Giant Cell Reparative Granuloma in the Temporal Bone of the Skull Base: Report of Two Cases

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ABSTRACT

Giant cell reparative granuloma (GCRG) in the temporal bone of the skull base is a very rare benign osteolytic lesion. Here, we report two cases that were initially misdiagnosed according to the patients' histories, clinical symptoms, and brain imaging prior to surgery. One case had a history of resection of a middle cranial fossa meningioma. The other case had a history of otitis media and mastoiditis. Pathological examination of the surgical specimens led to the diagnosis of GCRG for both cases. Both patients recovered well after surgical removal of the lesion without radiotherapy. Follow-up for 2 years indicated no recurrence of GCRG. These two cases support the hypothesis that repairing responses of bone tissue to either trauma or inflammation may underlie the pathogenesis of GCRG.

KEYWORDS: Giant cell reparative granuloma, temporal bone, trauma, inflammation, skull base

Giant cell reparative granuloma (GCRG) is an uncommon benign non-neoplastic osteolytic lesion that occurs mainly within the mandible and maxilla and occasionally in the small bones of the hands and feet. GCRG in the temporal bone is extremely rare and only a few sporadic cases have been reported.¹⁻³ Because of the characteristic that GCRG cells grow expansively and aggressively, GCRG often causes destruction of adjacent cortical bone and exhibits no significant changes in imaging, making it difficult to distinguish GCRG from other osteolytic bone lesions. Correct diagnosis is an interdisciplinary challenge, particularly when this lesion arises in an exceptional location.^{4,5} The etiology of GCRG is contentious and unclear. One view is that GCRG is the result of a repairing response of bone tissue to traumatic bleeding or inflammation. However, this

theory is challenged by the fact that not all patients have a clear history of traumatic bleeding or inflammation.⁶⁻⁸ In this communication, we report two cases of GCRG in the temporal bone of the skull base. One case had a history of previous tumor resection, and the other case had a history of chronic otitis media.

CASE REPORTS

Case one was a 38-year-old woman who was admitted to the hospital with a 4-month history of a gradual headache and 1-month history of right-limb weakness. The patient had a history of resection of a middle cranial fossa meningioma 4 years previously and had recovered well after the surgery. Clinical examination showed directional hemianopia to the top right, right hemiparesis,

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and a negative Babinski sign. Blood biochemical tests showed normal ranges of calcium, phosphorus, and potassium. Magnetic resonance imaging (MRI) demonstrated a $7 \times 6.2 \times 6.1$ -cm extra-axial lesion within the left middle cranial fossa resulting in moderate mass effect and uncus herniation. This lesion returned intermediate T1-weighted signal with some punctate foci of low T1-weighted signal and mixed intermediate, low, and high T2-weighted signal. There was heterogeneous gadolinium enhancement with some peripheral nonenhancing cystic or necrotic areas. There was thinning of the adjacent bone of the middle cranial fossa (Fig. 1).

On the basis of the patient's history, MRI, and physical signs, she was diagnosed with recurrent meningioma. Interdisciplinary surgical resection was performed using a combined transtemporal-subtemporal approach with craniotomy from the original left frontal temporal incision. The lesion was found to be dark red in color with a soft consistency, had abundant blood vessels, and had a clear boundary from the surrounding tissue. The lesion originated from the middle cranial fossa bone and had destroyed the adjacent bone. The lesion and the surrounding invaded bone tissue were removed completely, and the dura was repaired with a temporalis myofascial flap.

Microscopic examination of the tissue revealed fibrosis-like changes with a proliferation of fibroblasts

and multinucleated giant cells distributed within the stroma. Variably sized areas of hemorrhage with hemosiderin deposition were noted throughout the specimen. Osteoid formation and new bone formation were seen with diffuse infiltration of scattered inflammatory cells (Fig. 2). According to these pathological characteristics, the diagnosis was corrected to GCRG. The patient recovered well after surgery, and no GCRG had recurred after 2 years' follow-up.

Case two was a 46-year-old man, who presented with a 2-month history of right-sided ear pain and hearing loss. Clinical examination revealed secretory otitis media and mastoiditis. Further examination with Rinne and Weber tests revealed a right-sided conductive deafness. Computed tomography demonstrated an expansile bony lesion of the right middle cranial fossa measuring 2×1.6 cm in maximum axial dimensions. This was of low density with sclerotic molded bony edges (Fig. 3A, B). MRI showed a corresponding predominantly intermediate T1-weighted and high T2-weighted signal lesion with a thick rind of low T1-weighted and T2-weighted signal. There was a possible fluid-fluid level with dependent intermediate T2-weighted signal. Right-sided petromastoid air cell signal changes were also noted (Fig. 3C-E).

Figure 1 Magnetic resonance images from case one before surgical removal. An extra-axial lesion in the left middle cranial fossa resulted in moderate mass effect and uncus herniation. This lesion returned intermediate T1-weighted signal with some punctate foci of low T1-weighted signal and mixed intermediate, low, and high T2-weighted signal (A, B). There was heterogeneous gadolinium enhancement with some peripheral nonenhancing cystic or necrotic areas. There was thinning of the adjacent bone of the middle cranial fossa (C-E).

Figure 2 Microscopic examination of the tissue from case one revealed fibrosis-like changes with a proliferation of fibroblasts (A, $\times 200$), multinucleated giant cells distributed within the stroma, variably sized areas of hemorrhage with hemosiderin deposition throughout the specimen (B, $\times 400$), and osteoid formation and new bone formation with diffuse infiltration of scattered inflammatory cells (C, $\times 200$).

Combining the history and radiological findings, the lesion was considered to be bone destruction by an abscess, which was scheduled for surgical drainage. During surgery, the lesion extended into the extradural space of the inferior middle cranial fossa. It was jelly-like and dark red in color with a rich blood supply. Some bony tissue was involved.

Microscopic examination of the specimen revealed fibrosis with a large number of fibroblasts and variably sized areas of hemorrhage with associated hemosiderin deposition. The hemosiderin deposition was surrounded by a large number of multinucleated giant cells, and osteoid formation and new bone formation were also observed (Fig. 4). A characteristic feature of GCRG is

Figure 3 Computed tomography (CT) and magnetic resonance imaging (MRI) from case two before surgical removal. CT demonstrated an expansile bony lesion of the right middle cranial fossa measuring 2×1.6 cm in maximum axial dimensions. This was of low density with sclerotic molded bony edges (A, B). MRI showed a corresponding predominantly intermediate T1-weighted and high T2-weighted signal lesion with a thick rind of low T1-weighted and T2-weight signal. There was a possible fluid-fluid level with dependent intermediate T2-weighted signal. Right-sided petromastoid air cell signal changes were also noted (C–E).

Figure 4 Microscopic examination of the tissue from case two revealed fibrosis with a large number of fibroblasts (A, $\times 200$), variably sized areas of hemorrhage with associated hemosiderin deposition that was surrounded by a large number of multinucleated giant cells, osteoid formation (B, $\times 400$), and new bone formation (C, $\times 200$).

that the giant cells surround the areas of hemorrhage. The diagnosis of GCRG was rendered. The patient recovered well, and postoperative MRI indicated no recurrence of GCRG after 2 years' follow-up.

DISCUSSION

The term *giant cell reparative granuloma* was first proposed by Jaffe in 1953, and the corresponding pathological diagnostic criteria for GCRG were developed at that time to distinguish it from giant cell tumor, aneurysmal bone cyst, fibrous dysplasia, hyperparathyroidism of brown tumors, and other diseases.^{9,10} Since then, most GCRGs were reported to be located in the maxilla and mandible and occasionally in the small bones of the hands and feet. Cases with GCRG in the skull base are extremely rare. In 1974, Hirschl and Katz were the first to report GCRG in the temporal bone, and since then only sporadic cases have been reported.^{3,10-12} The correct diagnosis of GCRG before surgery is difficult, although some investigators have indicated that characteristic MRI findings include a thick low T1-weighted and T2-weighted signal rim with variable central signal.¹³⁻¹⁵ Indeed, several other lesions, and in particular giant cell bone tumor, also have similar imaging characteristics. It is very difficult to distinguish these diseases from GCRG on the basis of brain imaging.^{16,17}

The difficulty in the diagnosis of GCRG prior to surgery is partially due to the limited number of cases that have been documented and its unclear etiology. The possible GCRG etiologies include a proliferative response of bone tissue to traumatic bleeding and/or infection. According to this hypothesis, when the skull is subjected to trauma, bleeding within bone tissues occurs and macrophages migrate into the area to repair the damaged tissue. If the response is too excessive, it could generate a reparative granuloma. In chronic inflammation in the skull, the local hemodynamic changes often induce

responsive proliferation in the tissue, which is rich in new blood vessels and often accompanied by bleeding. Under this condition, macrophages migrate into the bleeding area to repair and, in some cases, to generate a reparative granuloma. Immunohistochemistry and electron microscopy studies have confirmed that the macrophages responsible for repair are the precursors of the giant cells in GCRG, supporting the idea that GCRG can be caused by trauma and inflammation.^{8,9,12} However, this hypothesis has been challenged by many other researchers because a considerable number of patients have no clear history of trauma and/or inflammation.⁶⁻⁸ The two cases we report here had a clear history of skull base meningioma resection and otitis media and mastoiditis, supporting the trauma and inflammation theory of GCRG.

Although brain imaging of GCRG is not specific, the pathology of GCRG has distinct characteristics. The GCRG lesion is mainly composed of a large number of fibroblasts intermingled with areas of hemorrhage, which can be surrounded by multinucleated giant cells. Another distinctive feature seen in some cases is the formation of osteoid in some of the hemorrhagic regions.^{12,18} The two cases reported in this article showed the typical pathological changes of GCRG. These pathological features can distinguish GCRG from other lesions occurring in the temporal bone. In addition, because GCRG contains a large number of fibroblasts, distributed bleeding loci, and osteoid formation, which make the tissue dark red in color, soft, and hemorrhagic,^{2,7,10,19,20} it is easy to distinguish it and remove it during surgery. However, removal of the lesion should be thorough and include any eroded bone to prevent recurrence.^{2,4,7,10,12,14,15,17,19,20} The recurrence of GCRG occurring in the temporal bone has not been reported, probably due to only a few documented cases. The two cases we report here recovered well after operation without radiotherapy. We did not find recurrence of these cases after follow-up for 2 years.

In conclusion, GCRG of the temporal bone is a rare benign osteolytic lesion and is difficult to distinguish from other osteolytic bone lesions. Although the exact etiology of GCRG is unclear, the two cases reported here support the hypothesis that trauma and inflammation contribute to the development of GCRG.

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