is believed that these tumors arise in these areas because the bones of the mandible, sphenoid, ethmoid, and parts of the temporal bone form largely through the process of endochondral ossification.<sup>22</sup> In contrast, the other cranial bones (i.e., frontal and parietal bones) arise from intramembranous ossification and are less frequently affected by GCTB.<sup>15,22</sup> Patients with GCTB of the temporal bone typically present with headache, conductive hearing loss, aural fullness, preauricular pain, or facial weakness.<sup>18,20,23</sup> In comparison, patients with GCTB of the sphenoid bone may present with symptoms such as headache, facial hypoesthesia, diplopia, blindness, or visual field defects.<sup>18,19</sup>

Both CT and MRI are used to identify and characterize GCTB of the lateral skull base. On CT imaging, GCTBs usually

**Table 1** Review of our case and cases in the literature of giant cell tumors of bone involving the lateral skull base

Study	Patient age (y)	Patient sex	Presentation	Location	Operative technique/ approach	Extent of resection	Adjuvant RT	Recurrence, follow-up (mo)
Carmody et al, 1983 <sup>35</sup>	16	M	Progressive diplopia, esotropia of R eye	Sphenoid bone and sinus, involvement of ST	Subfrontal craniotomy	STR	Y	N, 10
Wolfe et al, 1983 <sup>19</sup>	25	F	HA, blindness in L eye, visual field loss in R eye	Sphenoid bone and ST	Craniotomy (NFS)	STR	Y	N, 168
	16	F	HA, diplopia, blurred vision	Sphenoid bone and sinus w/ involvement of ST, clivus	Transseptal biopsy and surgical decompression	STR	Y	N, 96
	19	F	Diplopia, progressive loss of vision	Sphenoid bone and sinus	Frontal craniotomy	STR	Y	N, 132
	20	M	HA, blurred vision, facial nerve palsy, R-sided spastic hemiparesis	Sphenoid bone, petrous part of temporal bone, clinoid	Craniotomy (NFS)	GTR	Y	N, 12
Motomochi et al, 1985 <sup>36</sup>	69	M	Memory loss and expressive dysphasia	ST	Craniotomy (NFS)	GTR	N	N, 9 days
	35	M	HA	ST	Craniotomy (NFS)	STR x2	Y	N, 21
	16	M	Diplopia, visual field loss	Sphenoid bone and ST	Craniotomy (NFS)	STR	Y	N, 31
Kiwit et al, 1986 <sup>37</sup>	19	M	HA, diplopia, L eye pain, R-sided ptosis	Sphenoid bone and ST	Oropharyngeal biopsy, transsphenoidal biopsy, and decompression	STR	Y	N, 6
	38	M	Chronic R-sided otitis media	Temporal bone	Temporal craniectomy with Y-shaped incision and retroauricular approach	STR	Y	N, 11
Findlay et al, 1987 <sup>23</sup>	53	M	HA, dysphagia, dysarthria	Occipital bone	Suboccipital craniectomy	STR	Y	N, 26
	46	F	L-sided hearing loss and tinnitus, L facial palsy	Petrous part of temporal bone	NA	GTR	N	Y, 60
Tandon et al, 1988 <sup>38</sup>	23	M	R-sided hearing loss and otalgia, R facial palsy	Temporal bone	R ECA ligated preoperatively. R subtemporal approach	STR	Y	N, 8
	33	M	NA	Temporal bone w/ involvement of sphenoid bone	Ablative surgery with Weber-Fergusson incision and transection of zygoma	GTR	N	N, 11

(Continued)

**Table 1** (Continued)

Study	Patient age (y)	Patient sex	Presentation	Location	Operative technique/ approach	Extent of resection	Adjuvant RT	Recurrence, follow-up (mo)
Bertoni et al, 1992 <sup>15</sup>	63	F	Hx of neurofibromatosis	Sphenoid and ethmoid bones	NA	STR	Y	Y, 34
	61	F	HA, R-sided hearing loss and facial nerve palsy, unsteadiness, dizziness	Petrous part of the temporal bone w/ involvement of occipital and sphenoid bones	NA	STR	Y	N, 120
	8	F	R-sided preauricular swelling	Temporal bone	NA	GTR	N	Y, 31
	24	F	NA	Occipital bone w/ involvement of petrous part of temporal bone and sphenoid bone	NA	STR	N	N, 78
	28	F	NA	Clivus	NA	STR	Y	N, 84
do Amaral et al, 1994 <sup>39</sup>	58	F	NA	Occipital bone	NA	STR	N	Y, 18
	78	F	Blindness, prior hx of Paget's disease w/ skull involvement	Frontal bone	NA	GTR	N	Y, 48
	14	F	HA, visual disturbances	Sphenoid bone, involvement of anterior ethmoid sinus, and ST	Bicoronal flap w/ frontal craniotomy	GTR	Y	N, 48
Rock et al, 1994 <sup>40</sup>	32	F	L preauricular and temporal pain; hx of Turner syndrome	Sphenoid bone w/ involvement of zygoma	Preoperative embolization of tumor. Frontotemporal incision w/ preauricular infratemporal extension	GTR	N	N, 6
Saleh et al, 1994 <sup>13</sup>	36	M	R zygomaticotemporal swelling w/ jaw and temporoparietal pain, R-sided hearing loss, and tinnitus	Greater wing of sphenoid bone and squamous part of temporal bone	Infratemporal fossa approach	STR	N	N, 33
Silvers et al, 1996 <sup>41</sup>	55	F	R-sided otalgia and facial pain (previously dx as TMJ syndrome) w/ R-sided facial mass	Temporal bone w/ involvement of glenoid fossa	Preauricular infratemporal fossa approach	GTR	N	NA
Büter and Chilla, 1997 <sup>42</sup>	49	F	NA	Temporal and sphenoid bones w/ involvement of condylar fossa of the mandibular joint	Retroauricular approach	NA	NA	N, 36

Table 1 (Continued)

Study	Patient age (y)	Patient sex	Presentation	Location	Operative technique/ approach	Extent of resection	Adjuvant RT	Recurrence, follow-up (mo)
Li et al, 1997 <sup>43</sup>	36	F	Prior hx of GCTB of L temporal bone (local recurrence)	L glenoid fossa	Preauricular middle cranial fossa approach	GTR	N	N, 12
Kattner et al, 1998 <sup>44</sup>	9	F	Frontal cephalgia, diplopia	Sphenoid bone and sinus w/ involvement of clivus, cavernous sinus	Transseptal transsphenoidal hypophysectomy w/ second resection via transphenoidal route	STR	Y	N, 12
Omura et al, 1998 <sup>45</sup>	18	M	L TMJ pain and restricted jaw opening	Glenoid fossa and condyle	Preauricular approach	GTR	N	N, 24
Lee and Lum, 1999 <sup>12</sup>	45	M	L conductive hearing loss	Squamous, mastoid, and petrous portions of the L temporal bone	Sub- and transtemporal craniotomy w/ dissection of facial nerve	NA	NA	NA
Rosenbloom et al, 1999 <sup>46</sup>	33	F	R aural fullness, pulsatile tinnitus, hearing loss, and otalgia, dysequilibrium	Jugular foramen	Preauricular infratemporal fossa approach	GTR	Y	NA
Spallone et al, 1999 <sup>47</sup>	46	M	R-sided hearing loss	Temporal bone	Basal subtemporal transzygomatic approach	STR	N	N, 10
Sharma et al, 2002 <sup>25</sup>	36	M	Frontotemporal HA, R eye proptosis, epistaxis	Sphenoid bone	Frontozygomaticotemporal approach w/ R maxillectomy and orbital exenteration	STR	Y	N, 120
	17	M	Recurrent HA, b/l proptosis, blindness	Sphenoid bone	Anterior transbasal and transnasal transsphenoidal approach w/ b/l medial maxillectomies	STR	Y	N, 24
	40	M	HA, R eye proptosis w/ partial ophthalmoplegia	Temporal bone w/ involvement of sphenoid bone	Frontozygomaticotemporal craniotomy and R maxillectomy	STR	Y	N, 24
	18	F	Occipital HA, hearing loss, facial nerve palsy, dysphagia, ataxia	Petrous part of the temporal bone	Retromastoid retrosigmoid approach	STR	Y	N, 12
	12	F	Cervicooccipital pain, R-sided hearing loss, facial nerve palsy	Petrous part of the temporal bone	Retromastoid retrosigmoid approach	GTR	N	N, 12

(Continued)

Table 1 (Continued)

Study	Patient age (y)	Patient sex	Presentation	Location	Operative technique/ approach	Extent of resection	Adjuvant RT	Recurrence, follow-up (mo)
Bibas-Bonet et al, 2003 <sup>48</sup>	8	F	R-sided auricular pain, tinnitus, and hearing loss, R facial numbness, dysphagia, hoarseness, diplopia	Temporal and sphenoid bones w/ involvement of ST, clivus, and pontine cistern	Nonoperative care (per guardians)	None	Y	NA
Chan et al, 2003 <sup>49</sup>	77	M	Recurrent epistaxis, HA, hx of polyostotic Paget's disease	Sphenoid bone and sinus	Nonoperative care	None	N	N, 7
Harris et al, 2004 <sup>50</sup>	24	F	HA, tenderness and swelling over L inferoparietal and occipital regions	Occipital bone w/ intracranial extension	Occipital craniotomy	GTR	N	NA
Tang et al, 2003 <sup>51</sup>	61	F	Ataxia, facial palsy, dizziness, scalp mass over L temporozygomatic region	L temporal bone w/ expansion into L middle ear	Trans temporal approach	STR	Y	NA
Pai et al, 2005 <sup>52</sup>	26	M	Swelling of R temporal region, R-sided hearing loss, and tinnitus	Temporal bone w/ large intracranial extension causing uncus herniation	Frontotemporal approach	GTR	N	N, 12
Wang et al, 2006 <sup>5</sup>	64	F	Pressure in L ear, discomfort in L TMJ	Temporal bone	Preauricular approach w/ temporal craniotomy	GTR	N	N, 24
Zorlu et al, 2006 <sup>53</sup>	14	F	Frontal HA, diplopia	Sphenoid bone	Transsphenoidal approach	STR	Y	Y, 17
Elder et al, 2007 <sup>54</sup>	2	F	Preauricular mass	Temporal bone	Preoperative embolization of tumor vessels (90% occlusion); craniotomy (NFS)	GTR	N	N, 13
	0.13	F	Mass in L external auditory canal	Temporal bone	Craniotomy (NFS)	GTR	N	N, 11
Gupta et al, 2008 <sup>55</sup>	17	F	HA, diplopia, amenorrhea, worsening vision	Clivus w/ involvement of ST, sphenoid bone	LeFort I osteotomy	STR	Y	N, 24
Matsushige et al, 2008 <sup>56</sup>	77	F	Sudden-onset L temporal HA w/ emesis, horizontal nystagmus, reduced consciousness	Temporal bone	Subtemporal craniotomy	STR	N	N, 12

Table 1 (Continued)

Study	Patient age (y)	Patient sex	Presentation	Location	Operative technique/ approach	Extent of resection	Adjuvant RT	Recurrence, follow-up (mo)
Chiari et al, 2009 <sup>57</sup>	70	M	Swelling of the L TMJ, L-sided hearing loss, and tinnitus, HA	Temporal bone, TMJ	Craniotomy (NFS)	NA	N	N, 36
Isaacson et al, 2009 <sup>20</sup>	42	M	R-sided hearing loss	Temporal bone	Middle cranial fossa approach	GTR	N	N, 36
	47	M	L-sided otalgia and aural fullness. Previous STR of GCTB w/ local recurrence	Temporal bone w/ involvement of glenoid fossa, cochlea, and mandibular condyle	Revision L temporal craniotomy and infratemporal fossa approach	GTR	N	N, 120
Roeder et al, 2010 <sup>27</sup>	23	M	NA	Sphenoid bone	NA	STR	Y	N, 63
He et al, 2012 <sup>58</sup>	34	M	R TMJ pain and clicking	Temporal bone, TMJ	Preauricular approach	GTR	N	N, 6
Iizuka et al, 2012 <sup>59</sup>	32	M	L aural fullness, L-sided hearing loss and tinnitus	Temporal bone, TMJ	Mastoidectomy w/ transmastoid and middle fossa approach	GTR	N	N, 48
Venkatesh et al, 2012 <sup>60</sup>	30	M	Swelling of L temporal region w/ jaw pain and restricted jaw motion	L temporal bone	Pre/post-auricular and temporoparietal approaches	GTR	N	N, 12
Zhang et al, 2013 <sup>24</sup>	44	M	Involvement of CNs	Temporal bone	NA	GTR	Y	N, 21
	17	M	Proptosis of eye	Sphenoid bone	NA	STR	N	Y, 19
	34	M	TMJ pain	Temporal bone	NA	STR	N	Y, 18
	23	M	Involvement of CNs	Sphenoid bone	NA	STR	Y	N, 32
	18	M	Involvement of CNs	Sphenoid bone	NA	STR	Y	N, 27
	54	F	Subcutaneous mass	Temporal bone	NA	GTR	N	N, 7
	27	F	Involvement of CNs	Temporal bone	NA	STR	Y	N, 24
	19	M	Involvement of CNs	Temporal bone	NA	GTR	Y	N, 32
	19	F	HA, emesis	Occipital bone	NA	GTR	N	N, 31
	52	M	HA, emesis	Temporal bone	NA	STR	Y	N, 33
	29	M	Involvement of CNs	Sphenoid bone	NA	STR	N	Y, 46
	40	F	Subcutaneous mass	Sphenoid bone	NA	STR	N	N, 79
	42	F	HA, involvement of CNs	Sphenoid bone	NA	GTR	N	N, 99
	25	M	HA, involvement of CNs	Sphenoid bone	NA	STR	N	Y, 2
	59	M	HA, involvement of CNs	Sphenoid bone	NA	GTR	NA	NA

(Continued)

Table 1 (Continued)

Study	Patient age (y)	Patient sex	Presentation	Location	Operative technique/ approach	Extent of resection	Adjuvant RT	Recurrence, follow-up (mo)
Billingsley et al, 2014 <sup>21</sup>	32	F	HA, involvement of CNs	Sphenoid bone	NA	STR	NA	NA
	33	M	Involvement of CNs	Temporal bone	NA	GTR	N	N, 12
	35	F	HA, involvement of CNs	Temporal bone	NA	GTR	N	N, 10
	44	F	R otalgia and auricular fullness	Temporal bone	Postauricular infratemporal approach w/ subtemporal craniectomy, subtotal petrossectomy and mandibular osteotomy	GTR	N	N, 15
Prasad et al, 2014 <sup>8</sup>	36	M	Preauricular mass, hearing loss and tinnitus, temporoparietal pain	Temporal bone w/ involvement of greater wing of sphenoid bone, TMJ	Infratemporal fossa type B approach	GTR	N	N, 120
	48	F	Temporoparietal mass	Temporal bone w/ involvement of greater wing of sphenoid bone, TMJ	Infratemporal fossa type D approach	GTR	N	N, 108
	31	F	Hearing loss and tinnitus	Temporal bone w/ involvement of TMJ	Infratemporal fossa type B approach w/ temporal craniotomy	GTR	N	N, 96
	46	M	Temporal swelling, temporoparietal pain, hearing loss, and tinnitus	Temporal bone	Infratemporal fossa type B approach	GTR	N	N, 48
Freeman et al, 2016 <sup>18</sup>	67	M	Hearing loss and tinnitus, vertigo	Temporal bone	Transmastoid exploration w/ extended mastoidectomy	STR	Y	Y, 24
	39	M	HA, hearing loss	Temporal bone w/ involvement of greater wing of sphenoid bone, TMJ	Infratemporal fossa type B approach	GTR	N	N, 18
	57	M	Hearing loss and tinnitus	Temporal bone	Middle cranial fossa and infratemporal fossa type B approaches	GTR	N	N, 15
	27	M	R-sided hearing loss, HA	Mastoid portion of temporal bone	Cortical mastoidectomy	GTR	N	N, 6

Table 1 (Continued)

Study	Patient age (y)	Patient sex	Presentation	Location	Operative technique/ approach	Extent of resection	Adjuvant RT	Recurrence, follow-up (mo)
Carlson et al, 2017 <sup>61</sup>	43	F	R-sided TMJ swelling and pain	Middle, infratemporal, and glenoid fossae	Preauricular infratemporal fossa approach w/ condylectomy and resection of glenoid fossa	GTR	N	N, 166
	40	M	R-sided hearing loss	Middle, infratemporal, and glenoid fossae w/ involvement of mastoid, external auditory canal, and middle ear	Middle fossa craniotomy w/ tympanomastoidectomy 1-y later	STR	Y	N, 240
	58	M	L-sided aural fullness	Middle, infratemporal, and glenoid fossae w/ involvement of mastoid, external auditory canal, and middle ear	External beam RT (60 Gy) followed by temporal craniotomy w/ tympanomastoidectomy	STR	N	N, 226
	60	M	L-sided hearing loss, aural fullness, and pain	Middle and glenoid fossae w/ involvement of mastoid, external auditory canal, and middle ear	Middle fossa craniotomy w/ tympanomastoidectomy	GTR	N	N, 162
	57	M	L-sided hearing loss, tinnitus, aural fullness	Middle and glenoid fossae w/ involvement of mastoid, external auditory canal, and middle ear	Middle fossa craniotomy w/ tympanomastoidectomy	GTR	N	N, 156
	31	M	R-sided TMJ swelling and pain	Middle, infratemporal, and glenoid fossae w/ involvement of condyle	Preauricular infratemporal fossa approach w/ condylectomy and resection of glenoid fossa	GTR	N	N, 73
	42	F	Incidental finding	Middle, infratemporal, and glenoid fossae	Modified infratemporal fossa type B approach	GTR	N	N, 116
	49	M	L-sided trismus and pain	Middle, infratemporal, and glenoid fossae w/ involvement of external auditory canal, and middle ear	Middle fossa craniotomy w/ subtotal petrosectomy	STR	N	Y, 12
	79	M	R-sided hearing loss, aural fullness and otorrhea	Middle, infratemporal, and glenoid fossae w/ involvement of external auditory canal, and middle ear	Middle fossa craniotomy w/ subtotal petrosectomy	GTR	N	N, 29

(Continued)

**Table 1** (Continued)

Study	Patient age (y)	Patient sex	Presentation	Location	Operative technique/ approach	Extent of resection	Adjuvant RT	Recurrence, follow-up (mo)
	54	M	R-sided hearing loss and otorrhea	Middle, infratemporal, and glenoid fossae w/ involvement of external auditory canal, and middle ear	Middle fossa craniotomy w/ subtotal petrosectomy	STR	N	N, 53
	39	F	R-sided jaw pain and otalgia	Middle, infratemporal, and glenoid fossae	Middle fossa craniotomy w/ infratemporal fossa dissection	GTR	N	N, 7
Patibandla et al, 2017 <sup>62</sup>	20	M	Hemicranial pain, eyelid droop, vomiting	Clivus	Transnasal transsphenoidal	STR	Y	N, 3
Current study	22	M	HA, L face swelling, L-sided hearing loss	Temporal bone w/ involvement of frontal and zygomatic bones	Fisch-type approach w/ preauricular incision	GTR	N	N, 2

Abbreviations: b/l, bilateral; CNS, cranial nerves; ECA, external carotid artery; GTR, gross total resection; HA, headache; Hx, history; L, left; M/F, male/female; N, no; NA, not available; NFS, not further specified; R, right; RT, radiotherapy; ST, sella turcica; STR, subtotal resection; TMJ, temporomandibular joint; Y, yes.

present as soft tissue masses of mixed density with higher density spots and destructive expansion into the bone, sometimes sparing cortical bone.<sup>12,18,24,25</sup> CT alone is insufficient for the accurate diagnosis and differentiation of GCTB from other similar-appearing masses or tumors, such as osteitis fibrosa cystica (brown tumor) or giant cell reparative granulomas.<sup>12,18</sup> MRI provides better characterization and delineation of the tumor, showing intermediate signal intensity on T1-weighted imaging and hypointensity on T2-weighted sequencing.<sup>18</sup>

Surgical removal of GCTB of the skull with complete resection is the current treatment of choice.<sup>8,14,18</sup> The surgical management of GCTB of the lateral skull base can be difficult because of its proximity to critical neurovascular structures. Although gross total resection of the tumor is ideal, this may not be feasible depending on the extent of structural involvement by the tumor. In this setting, partial resection (i.e., maximal safe resection) followed by adjuvant radiotherapy may be a reasonable alternative.<sup>8,18,26,27</sup> A recent systematic literature review of GCTBs involving the skull reported 94 patients who underwent surgery, with 37 of those patients having received adjuvant radiotherapy.<sup>24</sup> In a subanalysis within this review, in 62 patients for whom survival data was available, the 5-year overall survival rate was 84%, with an event-free survival rate (i.e., survival rate without tumor recurrence) of 61.3%.<sup>24</sup> All 16 patients who had gross total resection (with or without adjuvant radiotherapy) were alive and event-free at 5 years.<sup>24</sup> In comparison, patients treated with subtotal resection and adjuvant radiotherapy ( $n = 33$ ) had an overall survival of 90.3% and event-free survival of 70.1%.<sup>24</sup> Patients treated with subtotal resection without subsequent radiotherapy ( $n = 13$ ) had an overall survival rate of 50% and an event-free rate of 15.4% at 5 years.<sup>24</sup> Because of the difficulty associated with the surgical management of GCTBs involving the lateral skull base, complications can arise during surgical resection (e.g., bleeding or the compromise of critical neural structures). Nevertheless, current evidence strongly suggests that gross total resection results in improved local control and survival outcomes.<sup>18</sup>

Adjuvant therapy is recommended for cases where complete resection cannot be achieved.<sup>25</sup> Radiation therapy is discussed in the literature as a possible treatment option following subtotal resection. Small retrospective studies and case reports have suggested a control benefit and marked symptom relief with adjuvant radiation therapy. Malone et al<sup>26</sup> reported local control in 19 of 21 patients treated with radiation therapy, with a mean follow-up time of 15.4 years. Most patients received 35 Gy in 15 fractions delivered daily over 3 weeks.<sup>26</sup> Other series have also demonstrated favorable local control rates, with Roeder et al<sup>27</sup> reporting local control in four of five patients treated with intensity-modulated radiation therapy to a median dose of 64 Gy using conventional fractionation. There are also reports on the use of Gamma Knife (stereotactic) radiosurgery in the treatment of GCTB of the skull base, with marked reduction in tumor size and a meaningful disease-free interval.<sup>28</sup> Although adjuvant radiation therapy appears to offer a control benefit,

the data are limited by their retrospective nature, small patient numbers, and short follow-up intervals. Given these limitations, general consensus regarding optimal dose and fractionation regimens are lacking. Moreover, there is concern that radiotherapy may contribute to malignant transformation.<sup>20,25</sup> This risk may be minimized by use of conventional fractionation regimens without compromising tumor control; however, longer follow-up is needed to better characterize this risk.<sup>15,25</sup>

Recently, several studies have investigated the role of targeted therapy with denosumab, a fully humanized monoclonal receptor activator of nuclear factor kappa-B ligand (RANK-L) antibody, which has shown promise as a potential effective chemotherapeutic treatment option in patients with GCTB.<sup>29</sup> The osteoclastic giant cells responsible for local bony destruction and invasion in GCTB have been shown to ubiquitously express RANK receptor.<sup>29–31</sup> Current evidence suggests that the neoplastic stromal cells promote the growth, proliferation, and osteolytic activity of the multinucleated osteoclastic giant cells through the overexpression of RANK-L, thus driving local bony destruction.<sup>30,32</sup> With ongoing clinical trials studying the effectiveness of denosumab in the treatment of GCTBs, the role of monoclonal therapy in GCTBs of the skull base has not yet been fully characterized.<sup>31,33,34</sup> Current evidence for the management of GCTBs of the skull recommends complete surgical resection with negative margins to achieve the highest rate of cure and lowest risk of recurrence.<sup>4,16</sup> Nevertheless, the inhibition of this pathway with a monoclonal RANK-L antibody may limit bony destruction and tumor progression, thereby making these tumors of the lateral skull base more amenable to complete surgical resection and therefore decreasing the morbidity and mortality of this disease.

## Conclusion

The skull is a relatively rare location for a GCTB to occur. When this tumor is found, it is normally found in the temporal or sphenoid bones. Although GCTB is a benign tumor, it is also locally aggressive and has the ability to recur or rarely metastasize. Gross total resection is the current treatment of choice in GCTB of the skull, but it can be difficult to achieve due to the proximity of the tumor to important neural and vascular structures. Subtotal resection with adjuvant radiotherapy may be a good alternative treatment in such cases. Although radiotherapy has been the adjuvant therapy of choice in GCTB treatment, recent literature shows that denosumab, a RANK-L antibody, may also prove to be effective in treating the tumor. Future studies should evaluate the efficacy of different adjuvant therapies used to treat partially resected GCTB of the lateral skull base.

### Disclosure

None.

### Compliance with Ethical Standards

This study was approved by the Institutional Review Board (IRB) of the University of Utah.

### Patient Consent

The patient/legal guardian/next of kin has consented to the submission of the case report for submission to the Journal of Neurological Surgery Reports.

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