Labyrinthine calcification in ears with otitis media and antineutrophil cytoplasmic antibody-associated vasculitis (OMAAV): a report of two cases

Tadao Yoshida, MD, PhD[1]; Masumi Kobayashi, MD, PhD[1]; Satofumi Sugimoto, MD, PhD[1]; Shinji Naganawa, MD, PhD[2]; Michihiko Sone MD, PhD[1]

1: Department of Otorhinolaryngology, Nagoya University Graduate School of Medicine, Nagoya, Japan

2: Department of Radiology, Nagoya University Graduate School of Medicine, Nagoya, Japan

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Address for correspondence:

Tadao Yoshida, MD, Ph.D.

Department of Otorhinolaryngology, Nagoya University Graduate School of Medicine

65 Tsurumai-cho, Showa-ku, Nagoya, 466-8550, Japan.

E-mail: tadaoy@med.nagoya-u.ac.jp

Abstract

Otitis media with antineutrophil cytoplasmic antibody-associated vasculitis (OMAAV) has been proposed as a new type of otitis media. The hearing loss caused by OMAAV can be expected to improve with early detection and intervention, but if it continues to worsen and leads to deafness, it is challenging to recover the patient's hearing. When bilateral deafness occurs, cochlear implant (CI) surgery is the only way to improve hearing. Here, Case 1 showed unilateral cochlear calcification, and Case 2 showed bilateral cochlear calcification. In Case 1, CI surgery was performed on the ear lacking calcification, and in Case 2 it was performed on the ear with milder calcification. In Case 2, granulation was present from the tympanic space to the mastoid, the round window was closed, and the basal turn of the cochlea was narrowed. Such calcification of the cochlea caused by OMAAV has not been reported so far. It is essential to detect these changes by computed tomography scans at an early stage and to perform CI surgery at an appropriate time, because hearing improvements are not expected in patients who become deaf because of OMAAV.

Keywords: otitis media with antineutrophil cytoplasmic antibody-associated vasculitis—cochlear implant—labyrinthine calcification

Introduction

The etiology of cochlear calcification includes otosclerosis, chronic otitis media, temporal bone fractures, idiopathic meningitis, and Cogan's syndrome. Calcification of the cochlea caused by otosclerosis is the most common form reported, and exclusive round window involvement of calcification has been seen in more than half of the cases reported [1]. Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of autoimmune diseases characterized by necrotizing vasculitis. Otitis media is one of the intractable symptoms of AAV. Otitis media with AAV (OMAAV) was defined as being caused by granulomatosis with polyangiitis (GPA), microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis, but did not meet the ordinary diagnostic criteria for systemic AAV. Calcification of the cochlea in cases of OMAAV has not been reported to date. The diagnostic criteria of OMAAV proposed by the Japan Otological Society are met if the following three criteria (A, B, and C) are fulfilled. (A) At least one of the following two features: (1) presence of intractable otitis media with effusion or granulation resistant to antibiotics and insertion of a tympanostomy tube, or (2) progressive deterioration of bone conduction hearing levels. (B) At least one of the following four features: (1) a previous diagnosis of AAV based on the involvement of other organs, (2) positivity for serum myeloperoxidase (MPO)- or proteinase 3 (PR3)-linked ANCA, (3) histopathology consistent with AAV, or (4) at least one accompanying sign/symptom of AAV-related involvement other than the ear. (C) Exclusion of the other types of intractable otitis media [2].

Clinical features of OMAAV obtained from a nationwide survey in Japan showed a predominance in female patients (71%), bilateral hearing loss (74%), facial palsy (32%), MPO-ANCA positive findings (60% or more), and PR3-ANCA positive findings (30% or less) [3]. The documented hearing outcomes for treated cases of OMAAV followed for 24 months were a complete/marked recovery (30%), partial recovery (30%), or nonrecovery (40%). Complete deafness was seen in 7.2% of cases, and complete bilateral deafness in 3.5%. There were cases of deafness at the first visit and progressive hearing loss; however, complete deafness was irreversible despite steroid or immunosuppressive treatment. Because cochlear implant (CI) surgery is a treatment that should be considered in such cases, there have been few previous reports of CI surgery in patients with OMAAV. One showed that CI placement in patients with OMAAV did not produce satisfactory listening results but was still a valid treatment option [4]. Here, we report two patients with bilateral profound or total deafness after the onset of OMAAV with calcification in the cochlea, making it challenging to insert a CI.

Case presentation

Case 1: a 64-year-old-woman

Three months before visiting our hospital, the patient had experienced a sensation of bilateral ear fullness, and progressive hearing loss in the right ear. On an initial examination in another hospital, she was diagnosed with bilateral otitis media with effusion and underwent insertion of a tympanostomy tube in both eardrums. After that, she had profound bilateral hearing loss (Fig. 1), bilateral complete facial paralysis and

mild floating sensation, so she visited our hospital. Although tests for PR3-ANCA were negative, the MPO-ANCA level was elevated to 26.0 U/mL in serum samples. Temporal bone computed tomography (CT) scans showed shadows in the middle ear cavity and mastoid but no calcification in the cochlea (Fig. 2-3A, B). A magnetic resonance imaging (MRI) performed around the same time showed no evidence of cochlear lymphatic space obstruction. No vestibular function tests were performed. Based on these findings, the patient was diagnosed with OMAAV and treated with 40-mg/day prednisolone, and 50-mg/day cyclophosphamide (CY) was initiated from 4 months after the disease onset. Oral administration of CY was continued for 5 months and then switched to azathioprine. Three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) MRI showed high signals both in the cochlea and vestibule (Fig. 4). By 5 months from onset, the deafness and hearing loss did not improve even though the MPO-ANCA levels had decreased, and the patient could not obtain satisfactory results with hearing aids. Temporal bone CT scans showed labyrinthine calcification in the right ear but no calcification in the left ear (Fig. 2-3C, D). Her preoperative speech discrimination test with hearing aids were 0%. We installed a CI into her left ear 24 months after the onset of symptoms, after waiting for her immunosuppressive treatment to be completed and the dosages of steroids to be reduced. All the CI electrodes could be inserted during surgery because the cochlea was not obstructed by calcification or granulation. At 60 months after the CI had been inserted (84 months after the disease onset), her hearing ability was rated at 60% recognition of monosyllables in quiet environments. Her percentage of correct word recognition was 56% for speech alone

and 96% for a combination of spoken and oral forms. She has no postoperative relapse of OMAAV, and the outcome of CI has been stable over time.

Case 2: a 69-year-old woman

Nine months before visiting our hospital, the patient experienced sudden profound hearing loss in the right ear and mild floating sensation. One month later, she developed otitis media and progressive sensorineural hearing loss in the left ear. Her bone conduction thresholds gradually worsened (Fig. 5), and she visited our department to consider the installation of a CI. Although the PR3-ANCA level was negative in serum samples, that for MPO-ANCA was elevated to 16.5 U/mL. Based on these findings, she was diagnosed with OMAAV according to the criteria listed above. She had no other severe systemic symptoms. Temporal bone CT scans revealed soft tissue density from the tympanum to the mastoid cavity on the left and a slight soft tissue density in the right tympanum. No obvious cochlear calcification was observed at first (Fig. 6A, B). T1 contrast-enhanced MRI scans around the same time revealed apparent contrast effects at both cochleae, indicating intracochlear bleeding and destruction of the blood–labyrinthine barrier but no obvious obstruction of lymph fluid. In addition, there were findings of hypertrophic dural inflammation. Treatment with 45-mg/day prednisolone and 575-mg/day CY was initiated 10 months after the disease onset. The patient's bilateral deafness and tinnitus did not improve, but the MPO-ANCA levels decreased, and the patient could not obtain satisfactory results with hearing aids. Caloric tests and the Romberg test showed no abnormalities. A CT scan performed 18 months after the

onset showed calcification in the basal turns of both cochleae (Fig. 6C, D). Her preoperative speech discrimination test with hearing aids were 0%. Although there was less calcification on the left side and soft tissue shading in the mastoid cavity, we opted for CI surgery to the left ear. A small amount of granulation was present in the mastoid cavity, and the round window was obstructed by intricate granulation. Lymphatic outflow was confirmed when the round window was opened. A depth gauge (Cochlear Ltd., Sydney, Australia) was inserted through the enlarged round window to check the space in the scala tympani, and then all CI electrodes were inserted. At 4 months after the CI was activated (23 months after the disease onset), her hearing ability was 15% recognition of monosyllables in quiet environments. The percentage of correct word recognition was 40% for speech alone and 76% for a combination of speech and oral forms.

Discussion

To date, seven cases—including these two—have been reported to have needed cochlear implants due to hearing loss caused by OMAAV. All cases were positive for either MPO or PR3-ANCA, and none were negative for ANCA [4, 5]. Complete hearing loss caused by OMAAV is rare but is characterized by an inability to respond to treatment with immunosuppressive drugs. When complete hearing loss does occur, CIs are the only way to improve hearing. Bilateral deafness occurred 3 months after onset in Case 1 and 7 months after onset in Case 2. Serum ANCA was positive in both cases, MPO-ANCA was positive, and PR3-ANCA was negative. In cases of MPO-ANCA-positive GPA,

granulation occurs in the middle ear, and in some of them granulation extends beyond the round window membrane into the scala tympani. In one study concerning the temporal bone, the stria vascularis was mildly atrophic, but the spiral ganglion was well preserved [6]. To improve the outcome of placing a CI, it is necessary to perform surgery as early as possible, before the spiral ganglion degenerates and with the OMAAV controlled. In Case 1, contrast-enhanced 3-Tesla 3D-FLAIR MRI showed a high signal in the cochlea and vestibule, and in Case 2, a high signal was detected using T1 contrast-enhanced MRI. These findings indicated that the labyrinthitis was very severe and irreversible. We have reported previously that a high MRI signal in the cochlea was positively correlated with the bone conduction threshold [7]. However, Case 1 showed better hearing after placement of a CI than those reported in the past. In previous reports, the percentage of correct word recognition in silence ranged from 0% to 40% in all but one case. The result was similar in Case 2, but Case 1 showed 56% recognition of words [4, 5]. The beneficial effect of a CI depends on how well the spiral ganglion is preserved. An important pathological factor in OMAAV is vasculitis, which is thought to cause damage to the spiral ganglion of the cochlea because of circulatory disturbances caused by vasculitis. The mechanism of permanent hair cell damage and inner ear damage caused by vasculitis involves the reduction of microcirculation in the spiral ligament and stria vascularis, which reduces endocochlear potential and causes structural dysfunction to the stria vascularis and ischemia in the inner ear [8]. Because currently there is no way to predict the degree of spiral ganglion damage in advance, we can only infer the degree of spiral ganglion preservation from the results of CI insertion.

These results were relatively good in Case 1, suggesting that the disease was not severe before treatment and that the spiral ganglion was better preserved. In addition, there have been no reports of OMAAV with calcification in the cochlea, but here we experienced two cases of OMAAV with calcification in the cochlea. The frequency of granulation and calcification in the cochlea in cases of OMAAV is unknown, but is probably milder than that of bacterial labyrinthitis. Vasculitis, ischemia, and necrosis of the middle ear cavity and labyrinth can cause such lesions around the round window and in the labyrinth. There is no report of calcification in the temporal bone pathology of cases with OMAAV, but there is a report of calcification of the renal cortex in a 'tram-line' pattern in a case of GPA caused by secondary renal failure [9]. The two cases reported here showed granulation in the tympanic space at the pretreatment stage, which shrank in response to treatment. In Case 1, the ear opposite to that with calcification was selected for CI insertion. Treatment with immunosuppressive drugs was successful, and intraoperative findings showed almost no granulation, so the CI surgery presented no particular problems. In the cochlea with calcification, a lesion was found in the mid-to-apical turn, making it difficult to insert a CI electrode. On the other hand, in Case 2, the patient underwent CI surgery early after immunosuppressive treatment. The preoperative CT scans demonstrated granulation in the tympanic space and the scala tympani. For such CI surgery, when granulation is found around the round window and space is found deep in the scala tympani, the use of a depth gauge to widen the window is considered to be a beneficial technique. Although granulation made surgery difficult, we could insert the CI electrodes completely because no gross calcification was

observed in the cochlea. Prolonged or high-dose steroid use and immunosuppressive therapy are known to be risk factors for delayed wound healing and surgical site infection [10]. The two patients in the present study were on steroid and immunosuppressive drug therapies but did not have wound healing problems, infections, or cerebral spinal fluid leakage. Because high doses of steroids are used initially in treating cases of OMAAV, it is desirable to perform CI surgery after the steroid doses have been reduced. Although the frequency is unknown, granulation and calcification in the cochlea might occur in cases of OMAAV. Patients with profound hearing loss who are eligible for CI surgery should undergo regular imaging studies even during immunosuppressive therapy to avoid losing the opportunity for such surgery.

Conclusions

Here we report two cases undergoing CI surgery for bilateral deafness caused by OMAAV. In one case, the cochlear calcification was unilateral, and the CI was placed on the contralateral side; in the other case the cochlear calcification was bilateral, and CI surgery was performed on the less calcified ear. The postoperative results were relatively good in both cases, suggesting that CI surgery should be considered even when the patient has mild calcification of the cochlea and surgery is difficult. In addition, it was thought necessary to take CT scans periodically to monitor the condition of the inner ear, even during immunosuppressive drug treatments.

Ethical standards

We obtained written informed consent from each participant and their guardians. The patients' anonymity has been preserved.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

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Figure legends

FIG. 1. Pure-tone audiometry of Case 1 at the first visit to our department.

FIG. 2. Axial temporal bone computed tomography (CT) centered on the mid-to-apical turn of the cochlea of Case 1. A and B are axial CT images immediately after the onset of the disease. There are shadows in the middle ear cavity and mastoid bone (arrow) but no calcification in the cochlea. C shows calcification of the mid-to-apical turn of the right ear (arrow); D shows no calcification of the cochlea. Reproduced in part from reference [7].

FIG. 3. Axial temporal bone CT centered on the basal turn of the cochlea of Case 1. A and B are axial CT images immediately after the onset of the disease. There are shadows in the middle ear cavity and mastoid bone but no calcification in the cochlea. C and D also show no calcification of the cochlea. Reproduced in part from reference [7].

FIG. 4. Three-dimensional fluid-attenuated inversion recovery magnetic resonance imaging (MRI) showed high signals in the cochlea and vestibule (arrow). Reproduced in part from reference [7].

FIG. 5. Pure-tone audiometry of Case 2 at the first visit to our department.

FIG. 6. Axial temporal bone CT scan and magnified images of Case 2. Panels A and B show axial CT images obtained immediately after the onset of the disease. There are shadows in the middle ear cavity and mastoid bone (arrow) but no calcification in the

cochlea. Panel C shows calcification of the scala tympani in the basal turn of the right cochlea (arrow) and thickening of the ossicular laminae. Panel D shows calcification of the scala tympani near the round window of the left cochlea (arrow).