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CASE REPORT

A Giant Silence – An atypical association of sensorineural hearing loss with Giant Cell Arteritis

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Abstract

Giant cell arteritis (GCA) is a chronic vasculitic disorder predominantly affecting medium to large sized arteries, prevalent in the 50 plus age group. This case illustrates an atypical presentation of this disease in the form of bilateral sensorineural hearing loss (SNHL). Apart from the presence of constitutional and vertiginous symptoms, there were essentially no classical features of GCA. Differentials were broad including infection, malignancy and medication toxicity as well as brain, eye and ear syndromes such as Cogan's syndrome, all of which were eventually excluded. Her diagnosis was ultimately confirmed on positron emission tomography, which highlights the diagnostic importance of this modality. She was managed with corticosteroids then tocilizumab and is making a gradual recovery. Literature review demonstrates that SNHL is more prevalent than previously suggested in GCA, although this does not have widespread recognition. Mechanisms of SNHL in GCA include vascular occlusion, immunological mechanisms including cross reactivity with viral antigens and direct viral infection. SNHL does appear to improve with corticosteroids. This case emphasizes the importance of considering GCA as an important differential in SNHL.

KEYWORDS
clinical aspects, disease etiology and pathogenesis, giant cell arteritis, sensorineural hearing loss, vasculitides

1 | BACKGROUND

Giant cell arteritis (GCA) is a chronic vasculitic disorder predominantly affecting medium to large sized arteries. It is the most common systemic arteritis in European and American populations, with a prevalence of 0.2% in those aged over 50 years.[1]

Aging is the biggest risk factor with individuals >50 years old predominantly affected, with peak incidence at age 70-80 years.[2] Other risk factors include Scandinavian ethnicity, female gender, family history and polymyalgia rheumatica.[3]

The classic symptoms of presentation include acute to subacute onset of headache, jaw claudication, scalp tenderness and constitutional symptoms.[4] Serious complications of visual loss and extra-cranial arterial manifestations such as aortic aneurysms can also occur.[4,5]

Sensorineural hearing loss (SNHL) represents an atypical presentation of GCA, with only a few documented case reports. This case illustrates a debilitating presentation of GCA and highlights GCA as an important differential in the consideration of SNHL.

2 | CASE PRESENTATION

A 67-year-old independent Chinese woman presented to the emergency department with a 4 days history of profound, progressive

bilateral hearing loss commencing in the left ear. This was accompanied by tinnitus and vertigo. Her symptoms began 4 days after receiving the ChAdOx1-S recombinant vaccine (Astra Zeneca).

Her tinnitus started in her left ear, progressed to her right the next day and resulted in bilateral complete hearing loss within 4 days. Constitutional symptoms included subjective fevers for 4 days at home and 5 kg of weight loss in the preceding months. She also described hip and shoulder girdle pain 12 months prior to presentation without formal diagnosis.

Other features included a dry cough which resolved weeks prior to this presentation and mild bilateral pain in her pinna. She had no history of head trauma. She did not experience headache, scalp tenderness, jaw claudication or visual disturbance.

Her medical comorbidities included ischemic heart disease, degenerative disc disease in the cervical spine, dyslipidemia, gastroesophageal reflux disease and smoking with a >20 pack year history.

On examination, she was febrile to 38.9°C, but all other vital signs were within normal limits. She had left-sided gaze-evoked nystagmus and an entirely absent response to auditory stimuli with a Weber test. The remainder of her cranial nerves and neurological exam were normal, although she had a slightly unsteady gait and equivocal Romberg's test. There were no signs of connective tissue disease and her cardiovascular, respiratory and gastrointestinal examinations were unremarkable. Ophthalmological examination revealed mild exophoria, bilateral myopia, early cataracts and possible left eye glaucoma. There were no features of optic nerve ischemia. Ear, nose and throat examination was essentially normal except for a small mucous retention cyst at right vallecula and mild bilateral erythema of the pinna suggestive of perichondritis.

3 | INVESTIGATIONS

Initial audiometry demonstrated complete bilateral sensorineural hearing loss and tympanometry showed normal middle ear pressure and compliance in both ears.

Laboratory studies demonstrated elevated inflammatory markers with white cell count of 11.1×10^9/L (reference range [RR] 3.9-9.5×10^9/L), with a neutrophil predominance of 9.6×10^9/L (RR 2.0-8.0×10^9/L), elevated C-reactive protein (CRP) to 168 mg/L (RR ≤ 4 mg/L) and erythrocyte sedimentation rate (ESR) of 127 mm/h (RR <12 mm/h). Autoimmune, myeloma, hemolysis and infection screening were all negative except for positive antinuclear antibodies at 1:80 with a speckled pattern. These include anti-neutrophil cytoplasmic autoantibodies, extractable nuclear antigen antibodies, immunoglobulin G subclasses, anti-cyclic citrullinated peptides, rheumatoid factor and antiphospholipid antibodies all testing negative or within normal limits. She had a normocytic anemia with a hemoglobin of 78 g/L (RR 115-165 g/L) and mean corpuscular volume of 85.2 fL (RR 80-100 fL). Iron studies were also suggestive of iron deficiency anemia in the context of anemia of chronic disease with reduced transferrin saturation of 9% (RR 20%-50%), iron levels of 3 μmol/L (RR 5-30.4 μmol/L) and a ferritin of 386 μg/L (RR 30-300 μg/L); however, a soluble transferrin receptor result would be more conclusive. COVID-19 polymerase chain reaction test was negative.

Of coagulation tests, international normalized ratio was normal and proteins C and S were elevated at 287% (RR 70%-180%) and 175% (RR 60%-150%) respectively. Further vaccine-induced thrombotic thrombocytopenia testing was not engaged in, due to platelet count persistently ranging in the normal to thrombocytosis range.

Computed tomography (CT) and magnetic resonance imaging of the brain were unremarkable and review by a neurologist, otolaryngologist and ophthalmologist yielded no further findings than as discussed earlier. CT scans of the chest, abdomen, pelvis were also normal.

A positron emission tomography (PET) scan (see Figure 1A–C) revealed significant uptake in the ascending thoracic aorta as well as in both internal carotid arteries and subclavian artery, suggestive of a large vessel vasculitis, most in keeping with GCA. Arterial temporal duplex study was normal with no evidence of halo sign or stenosis and the patient declined a temporal artery biopsy.

4 | TREATMENT

The patient was commenced on intravenous methylprednisolone (1 g daily) for 5 days and with addition of 6 total doses of intratympanic steroids (0.8 mL of 8 mg/2 mL) when there was minimal improvement. She was subsequently commenced on oral prednisone 50 mg daily with a progressive 26 week wean.

5 | PROGRESS

There was some improvement in audiometry (see Table 1).

In her left ear at 250 Hz, tones were only audible at 80 dBHL. In the right ear at 250 Hz, tones were audible at 90 dBHL, and at 500 Hz, they were audible at 100 dBHL. She was unable to distinguish voices.

Her inflammatory markers began to improve rapidly with CRP falling to <10 mg/L and ESR falling to 25 mm/h within 2 weeks.

Approximately 1 month after discharge from her hospital admission, she was commenced on methotrexate for 2 weeks. This was then switched to tocilizumab 162 mg fortnightly when stock became available as a steroid-sparing agent. She now remains on a 162 mg weekly dose. She has also been fitted with hearing aids and can understand loud voices. Her dizziness continues to improve.

6 | DISCUSSION

GCA is a large vessel vasculitis characterized by the formation of "giant cells" from the fusion of macrophages into multinucleated aggregates, an event driven by inflammatory cytokines released by T cells.[6,7] The exact pathogenesis is not yet completely understood.[8]

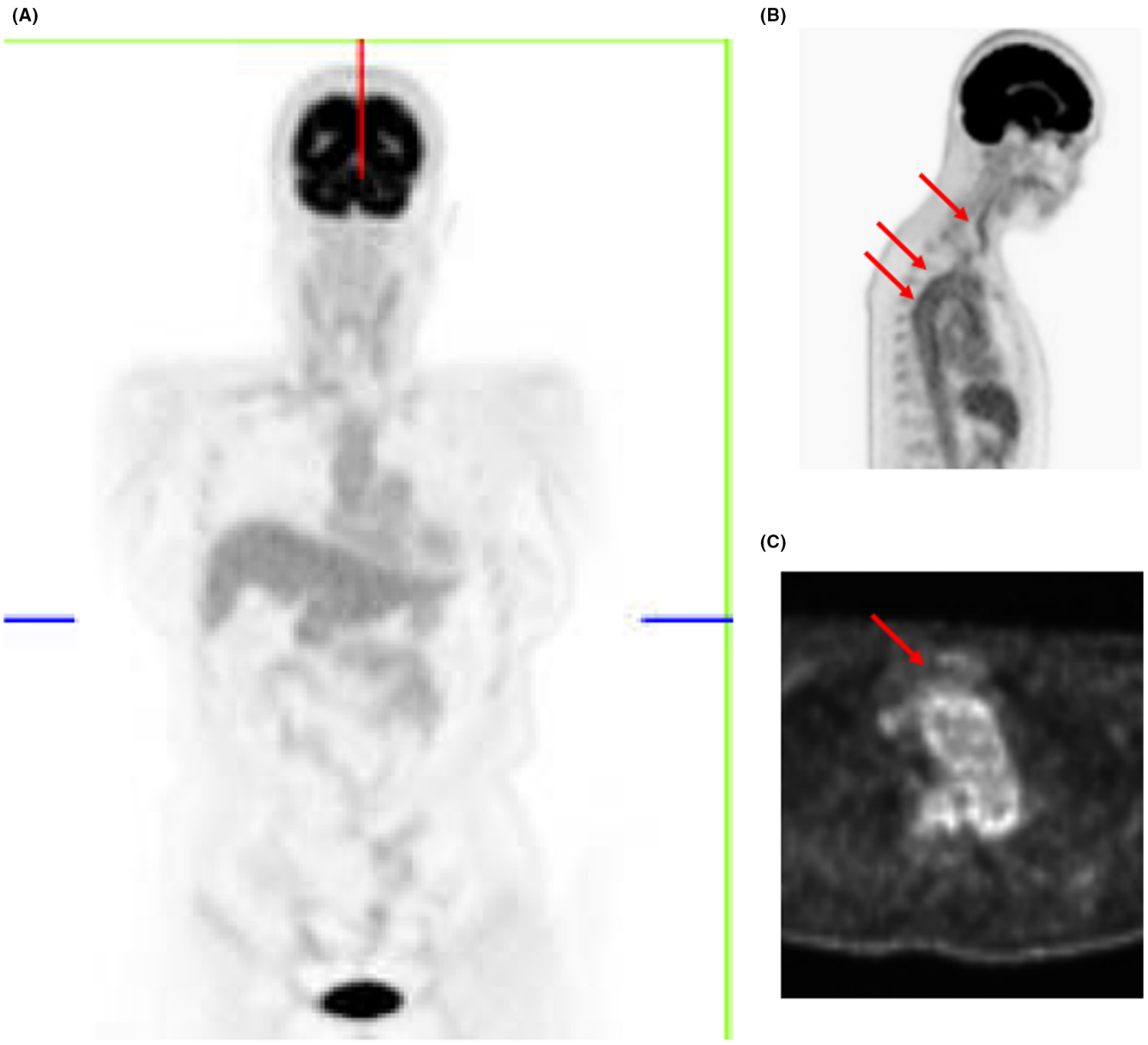

FIGURE 1 A. Whole-body positron emission tomography (PET) findings. B. PET image demonstrating increased metabolism in thoracic ascending aorta and both internal carotid arteries suggestive of large vessel vasculitis. C. PET image demonstrating increased metabolism in aortic arch, also suggestive of large vessel vasculitis

SNHL is an atypical complication of GCA, thought to be uncommon. Such cases have been reported since 1946[9] but there have only been a few. Subsequent isolated cases were illustrated by Malmvall and Bengtsson[10] which showed no hearing improvement after steroid administration.

Recent studies demonstrate that SNHL may not be as uncommon as previously thought. Saravanan[11] shows that 35% of GCA patients had concurrent hearing loss. Similarly, a retrospective study by Chu[12] of Chinese patients demonstrated hearing loss in 25% of patients, although again, neither study commented specifically on hearing loss in the absence of other classical features of GCA.

Improvement of hearing post-steroids occurs in 56% of patients,[11] with early administration of steroids important in the recovery of SNHL.[13] Recovery from vertiginous symptoms was not as pronounced as recovery of hearing loss.[11]

The mechanism of deafness is not entirely understood but may involve arterial wall inflammation of the posterior circulation or terminal cochleovestibular vasculature.[14] Multiple theories have been suggested regarding the exact mechanism, including vascular occlusion, immunological mechanisms and viral infection.[12] Vascular occlusion occurs when vasculitic vessels prone to thrombosis occlude and cause downstream ischemia and necrosis.[15] The immunological mechanism suggests circulating antibodies may cross-react with inner ear antigens and cause immune-mediated damage potentially through direct antibody-mediated damage of inner ear structures.[16] Direct viral infection has been postulated to damage the inner

TABLE 1 Timeline of clinical course

Time post-symptom onset	Event
D 0	Development of profound bilateral hearing loss
D 4	Hospital admission
D 4-20	Various inconclusive investigations and initial trial of intravenous methylprednisolone (D 5-11)
D 20	Positron emission tomography imaging demonstrating likely diagnosis of giant cell arteritis
D 30	Discharge from hospital and ongoing corticosteroid weaning
D 60	Commencement of methotrexate
D 77 - present	Commencement of tocilizumab and cessation of methotrexate

TABLE 2 Analysis of differentials

Differential	Supporting evidence	Conflicting evidence
Giant cell arteritis (GCA)	Diagnostic positron emission tomography (PET) findings Response to immunosuppressive therapy including tocilizumab Some constitutional clinical features suggestive of GCA	Absence of clinical features of cranial GCA
COVID vaccine-related audio-vestibular disorder	Proximity of sensorineural hearing loss (SNHL) with COVID vaccine Case reports of audio-vestibular disorder associated with COVID-19 vaccines documented	Unlikely vaccine-induced thrombotic thrombocytopenia due to normal platelet counts or thrombocytosis Recent cross-sectional study and case series finds no association between COVID-19 vaccination and SNHL Significantly more research required
Ototoxic medication	Association exists between mirtazapine and irreversible SNHL in 1 case report[21]	Mirtazapine is a regular medication, not recently started Does not explain other findings including PET results Hearing loss with mirtazapine initiation was rapid in reported case
Infectious agent	Presence of raised inflammatory markers and fever	Entire infection screen was negative with no infectious organisms either isolated or identified on polymerase chain reaction testing
Neoplastic process	Clinical features of SNHL and constitutional features such as weight loss and fever	Extensive imaging findings demonstrating no signs of mass lesion or metastases

ear structures. although no direct histopathological evidence has supported this. Alternately, viral antigens could trigger antibodies against inner ear antigens such as type 2 collagen or phospholipids, which could cause an acquired thrombophilia affecting the inner ear and triggering the immunological mechanism.[12]

This case was notable for the absence of features of cranial GCA. Although the patient did demonstrate some suggestive features including constitutional symptoms and biochemistry suggestive of an inflammatory process, the differentials remained broad. This included infection, ototoxic drugs, neoplasms, autoimmune causes, thrombosis after COVID-19 Astra Zeneca vaccine and vascular disorders. Specifically, brain, eye and ear syndromes were considered, such as Cogan's syndrome. However, these were eventually ruled out as she did not meet the criteria.

The other manifestations of cranial nerve VIII involvement including dizziness and nystagmus localized the lesion and its bilateral nature suggested a systemic inflammatory process; however, this was not definitive for GCA. The presence of a syndrome suggestive of polymyalgia rheumatica increased the clinical suspicion for GCA.

Vaccine-induced thrombotic thrombocytopenia was considered less likely due to persistently normal platelet count or thrombocytosis.

Specifically, COVID-19 vaccine-related audio-vestibular disorder was a possibility. Recent case reports illustrate its association with SNHL, including by Tsetsos et al and Medina et al,[17–19] which specifically cite involvement of the Astra Zeneca vaccine. In contrast, Ekobena et al reports associations of SNHL with only messenger RNA vaccines. However, a combined cross-sectional and case series

study by Formeister et al[20] involving 555 cases of SNHL demonstrated no association of COVID-19 vaccination with SNHL. With the highly suggestive PET findings, an association with GCA is favored over this key differential.

A tabular consideration of differential is included (see Table 2).

The literature thus demonstrates that SNHL is not as uncommon a manifestation of GCA as previously believed and highlights GCA as a key differential to be considered in SNHL, especially in the setting of a systemic inflammatory process. This case also illustrates the importance of PET imaging as an important diagnostic tool in GCA. Although temporal artery biopsy is the gold standard in the diagnosis of cranial GCA,[22] PET is demonstrated as an important method in diagnosis of extra-cranial GCA.[23]

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report.

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REFERENCES

1. Laldinpuii J, Sanchetee P, Borah AL, Ghose M, Borah NC. Giant cell arteritis (temporal arteritis): a report of four cases from north East India. *Ann Indian Acad Neurol*. 2008;11(3):185-189.
2. Kermani TA, Schäfer VS, Crowson CS, et al. Increase in age at onset of giant cell arteritis: a population-based study. *Ann Rheum Dis*. 2010;69:780-781.
3. Dejaco C, Brouwer E, Mason JC, Buttgereit F, Matteson EL, Dasgupta B. Giant cell arteritis and polymyalgia rheumatica: current challenges and opportunities. *Nat Rev Rheumatol*. 2017;13(10):578-592.
4. Calamia KT, Hunder GG. Clinical manifestations of giant cell (temporal) arteritis. *Clin Rheum Dis*. 1980;6:389-403.
5. Espitia O, Blonz G, Urbanski G, et al. Symptomatic aortitis at giant cell arteritis diagnosis: a prognostic factor of aortic event. *Arthritis Res Ther*. 2021;23:14.
6. Cid MC, Campo E, Ercilla G, et al. Immunohistochemical analysis of lymphoid and macrophage cell subsets and their immunologic activation markers in temporal arteritis. Influence of corticosteroid treatment. *Arthritis Rheum*. 1989;32(7):884-893.
7. Weyand CM, Goronzy JJ. Arterial wall injury in giant cell arteritis. *Arthritis Rheum*. 1999;42:844-853.
8. Koster MJ, Warrington KJ. Giant cell arteritis: pathogenic mechanisms and new potential therapeutic targets. *BMC Rheumatol*. 2017;1:1-2.
9. Francis DA, Boddie HG. Acute hearing loss in giant cell arteritis. *Postgrad Med J*. 1982;58(680):357-358.
10. Malmvall BA, Bengtsson BA. Giant cell arteritis. Clinical features and involvement of different organs. *Scand J Rheumatol*. 1978;7:154-158.
11. Saravanan V, Pugmire S, Smith M, Kelly C. Patient-reported involvement of the eighth cranial nerve in giant cell arteritis. *Clin Rheumatol*. 2019;38:3655-3660.
12. Chu X, Wang D, Zhang Y, et al. Comparisons of clinical manifestations and prognosis between giant cell arteritis patients with or without sensorineural hearing loss: a retrospective study of Chinese patients. *Medicine (Baltimore)*. 2019;98(17):e15286.
13. Junejo S, Ali Y, Abrudescu A. Giant cell (temporal) arteritis with persistent bilateral sensorineural hearing loss - A likely consequence of delayed institution of glucocorticoid therapy. *Am J Case Rep*. 2017;22(18):1233-1237.
14. Sofferman RA. Cranial arteritis in otolaryngology. *Ann Otol Rhinol Laryngol*. 1980;89:215-219.
15. Emmi G, Silvestri E, Squatrito D, et al. Thrombosis in vasculitis: from pathogenesis to treatment. *Thrombosis J*. 2015;13:15.
16. Berrocal JR, Ramírez-Camacho R. Sudden sensorineural hearing loss: supporting the immunologic theory. *Ann Otol Rhinol Laryngol*. 2002;111(11):989-997.
17. Ekobena P, Rothuizen LE, Bedussi F, et al. Four cases of audiovestibular disorders related to immunisation with SARS-CoV-2 mRNA vaccines. *Int J Audiol*. 2022;1-5.
18. Tsetsos N, Poutoglidis A, Vlachtsis K, Kilmpasanis A, Gougousis S. Sudden sensorineural hearing loss following the second dose of COVID-19 vaccine. *Cureus*. 2021;13(8):e17435.
19. Canales Medina M, Ramirez Gómez M. Tinnitus, sudden sensorineural hearing loss, and vestibular neuritis as complications of the Astra Zeneca COVID-19 vaccine. *Cureus*. 2022;14(1):e20906.
20. Formeister EJ, Wu MJ, Chari DA, et al. Assessment of sudden sensorineural hearing loss after COVID-19 vaccination. *JAMA Otolaryngol Head Neck Surg*. 2022;148(4):307-315.
21. Dursun E, Akpinar A, Battal B. Sudden hearing loss associated with mirtazapine therapy: a case report. *Klinik Psikofarmakoloji Bulteni*. 2009;19:417-419.
22. Ponte C, Martins-Martinho J, Luqmani RA. Diagnosis of giant cell arteritis. *Rheumatology (Oxford)*. 2020;59(Suppl 3):iii5-iii16.
23. Maz M, Chung SA, Abril A, et al. 2021 American College of Rheumatology/Vasculitis Foundation guideline for the management of giant cell arteritis and takayasu arteritis. *Arthritis Care Res (Hoboken)*. 2021;73(8):1071-1087.

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