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Giant Cell Tumors of the Skull Base: Case Series and Current Concepts

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Abstract

Objective: To study the clinical features, tumor characteristics and outcomes of giant cell tumors (GCTs) in the skull base based on long-term follow-up. We also report the largest series of GCTs in the temporal bone and the lateral skull base. *Materials and Methods:* A retrospective study was conducted of all GCTs managed at the Gruppo Otologico, a quaternary referral skull base institute, in Italy from 1993 to 2013. The clinical features, investigations, surgical management and follow-up were recorded. The surgical approaches used were infratemporal fossa approach (ITFA) type B and D and middle cranial fossa (MCF) approaches. *Results and Observations:* A total of 7 patients with GCTs of the skull base were treated at our institution. The principal complaints were hearing loss reported in 6 (85.71%) patients, tinnitus in 5 (71.43%) and swelling in 3 (42.9%). Pure-tone audiometry showed conductive hearing loss in 5 (71.43%) patients. High-resolution CT scan and MRI with gadolinium enhancement were done in all patients. Radiology showed involvement of the ITF and middle ear in 6 (85.71%) patients each, temporomandibular joint in 4 (57.14%) patients, invasions of the squamous part of the temporal bone, mastoid, MCF and greater wing of sphenoid in 3 (42.9%) patients each and the petrous bone in 2 (28.6%) patients. ITFA type B was applied as an approach for tumor removal in 5 (71.43%) patients, including a case where an additional MCF approach was employed, and ITFA type D and the transmastoid approach were applied in 1 (14.3%) patient each. Total tumor removal and successful cure was achieved in 6 (85.71%) patients. Subtotal removal leading to recurrence and eventual mortality was the result in 1 (14.3%) patient. *Conclusions:* A thorough knowledge of the anatomy of the skull base and the various skull base approaches is necessary to tackle GCTs. ITFA type B and D combined with MCF approaches provide good exposure of the tumor with minimal postoperative sequelae and good locoregional control. Recurrence due to either subtotal removal or suboptimal treatment may have disastrous consequences for the patient.

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Introduction

Giant cell tumors (GCTs) are a group of rare benign neoplasms that are most commonly found in the epiphysis of long bones. Around 1–2% of these lesions present in the head and neck [Cook et al., 1986; Lee and Lum, 1999; Gibbons et al., 2000; Leonard et al., 2001; Isaacson et al., 2009], with the skull base being a commonly reported site (temporal, sphenoid and ethmoid bones) and other sites including the mandible, maxilla, nasal cavity, thyroid, larynx, hyoid, tongue and the soft tissues of the neck. In the skull base the temporal bone is a common site of occurrence of GCTs. Although benign, these tumors have a locally destructive character which can be potentially dangerous in the presence of the intricate neurovasculature of the temporal bone and skull base. The management of GCTs of the skull base differs vastly from those in the long bones of other parts of the body both in terms of decision making and technique. The rarity of the disease has meant that the optimal treatment of this subset of tumors still remains elusive. Considering the rarity of these tumors in the skull base, we present the largest series in recent literature with 7 cases of GCTs in the skull base.

Materials and Methods

A retrospective study was conducted of all GCTs managed at the Gruppo Otologico, a quaternary referral skull base institute in Piacenza, Italy from 1993 to 2013. All tumors that were any variants or related tumors were excluded from the study. The clinical features, investigations, management and follow-up were recorded. All patients underwent blood tests, high-resolution CT scan (HRCT), MRI with gadolinium enhancement and four-vessel angiography wherever indicated. The surgical approaches used were as follows and have been described in detail elsewhere [Sanna et al., 2007].

(1) Infratemporal fossa approach (ITFA), type B: this approach consisted of a C-shaped extended postaural incision that provided access to the vertical and horizontal portions of the internal carotid artery (ICA), petrous apex and mid-to-lower clivus. A subtotal petrosectomy was performed, the anterior wall of the external auditory canal (EAC) was removed and the VII nerve was left in its anatomical position. The mandibular condyle was retracted and the ITF exposed to isolate the tumor.

(2) ITFA, type D: this approach consisted of a preauricular incision with a plane of dissection anterior to the middle ear, petrous horizontal ICA and the eustachian tube giving access to the nasopharynx, the pterygopalatine fossa and the upper parapharyngeal space. Mastoidectomy was not performed, and the middle ear and the eustachian tube were left intact.

(3) Middle cranial fossa (MCF) combined with ITFA: a square craniotomy was added to the ITFA type B to expose the floor of the MCF and extension of the tumor therein.

All patients were followed up with CT and MRI.

Results

A total of 7 patients with GCTs of the skull base were treated at our center (table 1); 5 of the patients were male and 2 were female. The principal complaints were hearing loss reported in 6 (85.71%) patients, tinnitus in 5 (71.43%), external swelling in 3 (42.9%) and vertigo, headache and pain in 1 patient each (14.3%). The mean time of clinical presentation after onset was 13.7 months. The tympanic membrane (TM) was intact in all cases and none of the tumors presented externally for biopsy. Pure-tone audiometry showed conductive hearing loss (CHL) in 5 (71.43%) patients and mixed hearing loss in 1 (14.3%) patient. HRCT and MRI with gadolinium enhancement were done in all patients. Radiology showed involvement of the ITF and middle ear in 6 (85.71%) patients each, temporomandibular joint (TMJ) in 4 (57.14%) patients, invasions of the squamous part of the temporal bone, mastoid, MCF and greater wing of sphenoid in 3 (42.9%) patients each and the petrous bone in 2 (28.6%) patients. ITFA type B was applied as an approach for tumor removal in 5 (71.43%) of the patients, including a case where an additional MCF approach was employed. ITFA type D and the transmastoid approaches were employed in 1 (14.3%) patient each. Total tumor removal was achieved in 6 (85.71%) of the patients. All described cases fulfilled the histological criteria of osseous GCT, i.e. composed by two main cellular components, spindle cells (stromal cells) and giant multinucleated osteoclast-like cells homogeneously scattered among them (fig. 1). The mean duration of follow-up was 5.6 years. Successful cure was achieved in 6 (85.71%) patients; 1 patient (14.3%) died as a result of tumor recurrence.

Below, in chronological order, are the 7 cases managed in our institution.

Case 1

A 36-year-old male presented with 8 months of right-sided preauricular swelling associated with ipsilateral hearing loss and tinnitus. This was followed by recent onset of pain along the parietotemporal area. On examination, there was a firm, ill-defined subcutaneous mass over the zygomaticotemporal area. Otoscopy showed swelling over the anterosuperior part of the EAC over an intact TM. Pure-tone audiometry revealed CHL with a pure-tone average (PTA) air-bone gap (ABG) of 25 dB. HRCT showed a 4-cm (largest diameter) osteolytic lesion involving the squamous part of the temporal bone and the floor of the MCF. There was erosion of the tegmen, middle ear, anterior wall of the EAC, TMJ, greater wing of the sphenoid and ITF. The MRI showed a hypointense mass in both T1- and T2-weighted images. Total tumor removal was achieved through the ITFA type B with blind sac closure of the EAC. There were no significant postoperative sequelae. The patient is disease free after a 10-year follow-up.

Table 1. Analysis of 6 patients with GCT of the skull base

| Case No./side	Age/sex	Presenting symptoms	Duration since onset, months	Signs	Radiological findings	Surgical approach	Tumor removal	Follow-up
1/R	36/M	preauricular mass, hearing loss, tinnitus, temporoparietal pain	8	ill-defined temporozygomatic mass, anterosuperior EAC bulge, CHL, intact TM	4-cm osteolytic lesion involving squamous and petrous TB, floor of MCF, ME, EAC, greater wing of sphenoid, TMJ, ITF	ITFA type B	total	10 years, no recurrence
2/R	48/F	temporoparietal mass	6	ill-defined hard mass in zygomaticoparietal, otoscopy normal	6-cm osteolytic lesion involving squamous and zygomatic process TB, greater wing of sphenoid, TMJ, ITF	ITFA type D	total	9 years, no recurrence
3/L	31/F	hearing loss, tinnitus, HTN, stroke with hemiparesis, SLE	2	left hemiparesis, SOM, edematous discharging EAC, CHL	2.5-cm osteolytic lesion involving ME with tegmen erosion, TMJ, ITF	ITFA type B + temporal craniotomy	total	8 years, no recurrence
4/L	46/M	temporal swelling, hearing loss, tinnitus, temporoparietal pain	8	ill-defined temporal mass, superior EAC bulge, CHL	3.5-cm osteolytic lesion involving squamous TB, ME, EAC, ITF	ITFA type B	total	4 years, no recurrence
5/L	67/M	hearing loss, tinnitus, vertigo, DM, HTN, vocal cord palsy due to previous thyroid surgery	12	nonspecific thickening of TM, CHL	5.5-cm osteolytic lesion involving ME, mastoid extending into PCF and sigmoid and abutting JB	transmastoid exploration resulting in an extended mastoidectomy	sub-total	RT followed by second-stage surgery (TLA) followed by CT, 2 years, deceased
6/L	39/M	hearing loss, headache[1]	36	intact TM with T-tube, MHL	5-cm osteolytic lesion involving ME, mastoid, MCF, greater wing of sphenoid, TMJ, ITF	ITFA type B	total	18 months, on FU, no recurrence
7/L	57/M	hearing loss, tinnitus	24	tympanosclerosis of TM, SOM, CHL	6-cm osteolytic lesion involving ME, mastoid, petrous TB, MCF, ITF	MCF + ITFA type B	total	15 months, on FU, no recurrence

MHL = Mixed hearing loss; TB = temporal bone; ME = middle ear; HTN = hypertension; SLE = systemic lupus erythematosus; SOM = secretory otitis media; JB = jugular bulb; RT = radiotherapy; TLA = translabyrinthine approach; FU = follow-up.
[1] Patient was operated 8 months earlier via a frontotemporal approach achieving subtotal removal.

Case 2

A 48-year-old female presented with a 6-month history of a painless subcutaneous mass in the right supra-auricular area. General and ENT examination was normal and the only finding on examination was a unilateral hard mass in the parietal and zygomatic regions. The otoscopic examination and pure-tone audiometry were normal. HRCT and MRI showed a 6-cm osteolytic lesion involving the squamous and zygomatic process part of the temporal bone, the greater wing of sphenoid, the TMJ and the ITF. An ITFA type D was used to excise the mass. Intraoperatively, the tumor was found to have eroded the floor of the MCF without intradural invasion. Total tumor removal was achieved without neurological deficits and hearing was preserved at preoperative levels. The patient is disease free after a 9-year follow-up.

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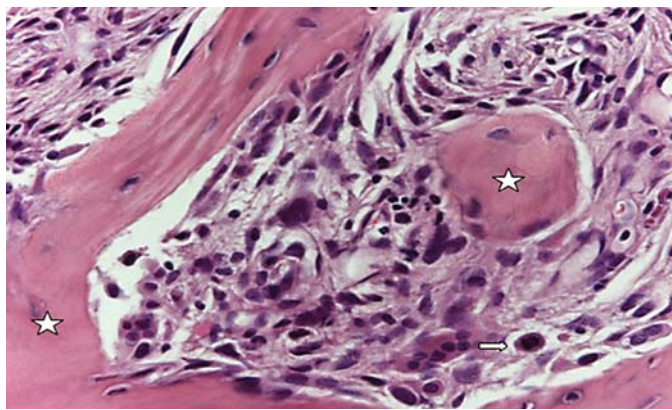
Fig. 1. Histopathology of GCT. Spindle and giant cell proliferation spreading between bony tissue (stars). Mitotic activity was evident in giant cells (arrow).

Case 3

A 31-year-old female with a past history of hypertension and systemic lupus erythematosus on oral corticosteroid treatment presented to the outpatient clinic with 2 months of left-sided hearing loss and unilateral tinnitus. General examination showed signs of left hemiparesis caused by a cerebral ischemic attack 6 years earlier. Otoscopic examination of the left ear showed an edematous EAC with otorrhea. Pure-tone audiogram showed a CHL with a PTA ABG of 30 dB on the left side. HRCT demonstrated a 2.5-cm osteolytic lesion involving the middle ear cavity, with erosion of the tegmen tympani and anterior extension to the TMJ and ITF. MRI ruled out any dural involvement. Total removal of the tumor was achieved using an ITFA type B with temporal craniotomy. Postoperatively, there were no significant complications. Apart from pain during mastication in the first postoperative month, there were no significant postoperative sequelae. The patient is disease free after 8 years of follow-up.

Case 4

A 46-year-old male presented with a 7-month history of left temporal swelling, left-sided hearing loss and unilateral tinnitus. Examination revealed a diffuse but firm subcutaneous mass in the temporal region and otoscopy showed a smooth mass in the EAC obscuring the TM. Pure-tone audiogram showed a CHL with a PTA ABG of 50 dB. HRCT scan demonstrated a 3.5-cm osteolytic lesion in the squamous part of the temporal bone, the EAC, the middle ear and the ITF. MRI showed a 2-cm intradural invasion. The tumor was approached with an ITFA type B with blind sac closure of the EAC. Intraoperatively, the mass was seen involving the EAC and the middle ear, exposing the horizontal segment of the ICA and extending into the MCF to involve the maxillary branch of the trigeminal nerve. The intraoperative histopathological exam demonstrated infiltration of the zygomatic arch. Total removal of the tumor with dural reconstruction was done with no significant complications. At 4 years of follow-up the patient is disease free, with mild paresthesia on the ipsilateral side of the face being the only postoperative sequelae.

Case 5

A 67-year-old male with a past history of diabetes mellitus and hypertension presented with left-sided hearing loss, unilateral tin-

nitus and vertigo of 12 months' duration. Incidentally, the patient had right vocal cord paralysis due to previous thyroid surgery. On otoscopy, the only finding was a nonspecific TM opacity on the affected side. The pure-tone audiogram showed a CHL with a PTA ABG of 40 dB. HRCT showed a 5.5-cm mass invading the middle ear and mastoid and eroding the bone over the posterior cranial fossa (PCF) and the sigmoid sinus. MRI confirmed invasion of the PCF dura, the sigmoid sinus and the jugular bulb. The patient underwent exploratory surgery via a transmastoid approach resulting in an extended mastoidectomy. Due to the proximity of the tumor to the lower cranial nerves, a part of the tumor was left behind, achieving a subtotal removal which was reported to be GCT by histopathology. This was followed by multiple radiotherapy sessions for the residual tumor. Subsequently, postoperative scans showed a rapid increase in the size of the tumor by 1 year with involvement of vital intracranial structures. A second salvage surgery was performed via a translabyrinthine approach for tumor excision but this attempt also failed to remove the tumor completely without causing damage to the lower cranial nerves and additional morbidity. The patient underwent further adjuvant radiotherapy. Despite all efforts, the tumor continued to grow. Finally the patient died secondary to brainstem compression 2 years after diagnosis.

Case 6

A 39-year-old male presented with a history of surgery 8 months earlier in another center where a frontotemporal approach was used to remove a left-sided tumor. A subtotal removal was achieved and the histopathology was reported as fibrous dysplasia. On examination the patient was found to have mixed hearing loss with an intact TM with a ventilation tube. HRCT scan showed a 5-cm osteolytic lesion involving the middle ear, mastoid, MCF, greater wing of the sphenoid, TMJ and ITF (fig. 2). Total tumor excision was achieved using an ITFA type B. Postoperatively, the patient did not have any major sequelae and has been free of disease for the last one and a half years (fig. 3).

Case 7

A 57-year-old male complained of progressive hearing loss and tinnitus in the left ear for more than 2 years. Otoscopic examination showed a tympanosclerotic plaque and otitis media with effusion. The pure-tone audiogram revealed a moderate CHL with a PTA ABG of 40 dB. HRCT and MRI showed an effusion in the middle ear with a 6-cm tumor involving the middle ear and mastoid, with erosion of the tegmen and extension into the petrous apex and the ITF, reaching the lateral aspect of the horizontal portion of the ICA (fig. 4). The tumor was seen abutting the temporal lobe without invading the MCF dura. Total tumor removal was achieved via the combined MCF and ITFA type B. The postoperative course was uneventful. The patient is disease free at 15 months of follow-up (fig. 5).

Discussion

GCTs are distinct clinical-radiological-pathological entities that have been intensely researched in the last few decades and clarity has developed with regard to the molecular biology, histopathology, classification and behav-
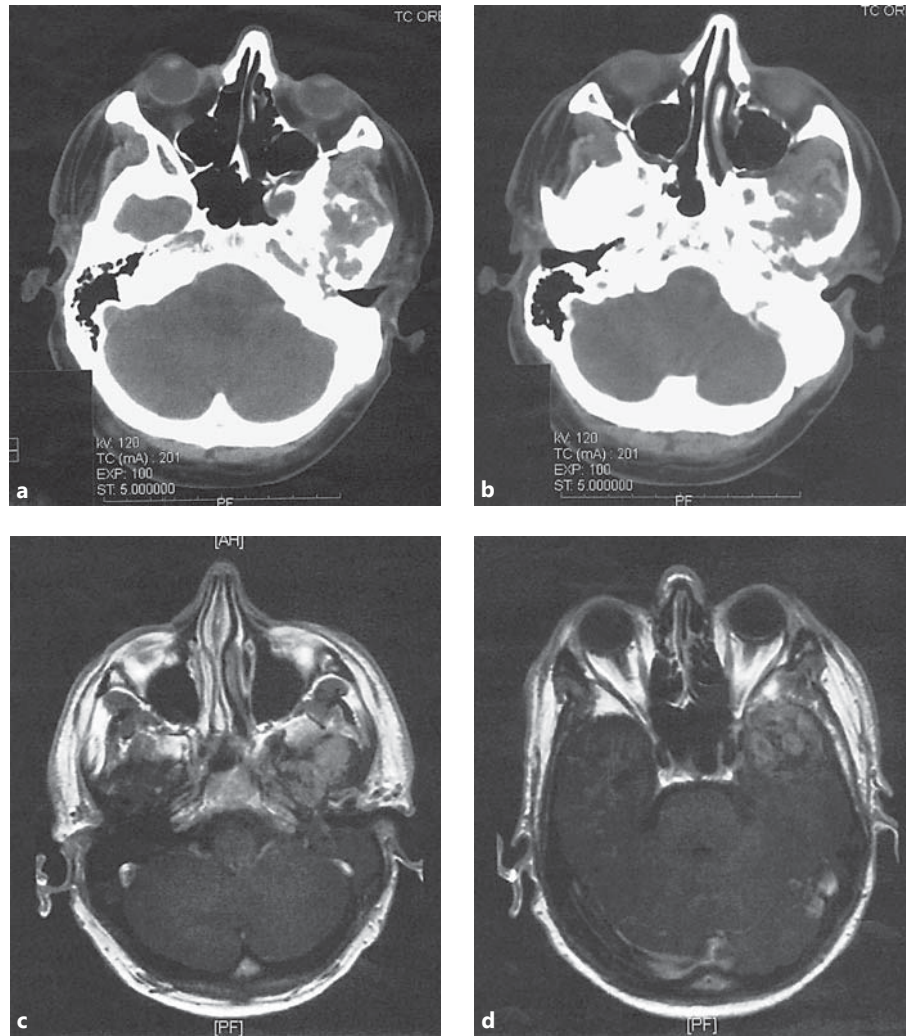
Fig. 2. Preoperative CT scan (**a**, **b**) and MRI (**c**, **d**) showing a 5-cm osteolytic lesion involving the middle ear, mastoid, MCF, greater wing of the sphenoid, TMJ and ITF.
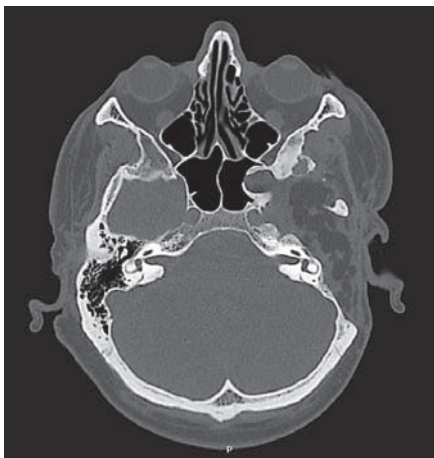

Fig. 3. Postoperative CT of the same patient showing complete tumor eradication after one and a half years.

ior of these tumors. However, uncertainty still remains about the optimal treatment for such tumors. In what would come to be known as 'giant cell tumor', Cooper and Travers [1818] described an expansive lesion of the fibular head through the first gross pathological drawings of a GCT. They named the lesion 'fungus medullary exostosis' and until the advent of the clinical use of the microscope in 1845, this categorization of bone tumors prevailed. In 1854 Sir James Paget provided the first microscopic description of the tumor in the English literature [Kim et al., 2012]. In 1912, Bloodgood [1912] coined the term 'giant cell tumor' but it was not until 1940 that a detailed clinical-radiographical-histological identity of GCTs was published by Jaffe et al. [1940]. Subsequently, as studies showed the benign nature of the disease, the earlier term of osteoclast sarcoma was omitted to yield the

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Fig. 4. Preoperative CT scan (**a**) and MRI (**b**) of the patient with tumor involving the middle ear and mastoid, with erosion of the tegmen and extension into the petrous apex and the ITF.
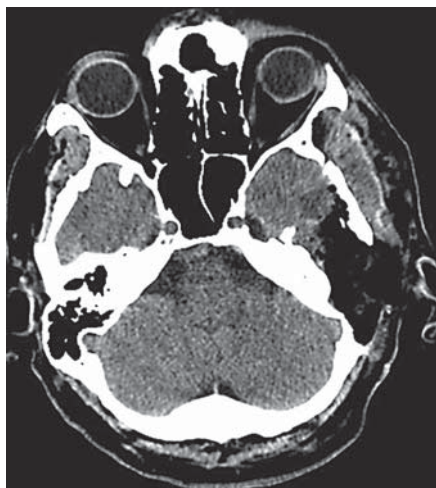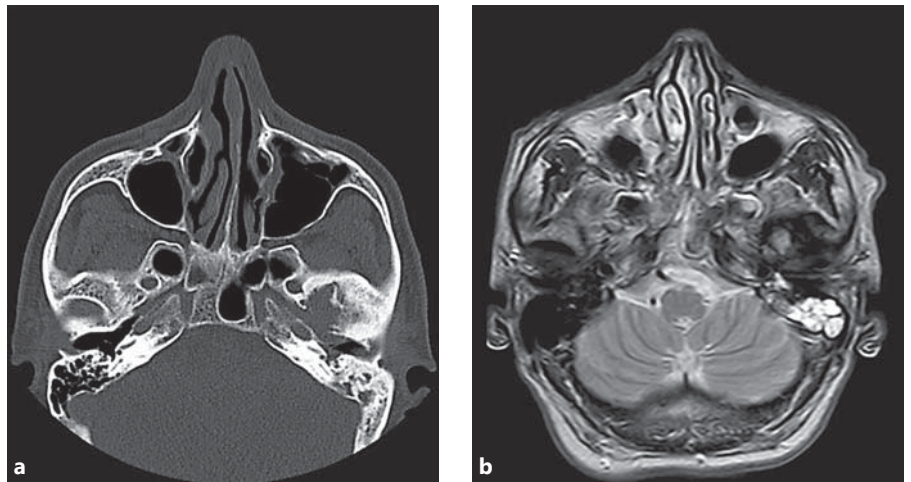

Fig. 5. CT scan of the same patient 1 week after surgery, which shows total eradication of the tumor.

name osteoclastoma [Kim et al., 2012]. However, the name 'giant cell tumor' is a misnomer as it gives an unintended impression that the giant cells are the major neoplastic components of the tumor, which is not true. Based on current cellular and molecular evidence, GCT stromal cells are the major neoplastic or disease components. Resorptive giant cells are the byproducts of interactions between GCT stromal cells and recruited monocytes which subsequently fuse to form tumor osteoclasts [Liao et al., 2005; Kim et al., 2012].

As the description of GCTs become clearer, more reports are emerging of such tumors in the head and neck area. The skull bones are reported to be more frequently involved than other parts of the face like the mandible or the maxilla. The difference between dealing with GCTs in other parts of the body, especially the long bones, and in the skull base is manifold. Firstly, the surgical anatomy of the skull base is extremely complicated and hence requires great expertise and skill in the excision of these tumors. Secondly, total tumor removal is imperative in the first sitting because a recurrence in this complex area would be particularly difficult to treat. Thirdly, it is difficult to be radical in tumor removal of the skull base as resection or injury to vital neurovascular structures leaves an unacceptable degree of morbidity. Finally, the GCTs of the skull base are dealt with by the otology/skull base surgeons, ENT/head and neck surgeons or maxillofacial surgeons who bring with them their expertise and familiarity of the use of the microscope and the microdrill that facilitates precise tumor identification and removal. Our institution is a quaternary referral skull base center where our surgeons deal with all pathologies of the skull base and our experience in treating over 3,500 skull base lesions helped us achieve a total cure for GCTs in 6 of the 7 patients who presented to us.

Clinical Features

Hearing loss, tinnitus and subcutaneous masses are the most commonly reported symptoms in GCTs of the skull base. TM is often intact as the tumor is anteromedial to it. Pain is uncommon and facial nerve and lower cranial nerve involvement is seen in later stages. Hearing loss is most likely to be conductive as a result of occlusion of the eustachian tube from tumor involvement of the

skull base as seen in our series. Sensorineural hearing loss is seen when the tumor extends into the otic capsule, internal auditory canal or cerebellopontine angle. Clinical and radiological features show that GCTs are predominantly tumors of the anterolateral skull base extending anteriorly and inferiorly into the ITF, posteriorly into the middle ear and mastoid, superiorly into the MCF, laterally into the zygoma and TMJ and medially as far as the petrous bone and the sphenoid sinus. Extensions into the PCF are rare and are associated with a poor prognosis as seen in case 5 of our series.

Histopathology

GCTs are characterized by the presence of multinucleated giant cells. The stromal cells are homogeneous mononuclear cells with a round or ovoid shape, large nuclei and indistinct nucleoli. The nuclei of the stromal cells are identical to the nuclei of the giant cells, a feature that distinguishes GCTs from other lesions that also contain giant cells. Another feature of a GCT is that the giant cells may contain very large numbers of nuclei, often several hundred. Multinucleated giant cells act like osteoclasts resorbing bone, hence the name osteoclastoma. GCTs are well studied in radiological and histological arenas, but the pathogenicity remains elusive [Kim et al., 2012]. According to Dahlin's bone tumors, GCT is a distinct neoplasm of undifferentiated cells [Unni and Dahlin, 1996]. The multinucleated giant cells apparently result from fusion of the proliferating mononuclear cells, and although they are a constant and prominent part of these tumors, the giant cells are probably of less significance than the mononuclear cells. The basic proliferating cell has a round-to-oval or even spindle-shaped nucleus in the field that is diagnostic of a true GCT. The GCT stromal cells are now widely understood to be the major neoplastic and proliferative component of GCTs [Wulling et al., 2001, 2003].

Differential Diagnosis

Histological diagnosis of a GCT is an extremely challenging task for the histopathologist. In particular, in skull and maxillofacial bones, one of the most intriguing differential diagnoses is represented by giant cell reparative granuloma (GCRG), a benign reactive granulomatous response to intraosseous hemorrhage or inflammation after trauma, which usually affects younger patients, especially adolescents, and involves mainly the maxilla and mandible. A recent hypothesis suggests that in the skull bones GCT and GCRG may be part of a spectrum of a single disease process due to the occurrence of border-line cases showing features of both GCT and GCRG [Saw et al., 2009]. Histopathologically, GCTs must also be differentiated from chondroblastomas, chondromyxoid fibromas, aneurysmal bone cysts, nonossifying fibroma, fibrous dysplasias, pigmented villonodular synovitis, foreign body reactions and the brown tumors associated with hyperparathyroidism. When an aggressive growth pattern is evident, one should consider the possibility of chondrosarcoma, osteosarcoma, malignant fibrous histiocytomas and a metastatic lesion until confirmation by histological examination [Park et al., 2012]. The malignant variant of GCT is rarely to be the first diagnosis but it must be borne in mind when there is a history of previous radiotherapy and when there are features of distant metastasis.

Imaging Characteristics

The radiological picture of a GCT is an osteolytic lesion. Both CT and MRI are essential for tumor staging and management. Although CT is superior to MRI in outlining tumor extent and bony destruction of the skull base, MRI is currently the best imaging modality for GCT because of its superior contrast resolution and multiplanar imaging capabilities that allow accurate tumor delineation [Manaster and Doyle, 1993; Purohit and Pardiwala, 2007]. GCT shows low intensity on T1-weighted images and heterogeneous high intensity on T2-weighted images. Gadolinium enhancement reveals areas of hypervascularity and enhancement with a very heterogeneous signal pattern. Though GCT shows increased uptake of technitium-99m but it is nonspecific and unreliable in defining the extent of the tumor and its use is limited to evaluation of the rare patient with multicentric or metastatic GCT. PET scan is useful in the diagnosis of malignant tumors and their recurrence and in monitoring the response to therapy [Purohit and Pardiwala, 2007].

Surgical Management

Surgical resection is the treatment of choice for GCTs of both head and neck and long bones. In GCTs of the skull base, a thorough knowledge of the surgical anatomy is essential to attempt tumor removal and is guided by the principles of skull base surgery [Sanna et al., 2007]. Total tumor clearance with preservation of the facial nerve and the lower cranial nerves is the goal of surgery, which was achieved in all our cases. The surgical approach depends on the position and extent of the tumor. Since most GCTs are found to involve the temporal bone and the ITF, the ITFA described by Ugo Fisch, especially types B and D, provide the ideal approach and exposure to these tumors

Table 2. Comparison of recent reports of other authors who managed GCTs

Year	Authors	Age/sex/side	Clinical features	Location	Approach	Extent of excision	Adjuvant therapy	Postoperative sequelae	Follow-up
1987	Findlay et al.	23/M/R	hearing loss, otalgia, partial FN paralysis, V nerve hypesthesia, CHL	M-, P-TB, MCF, ITF	subtemporal craniotomy with section of zygomatic arch	? total removal	RT	total FN paralysis	DF at 8 months
1994	Rock et al.	32/F/L	preauricular pain, temporomandibular symptoms, inframtemporal mass	destructive and expansile mass involving S-, Z-TB, sphenoid, ITF, MCF	frontotemporal incision with ITF extension with cranioplasty of lateral skull base defect, preoperative embolization	total removal	none	none	DF at 6 months
1994	Saleh et al.[1]	36/M/R	preauricular swelling, hearing loss, tinnitus, temporoparietal pain	S-, M-, P-TB, ITF, sphenoid greater wing, TMJ	ITFA type B	total removal	none	none	DF at 2 years 9 months
1996	Silvers et al.	55/F/R	otalgia, facial pain, facial/scalp mass	anterior portion of right TB	ITFA, preoperative embolization	total removal	none	none	NA
1999	Lee et al.	45/M/L	hearing loss	S-, M-, P-TB, MCF, ITF	subtemporal craniotomy	NA	NA	NA	NA
		60/F/L	difficulty in chewing	S-TB, TMJ	NA	NA	NA	NA	NA
2000	Gibbons et al.	44/M/R	hearing loss, vertigo, tinnitus, otorrhea, EAC mass, mild FN paralysis	S-, M-, P-, Z-TB, ITF, MCF, otic capsule	ITFA type B	total removal	none	seroma, 1 episode of seizure	DF at 4 years
2003	Tang et al.	61/F	facial palsy, dizziness, vomiting, weight loss	TB	transtemporal	partial removal	RT		
2005	Pai et al.	26/M/R	hearing loss, tinnitus, swelling, FN paralysis, CHL	S-, M-, P-, Z-TB, MCF	temporoparietal craniotomy	total removal	none	total FN paralysis	DF at 1 year
2007	Elder et al.	2/F/R	mass behind ear, aural discomfort	TB	temporoparietal craniotomy	total removal	none	none	
		7 weeks/F	mass in the EAC	TB	temporoparietal craniotomy	total removal	none	total FN paralysis	
2008	Matsushige et al.	77/F/L	headache, vomiting dizziness, temporal hemorrhage	left temporal extradural mass, ITF	ITFA type B	total removal	none	none	NA
2009	Isaacson et al.	42/M/R	total hearing loss, EAC bulge	S-, M-, P-TB, MCF, otic capsule, TMJ	combined MCF/subtotal petrosectomy	total removal	none	↑ lacrimation of eye	DF at 3 years
		47/M/L	recurrence with otalgia and aural fullness, prior surgery with MCF and subtotal clearance, MHL	S-, M-, P-TB, TMJ	revision MCF, ITFA, reconstruction of floor of MCF with split calvarial BG	total removal	none	labyrinthectomy for severe giddiness	DF at 10 years
2012	Iizuka et al.	32/M/L	left aural hearing loss, tinnitus, fullness, EAC bulge, CHL	M-TB, TMJ, MCF	transmastoid MCF, ossiculoplasty	total removal	none	mild FN paralysis recovered after 1 year, hearing ↑	DF at 4 years

FN = Facial nerve; V nerve = trigeminal nerve; MHL = mixed hearing loss; M- = mastoid; S- = squamous; P- = petrous; Z- = zygomatic; Sp- = sphenoid TB; TB = temporal bone; RT = radiotherapy; NA = not available; DF = disease free.
[1] This case report has been included as case No. 1 in our series.

Giant Cell Tumors of the Skull Base: Case Series

with a blind-sac closure of the EAC. For tumors involving the MCF with or without dural invasion, an MCF craniotomy must be performed. For additional exposure any of the skull base procedures may be added. Posterior extensions into the PCF, though rare, can be aggressive and extremely challenging to treat as seen in case 5 of our series. The reports of GCTs by other authors [Cook et al., 1986; Findlay et al., 1987; Rock et al., 1994; Saleh et al., 1994; Silvers et al., 1996; Lee and Lum, 1999; Gibbons et al., 2000; Tang et al., 2003; Pai et al., 2005; Elder et al., 2007; Matsushige et al., 2008; Isaacson et al., 2009; Iizuka et al., 2012] show that most authors achieved radical tumor removal through lateral skull base or neurosurgical procedures with adequate locoregional control (table 2). The facial nerve and the lower cranial nerves were preserved during surgery in all our cases.

Radiotherapy is reserved for tumors which are incompletely resected or recurrent. The role of primary radiotherapy for the treatment of these tumors is controversial due to earlier reports that GCTs could turn malignant after radiotherapy [Glasscock and Hunt, 1974]. A multi-institutional study of 58 patients with GCTs treated by radiotherapy in European and North American academic centers by Bhatia et al. [2011] reported no malignant transformation in any of the cases. They reported 5-year overall survival of 94% and 5-year disease-free survival of 81%. Their univariate analysis also showed that, except for age, there were no other associations for disease transformation, including gender, histology, grade, tumor type, location, size, type of recurrence or radiation dose. In another series of 5 cases, Roeder et al. [2010] reported overall survival of 100% but did not find significant decrease in tumor size after radiotherapy.

Embolizations have been successfully carried out in GCTs outside the head and neck either as a primary modality or as a neoadjuvant therapy [Owen, 2010]. In the skull base, Rock et al. [1994] and Silvers et al. [1996] have reported on the use of preoperative embolization in the head and neck. However, since GCTs are not particularly vascular tumors the usefulness of embolization is under question and such reports need further validation.

Conclusion

Although GCTs are benign they are locally aggressive and this makes surgical management difficult in the skull base due to the complex anatomy. A thorough knowledge of the anatomy of the skull base and the various skull base approaches is necessary to treat this subset of tumors. Our series is one of the largest series in recent times and we have achieved successful results in 6 of the 7 cases. The ITFA type B and D combined with MCF approaches provide good exposure of tumor with minimal postoperative sequelae and good locoregional control. Recurrence, due either to subtotal removal or suboptimal treatment, may have disastrous consequences for the patient.

Disclosure Statement

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