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Multifocal Inflammatory Pseudotumor of the Temporal Bone, Maxillary Sinus, and Orbit

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Objective: This is the first report of multifocal inflammatory pseudotumor (IPT) involving the temporal bone, orbit and paranasal sinus, and the use of rituximab as adjunctive therapy in multifocal temporal bone IPT.

Patient: We describe a 46-year-old man with orbital and maxillary sinus IPT, whose disease progressed despite radiation and steroid burst. He then developed contralateral mastoid disease, otalgia, aural fullness, and hearing loss.

Intervention: He was initiated on rituximab and prednisone therapy. Mastoidectomy with near-total tumor removal was accomplished and histopathology confirmed IPT. A literature review was also performed.

Main Outcome Measure: Tumor regression or recurrence.

Result: Despite disease progression after radiation and steroids, his orbital, sinus, and mastoid disease improved after surgery, steroids, and rituximab. A review of four other previously reported cases of multifocal disease involving the

temporal bone suggest that multifocal disease may be a more aggressive entity with higher recurrence rate compared with solitary disease. Although surgery and steroids are typically recommended, there is currently no consensus treatment recommendation.

Conclusions: Multifocal IPT of the temporal bone is a rare but aggressive entity for which surgery and steroid combination therapy should be first line treatment. We suggest rituximab may be an effective adjunctive treatment particularly for recurrent disease or where systemic therapy may be favored. **Key Words:** Fibrous xanthoma—Histiocytoma complex—Inflammatory myofibroblastic tumor—Inflammatory myofibrohistiocytic proliferation—Inflammatory pseudotumor—Plasma cell granuloma—Rituximab—Xanthomatous pseudotumor.

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Inflammatory pseudotumor (IPT), first described by Brunn in 1939, is a benign, fibro-inflammatory lesion (a.k.a, plasma cell granuloma, inflammatory myofibroblastic tumor, histiocytoma complex, xanthomatous pseudotumor, fibrous xanthoma, and inflammatory myofibrohistiocytic proliferation) (1,2). Clinically and radiographically, IPT can mimic malignant disease. The lesion can appear locally erosive on computed tomography (CT) and as low intensity lesions on magnetic resonance imaging (MRI) T1 and T2 sequences. Although the pathogenesis is not well understood, it has been associated with previous inflammation, trauma, infection, surgery, and an altered immune-mediated response (3,4).

IPT is most common in the lung but can occur anywhere (5). IPT of the head and neck accounts for less than 5% of all extrapulmonary cases (6). Within the head and neck, the most common location is the orbit, followed by the meninges, paranasal sinuses, infratemporal fossa, and nasopharynx (7). Temporal bone manifestation is rare, only ~40 cases have been reported (8), and those with distant multifocal disease are exceedingly rare, only four reported cases (9–12) (Table 1). To the best of our knowledge, this is the first case of simultaneous involvement of the temporal bone and contralateral orbit and maxillary sinus. Steroids and surgery are the most common treatment modalities, with occasional use of radiation or chemotherapy. The use of biologic therapy has only been reported in two cases of solitary temporal bone IPT. We report the first successful use of rituximab for adjunctive therapy in recurrent multifocal IPT of the temporal bone.

CASE REPORT

A healthy 45-year-old man presented with 6 weeks of epistaxis, left facial pain, nasal obstruction, and 1 week of

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TABLE 1. Characteristics of cases of multifocal inflammatory pseudotumor involving the temporal bone reported in the literature

Author	Age/Gender	Symptoms	Location	Treatment	Outcome
Rodgers et al. (9)	48 M	FP/HL/vertigo/headache/seizure	Bil Temp	Surgery/steroid	Remission
Tian et al. (10)	51 M	HL/neck swelling	L Temp/L parotid	Surgery/steroid/XRT/Chemo	Three recurrences, remission
Goh et al. (11)	27 F	Ota/HL	Sinus/Bil Temp	Surgery/steroid	Two recurrences, NED
Lee et al. (12)	39 M	HL/RP/diplopia	R Temp/Lung	Surgery/steroid	NED

Bil indicates bilateral; Chemo, cyclophosphamide; FP, facial palsy; HL, hearing loss; L, left; M, mastoid; ME, middle ear; NED, no evidence of disease at the last follow-up; Ota, otalgia; R, right; RP, retrobulbar pain; Temp, temporal bone; XRT, radiotherapy.

diplopia. CT showed a left maxillary sinus and ethmoid mass with erosion of the lamina papyracea. MRI revealed a circumferential enhancing tumor within the left maxillary sinus with enhancement of the medial rectus but no infiltration of the orbit. Endoscopic maxillary antrostomy and biopsy were performed. Diagnosis of IPT was made on histopathology. Per recommendation by the multidisciplinary tumor board, the patient was treated with 4 weeks of radiation therapy at 27 Gy followed by a prednisone burst.

Unfortunately, symptoms progressed with proptosis, vision loss, and restricted extraocular movement. Repeat MRI revealed persistent disease in the maxillary sinus (Fig. 1A, arrowhead), new diffuse infiltration of the left orbital fat (Fig. 1B, arrow), and evolution of a new right mastoid lesion (Fig. 1A, arrow). The patient was restarted on 40 mg prednisone. Despite treatment, his orbital symptoms worsened with development of optic nerve enhancement on MRI. At this point, rituximab was initiated with a 1000 mg/m² rituximab induction two times followed by 375 mg/m² weekly for 14 weeks. The patient then underwent endoscopic sinus surgery with orbital decompression.

During this time, the patient developed right-sided otalgia, aural fullness, hearing loss, and a new right mastoid lesion on MRI that was not present before radiation. He was thus referred to Neurotology clinic. CT revealed opacification and destruction of the right mastoid air cells with dehiscence of tegmen mastoideum (Fig. 2, arrows) and erosion of the fallopian canal (Fig. 2, arrowhead). Otomicroscopy and facial nerve function were normal and there was no sign of labyrinthine fistula. Pure tone audiometry demonstrated conductive hearing loss with a 5 to 10 dB air-bone gap in the right ear. The patient underwent an intact canal wall mastoidectomy. Intraoperatively, the tumor was noted to be fibrotic, strongly adherent to surrounding structures, and quite vascular. Extensive bony erosion was seen along the tegmen. The ossicles were intact and the mesotympanum was free of disease. Intraoperative frozen sections showed no evidence of malignancy. Near-total tumor removal was achieved.

The final histopathologic diagnosis confirmed IPT of the mastoid (Fig. 3). There was mixed inflammatory infiltrate composed predominantly of mature plasma cells, frequent neutrophils, and scattered eosinophils.

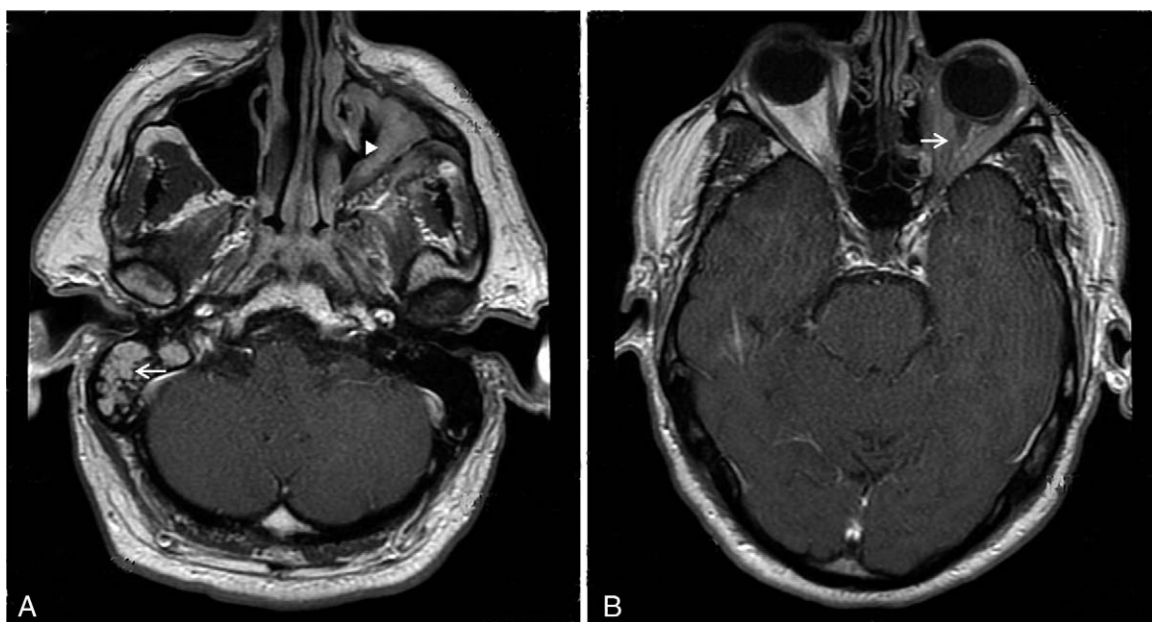


FIG. 1. T1-weighted MR images with contrast. There are homogenous enhancing lesions in right mastoid region (A, arrow) and left maxillary sinus (A, arrowhead) and infiltration of left orbital fat (B, arrow). MR indicates magnetic resonance.



FIG. 2. High-resolution CT of temporal bone. Axial (A) and coronal view (B) showed complete opacification in right mastoid with extensive erosion of tegmen (arrows) and partial erosion of vertical segment of fallopian canal (arrowhead). CT indicates computed tomography.

No epithelioid granulomas or giant cells were noted. Plasma cells were immunoreactive for both kappa and lambda light chains. IgG4 to IgG positivity was less than 10%. Flow cytometry was negative for lymphoma. He was restarted on a second course of rituximab (two inductions at 1000 mg/m², 4 weeks of maintenance 375 mg/m² weekly). He continued to remain on steroids.

The patient is now 21 months since presentation and 9 months since mastoidectomy. Long-term steroids and second course of rituximab treatment were completed 4 months ago. His most recent MRI shows resolution of temporal bone, sinus and orbital disease with improved appearance of the optic nerve. His aural symptoms,

proptosis and extraocular movement have been restored but his vision has not.

DISCUSSION

IPT is characterized histologically by non-neoplastic proliferation of spindle cells, with varying proportions of lymphocytes, plasma cells, histiocytes, fibrocytes, and extracellular collagen (5,7,10). Recently, there have been reports to suggest an association between IPT and IgG4 (8). Our periorbital pathology showed that nearly all plasma cells were IgG positive and that IgG4 positivity neared 20%. This is however much less than what is expected for IgG4 disease. Most acceptable cutoff criteria for IgG4 disease are set at more than 40% (13). Interestingly, the mastoid sample obtained 6 months after initiating rituximab and steroids yielded low IgG4 (<10%) content. This may represent tumor response to rituximab and steroids. Whether IPT is a subtype of IgG4 disease is unclear at this point.

Compared with pseudotumor in other locations, lesions of the temporal bone tend to be more aggressive (14). The locally destructive tumor has been reported to invade surrounding dura, sigmoid sinus, tentorium, facial nerve, and otic capsule and have perineural involvement.

Literature review suggests that multifocal disease involving the temporal bone is even more aggressive than solitary temporal bone IPT. Of ~40 cases with IPT of the temporal bones that have been described, only four cases are reported with additional distant sites (Table 1). Among these four, there is a male preponderance (3:1) (4:1 including this case). Two cases had bilateral lesions of the temporal bones. Extra-temporal sites include parotid gland, paranasal sinus, and lung. Our case is

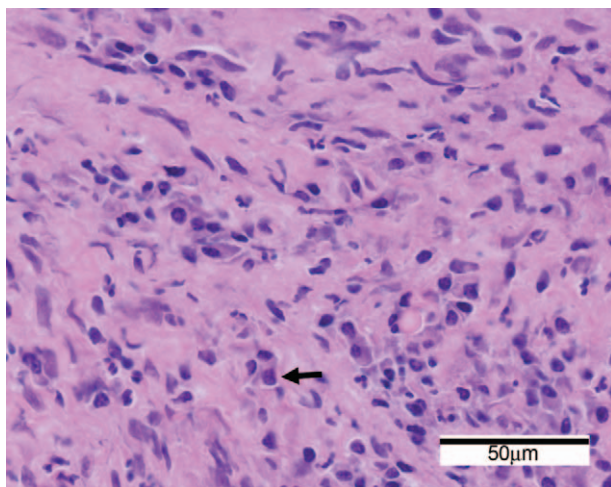


FIG. 3. Histopathology of the mastoid biopsy, Hematoxylin and eosin stain, 40× magnification. Spindle cell proliferation with plasmacytic, lymphocytic, and histiocytic infiltrate (arrow).

the first to report the involvement of both temporal bone and orbit. All patients underwent a combination of surgery and steroids. Of the four cases, two showed no evidence of disease and two had multiple recurrences requiring additional surgery or adjunctive treatment (radiation and cyclophosphamide). In our case, there was progression of disease despite radiation therapy and steroid burst. Overall, solitary temporal bone disease has a recurrence rate of ~10% compared with more than 50% in multifocal disease. The high likelihood of recurrence or failure of treatment in multifocal IPT may suggest that this may be a more aggressive entity.

Temporal bone IPT occurs infrequently and there is no consensus treatment. Any combination of steroids, surgery, radiation, and chemotherapy has been reported. Surgery is performed in a majority of cases (82%)—it is the mainstay of treatment and it is indicated to obtain tissue for pathologic diagnosis and ruling out malignancy. For lesions involving the lateral skull base, combination therapy which includes surgical excision shows better outcome (2). Nearly all are treated with steroids if tolerated. Approximately 10% will recur within a few months. Patients who recur or are unable to tolerate steroids may require additional therapies. Approximately 20% undergo radiation as an adjunctive therapy. Rarely, immunosuppressants such as cyclophosphamides and mycophenolate are also used, but these treatments are associated with major side effects. In the last decade, a biologic immunosuppressant, rituximab, a monoclonal antibody targeting B-cells, has been reported to be successful in treating various inflammatory orbital disease (15) with only sporadic use in orbital (16) and intracranial IPT (17). There are only two cases of its use in isolated temporal bone IPT in conjunction with surgery and steroids (8), but none reported for multifocal temporal bone disease. Its use in IPT is currently off-label. Our case suggests that the use of rituximab combined with steroids and surgery is beneficial for multifocal temporal bone IPT. One benefit of rituximab is that systemic therapy may be favored for multifocal disease over radiation, which would require multiple localized treatments. Also, chemotherapy such as cyclophosphamides and mycophenolate have significant side effects and need for frequent laboratory testing, which makes rituximab a more preferable systemic therapy.

CONCLUSION

IPT of the temporal bone is a rare but locally aggressive entity that can be associated with severe neurologic complications. A review of the literature reveals only five patients, including our case, that have temporal bone IPT with distant multifocal disease. At this point, it is unclear if IPT is indeed a subtype of IgG4 disease, but we do find

elevated levels of IgG4:IgG levels. There appears to be a slight male preponderance. We conclude that 1) multifocal IPT is more aggressive and likely to recur than isolated temporal bone IPT and 2) our case shows that combination therapy which includes surgery, steroids, and rituximab was successful in disease remission. Surgical excision followed by immunosuppressive therapy including corticosteroids is the mainstay of treatment and the addition of rituximab may be helpful for recurrent or persistent disease. Early recognition and treatment should result in favorable outcomes, and long-term follow-up is indicated due to the tendency of the disease to recur.

REFERENCES

1. Patnana M, Sevrakov AB, Elsayes KM, et al. Inflammatory pseudotumor: the great mimicker. *AJR Am J Roentgenol* 2012;198:W217–27.
2. Spinazzi EF, Desai SV, Fang CH, et al. Lateral skull base inflammatory pseudotumor: a systematic review. *Laryngoscope* 2015;125:2593–600.
3. Cho AH, Lee BH, Kwak KW, et al. Inflammatory pseudotumor of temporal bone with pachymeningitis, cranial neuropathies and uveitis. *Eur Neurol* 2004;51:238–40.
4. Dehner LP. Inflammatory myofibroblastic tumor: the continued definition of one type of so-called inflammatory pseudotumor. *Am J Surg Pathol* 2004;28:1652–4.
5. Alyono JC, Shi Y, Berry GJ, et al. Inflammatory pseudotumors of the skull base: meta-analysis. *Otol Neurotol* 2015;36:1432–8.
6. Coffin CM, Watterson J, Priest JR, et al. Extrapulmonary inflammatory myofibroblastic tumor (inflammatory pseudotumor). A clinicopathologic and immunohistochemical study of 84 cases. *Am J Surg Pathol* 1995;19:859–72.
7. Park SB, Lee JH, Weon YC. Imaging findings of head and neck inflammatory pseudotumor. *AJR Am J Roentgenol* 2009;193:1180–6.
8. Ortlip TE, Drake VE, Raghavan P, et al. Inflammatory pseudotumor of the temporal bone: a case series. *Otol Neurotol* 2017;38:1024–31.
9. Rodgers B, Bhalla V, Zhang D, et al. Bilateral inflammatory myofibroblastic tumor mastoiditis. *Head Neck* 2015;37:E142–5.
10. Tian H, Liu T, Wang C, et al. Inflammatory pseudotumor of the temporal bone: three cases and a review of the literature. *Case Rep Med* 2013;2013:480476.
11. Goh BS, Tan SP, Husain S, et al. Metachronous inflammatory myofibroblastic tumour in the temporal bone: case report. *J Laryngol Otol* 2009;123:1184–7.
12. Lee JH, Jung MK, Song CE, et al. Concomitant inflammatory pseudotumor of the temporal bone and lung: a case report. *Ear Nose Throat J* 2007;86:614–6.
13. Deshpande V, Zen Y, Chan JK, et al. Consensus statement on the pathology of IgG4-related disease. *Mod Pathol* 2012;25:1181–92.
14. Strasnick B, Vaughan A. Inflammatory pseudotumor of the temporal bone: a case series. *Skull Base* 2008;18:49–52.
15. Lim L, Suhler EB, Smith JR. Biologic therapies for inflammatory eye disease. *Clin Exp Ophthalmol* 2006;34:365–74.
16. Schaffranski MD. Idiopathic orbital inflammatory disease successfully treated with rituximab. *Clin Rheumatol* 2009;28:225–6.
17. Garcia BA, Tinsley S, Schellenberger T, et al. Recurrent inflammatory pseudotumor of the jaw with perineural intracranial invasion demonstrating sustained response to Rituximab. *Med Oncol* 2012;29:2452–5.