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A Case Series of Granulomatosis With Polyangiitis Primarily Diagnosed by Otological Manifestations

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Abstract

Objective: To describe a case series of previously undiagnosed granulomatosis with polyangiitis (GPA) patients who presented primarily with otological manifestations.

Method: We report a series of patients visited at a neurotology clinic who were eventually diagnosed with GPA based on their otologic complaints and had no prior knowledge of having this condition.

Results: In this series, 10 (91%) patients presented with hearing loss (HL), more than half of which were bilateral (60%). Upon audiometric examination, all but 1 patient had mixed, conductive, or sensorineural HL. All patients presented with eustachian tube dysfunction (ETD), otitis media with effusion (OME), or both. Nasal endoscopy showed intranasal pathology in 3 (27%) patients. Otologic symptoms were improved in all patients after treatment with an average of 4 in-office follow-up appointments.

Conclusion: GPA should be included in the differential diagnosis of adults with unexplained mixed hearing loss, new onset serous effusion, or acute otitis media in the absence of a previous history of ETD. Laboratory tests (ie, anti-neutrophil cytoplasmic autoantibody, erythrocyte sedimentation rate, and C-reactive protein) along with a urinalysis can aid in screening these patients. In cases in which the index of suspicion is high, repeated testing could reduce the risk of false negative findings.

Keywords

granulomatosis with polyangiitis, Wegener's granulomatosis, otology, hearing loss, ANCA associated vasculitis

Introduction

Granulomatosis with polyangiitis (GPA), previously known as Wegener's granulomatosis, is a rare multisystem autoimmune disorder, characterized by necrotizing granulomatous inflammation and pauci-immune vasculitis. GPA typically affects the upper and lower respiratory tracts and kidneys; however, any organ may be involved. The pulmonary nodules with necrotizing inflammation of upper respiratory tract and glomerular nephritis are common systemic features seen in GPA. Pulmonary symptoms including recurring bloody rhinorrhea, rhinosinusitis, and nodular lesions in the lungs are seen in 45% of the cases on presentation and 87% during the course of the diseases.[1,2] Ocular involvement is frequent and may range from mild conjunctivitis to dacryocystitis, scleritis, episcleritis, uveitis, ciliary vessel vasculitis, and retro-orbital mass lesion.[3]

In the United States, GPA has a 5-year period prevalence of 2.6 to 3.2 cases per 100 000 persons.[4] Of those patients with involvement of head and neck area, 85% to 100% have nasal cavity and paranasal sinuses symptoms, including chronic sinusitis, rhinitis, and epistaxis.[5,6] Most notably, otologic symptoms are often the first and only clinical manifestations of GPA, with the presence of symptoms existing 19% to 61% of the time.[5] In particular, the presence of otitis media with effusion (OME) makes up a large portion (40%-70%) of the presenting cases.[7,8] Herein, we describe a series of patients who presented with otologic findings that led to the diagnosis of GPA.

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Table 1. Demographic and Clinical Characteristics of the Patients.

Patient	Age	Sex	Otologic Findings	Otalgia	Type of HL	Pattern of HL	Otologic Intervention	Other Findings
1	36	F	OME/ETD	N	Conductive	Unilateral	PE tube	Hx of SLE
2	41	F	OME/ETD	Y	Conductive	Unilateral	PE tube	Developed subglottic stenosis
3	51	M	OME	Y	Mixed	Bilateral	PE tube	
4	52	M	OME	Y	Mixed	Unilateral	PE tube	
5	51	F	OME/ETD	Y	Mixed	Bilateral	PE tube	
6	46	F	ETD	N	Conductive	Bilateral	Observation	
7	78	M	OME/ETD	N	Sensorineural	Bilateral	Observation	
8	43	F	OME	Y	None	N/A	Observation	
9	60	M	OME	Y	Mixed	Unilateral	Observation	Facial paralysis
10	19	F	OME	N	Mixed	Bilateral	PE tube	Hx of vision loss, which returned
11	65	F	OME/ETD	N	Sensorineural	Bilateral	PE tube	

Abbreviations: ETD, Eustachian tube dysfunction; HL, hearing loss; Hx, medical history; OME, otitis media with effusion; PE tube, pressure equalization tube; SLE, systemic lupus erythematosus.

Case Series

A retrospective chart review spanning 2010 to 2016 was performed with Institutional Review Board approval at a tertiary care neurotology clinic to identify patients who were eventually diagnosed with GPA but had no prior knowledge of having this condition. All patients underwent audiometric testing, nasal endoscopy, and flexible laryngoscopy. After review of these clinical examinations and laboratory testing, all patients included were determined to have a diagnosis of GPA. Diagnostic reasoning aligned with the American College of Rheumatology (ACR) classification criteria[9] as well as the Chapel Hill Consensus Conference (CHCC) criteria for GPA.[10] Diagnosis of GPA was further confirmed with an elevated anti-neutrophil cytoplasmic autoantibody (c-ANCA).

A total of 11 patients presented with otologic symptoms with no previous diagnosis of GPA (Table 1) were identified. There were 4 men and 7 women with an average age of 49.2 years (range, 19-78 years). One patient was of Asian descent, and the remaining 10 were Caucasian. Upon examination, 10 out of 11 patients had OME, 1 one had eustachian tube dysfunction (ETD) without an effusion (Table 1). The most common otologic finding was hearing loss (HL), which was observed in 10 patients, while 6 patients endorsed otalgia. Of the 10 patients in whom audiometry was available, 8 had conductive hearing loss, and 7 had sensorineural hearing loss (SNHL). Five of the patients had both conductive and sensorineural hearing losses. In other words, 7 of these 10 patients had evidence of both middle and inner ear diseases. The pattern of HL was unilateral in 4 patients. Other related head and neck findings included 1 patient with facial paralysis. Nasal endoscopy showed evidence of intranasal granulation in 3 patients. When applicable, for example, asymmetric SNHL and/or facial paralysis, magnetic resonance imaging (MRI) was performed with gadolinium. The only finding was mucosal inflammation in the middle ear or mastoid and no abnormalities of the nerves were found. Computed tomography (CT) imaging generally showed an opacified mastoid with normal bony architecture of a well-developed mastoid.

After diagnosis, all patients received immunosuppressive therapy for the systemic disease process; otologic intervention is outlined in Table 1. To induce remission, patients received prednisone 1 mg/kg/d up to 80 mg daily in combination with methotrexate (0.3 mg/kg/wk). For remission maintenance, our rheumatology colleagues combined methotrexate with anti-TNF therapy (adalimumab most commonly). One patient with an isolated ear disease (negative c-ANCA) received trimethoprim 80 mg/sulfamethoxazole 400 mg daily after going into remission to maintain the remission. GPA was suspected and confirmed in all patients with either gingival or sinonasal biopsy or c-ANCA positivity. Histopathologic criteria for the diagnosis of GPA included fat necrosis, lipid-laden macrophages and giant cells, micro abscesses, granulomatous inflammation/foci, polymorphous inflammation featuring plasma cells, lymphocytes, neutrophils, as well as collagen necrosis and vasculitis.[11] The diagnosis was confirmed with a positive c-ANCA on all patients eventually. Two patients had initially a negative c-ANCA, but high suspicion of the clinicians and positive exam findings led to a biopsy and diagnosis. Follow-up c-ANCA testing was positive in both patients. The third patient with negative c-ANCA initially had no other examination findings and had a repeated c-ANCA testing a few weeks later due to a high suspicion, which was positive. All patients experienced improvement

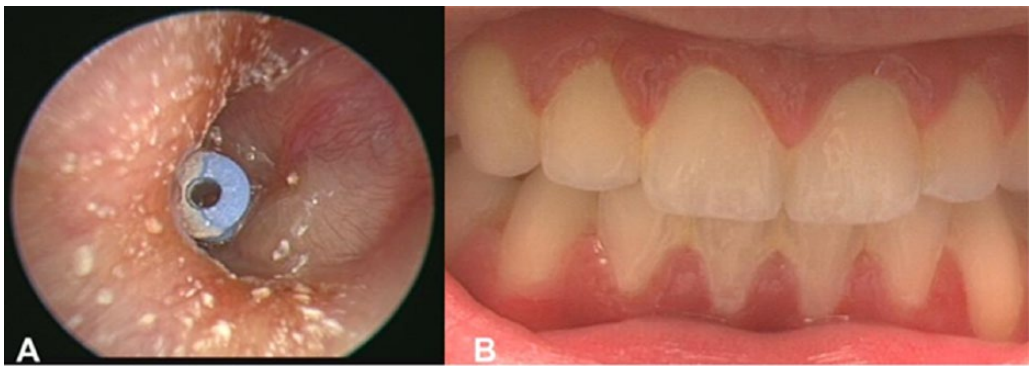

Figure 1. Otological and oral manifestations of granulomatosis with polyangiitis (GPA). (A) Otologic examination of patient with GPA. Pale granulation behind the tympanic membrane (TM) can be seen in posterior TM. (B) Gingival manifestations of GPA at the margin of the teeth can be seen.

of otologic symptoms after treatment (immunosuppressants or pressure equalization [PE] tube placement), with an average of 4 in-office follow-up appointments.

Discussion

This case series illustrates the importance of thoroughly considering GPA as the underlying diagnosis in adults presenting with specific otologic complaints. In the United States, GPA has an approximate incidence rate of 1.3 to 2.0 per 100 000 person per year[4] and occurs more frequently than vestibular schwannomas, which have an incidence of 0.3 to 1 per 100 000 population per year.[12] In an otolaryngology or tertiary neurotology practice, GPA patients should, in theory, be seen as frequently as those with vestibular schwannomas. The higher prevalence of GPA may suggest some GPA patients may be missed when these patients present to an otolaryngologist or otologist, possibly due to a low index of suspicion.

The otologic manifestations of GPA are commonly the only presenting symptom that can aid in the diagnosis of GPA.[5,13] Others have reported that 25% of GPA patients present with OME and HL as the second most common symptom in 6% of patients.[14] We similarly demonstrated a high prevalence of both OME (82%) and HL (91%) in our previously undiagnosed GPA patients. Furthermore, our findings align with others who have demonstrated significant otalgia or facial paralysis in the presence of serous middle ear effusion as diagnostic indicators of GPA.[15] Other features demonstrated in our case series were pale granulation in the middle ear with apparent serous otitis media (Figure 1A), otalgia in the presence of serous effusion, mixed hearing loss in patients with serous effusion, gingival lesions (Figure 1B), nasal granulation, and subglottic stenosis.

Therefore, in patients presenting with unexplained serous otitis without a history of upper respiratory infection, allergic rhinitis, or ETD, GPA should be included in the differential diagnosis. Serous otitis in the presence of a new-onset SNHL or significant pain should raise the suspicion of GPA. An initial screening with c-ANCA, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and urinalysis may help in the diagnosis. The ESR, CRP, and urinalysis are nonspecific tests that are useful when the c-ANCA is negative to help point to the diagnosis when the suspicion is high. All patients with a positive c-ANCA had highly elevated ESR and CRP. The remaining 3 patients had a mildly elevated ESR and CRP. Two patients with a negative initial c-ANCA had a positive urinalysis showing proteinuria or hematuria. The positive urinalysis contributed to the decision to recheck the c-ANCA later. Nasal endoscopy should be performed to screen for granulation tissue, and a biopsy should be done to help confirm the diagnosis. In the presence of a high index of suspicion, the testing should be repeated to help rule out the diagnosis.

In the workup of patients with previously undiagnosed GPA, 3 patients had an initially negative c-ANCA test, which became positive on follow-up testing, which was obtained due to a high index of suspicion. All patients with an initially false negative test were on steroids to treat the SNHL, facial paralysis, or serous otitis at the time of testing. In our experience, it is imperative to retest patients 2 to 3 weeks after cessation of steroid treatment with clinical suspicion of GPA. Reassessment with nasal endoscopy and biopsy of endonasal granulation tissue can assist in the diagnosis of GPA when ANCA testing is negative. In addition, in the context of otologic complaints described previously, combined with a high ESR, CRP, or an abnormal urinalysis, the suspicion of GPA should remain even when ANCA testing is normal.[16]

Following diagnosis, GPA patients are responsive to immunosuppressive therapy with or without PE tube placement and can have near complete symptomatic resolution of all otologic symptoms. In our series, SNHL did not fully return to normal in all patients, but the 1 patient with facial paralysis did experience a return of function from grade VI to grade III.

Conclusion

Clinicians should maintain a high index of suspicion for patients presenting with mixed or conductive HL with new onset serous effusion, particularly in the absence of previous ETD. All patients in this series were previously undiagnosed with GPA, but their otologic symptoms were suspected to be manifestations of GPA. As demonstrated in patients included here, we recommend initial screening with ANCA, ESR, CRP, urinalysis, and nasal endoscopy for GPA. Cessation of steroid treatment prior to ANCA testing or endonasal granulation tissue biopsy can assist in GPA diagnosis, while repeated testing can help rule in/out the diagnosis, especially when suspicion for GPA is high.

Authors' Note

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Declaration of Conflicting Interests

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