

Successful treatment with adalimumab for autoimmune sensorineural hearing loss in a patient with Behçet's disease

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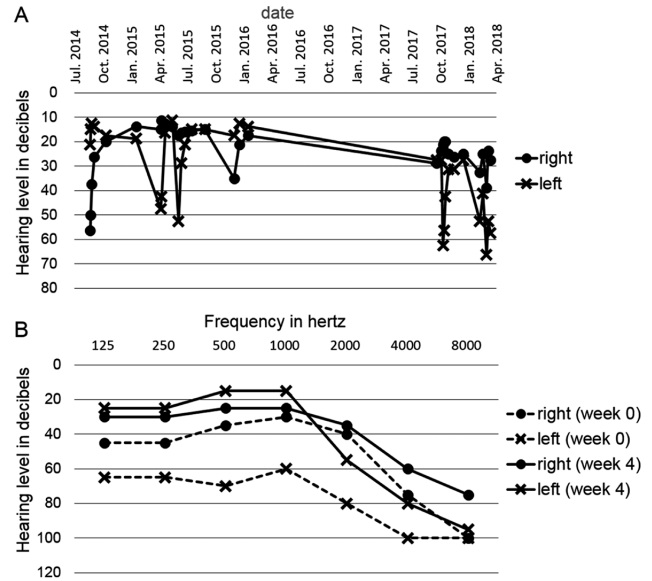
Autoimmune sensorineural hearing loss (ASHL) is either a primary disease, or a disease secondary to systemic autoimmune diseases characterised as a rapidly progressive, unilateral/bilateral sensorineural disorder that can cause hearing loss (1). There are some studies in which the frequency of inner ear disease is significantly increased among patients with Behçet's disease (BD), up to 60% (2). ASHL would be seen in the course of other systemic vasculitic or inflammatory syndromes besides BD (3-5). Glucocorticoids (GCs) are effective in improving ASHL; however, the response is generally temporary and the effects decrease with GC dose reduction (6). Recent reports have shown the usefulness of tumor-necrosis factor- α (TNF- α) inhibitors for ASHL (3). In the presenting case, the patient was diagnosed as ASHL. However, GC therapy was unable to be continued because of GC-associated glaucoma.

In March 2011, a 52-year-old woman was diagnosed with BD based on acute bilateral panuveitis, oral aphtha, and genital ulcers. She also developed glaucoma secondary to uveitis. Her symptoms and intraocular pressure were controlled via symptomatic therapies without using systemic immunosuppressive agents.

In August 2014, she was admitted to the otolaryngology department in our hospital due to sudden hearing loss on her right side. On physical examination, no nystagmus and dizziness were found. Otoloscopic examination revealed no abnormalities in her ear canal and eardrum. Audiometry showed 56 decibels (dB) and 21 dB in her right and left ear without air-bone gap, respectively. Brain magnetic resonance imaging (MRI) findings were normal. The diagnosis of sudden sensorineural hearing loss was established. Prednisolone 80 mg/day was administered and her hearing loss immediately improved. Prednisolone was gradually tapered and stopped over two weeks. Thereafter, from August 2014 to October 2017, she had experienced five episodes of unilateral or bilateral sensorineural hearing loss without any recurrent sign related to BD, and GC therapy was repeated as the hearing loss relapsed (Fig. 1A). Based on the clinical course, she was diagnosed with GC-dependent ASHL.

In October 2017, she developed the fifth attack of ASHL. The initiation of prednisolone 60 mg/day ameliorated her hearing loss. However, she complained of bilateral ocular pain and her intraocular pressure elevated to over 50 mmHg. GC therapy for ASHL recurrence induced severe deterioration of glau-

Fig. 1. Audiograms of the patient. (A) Recurrences of autoimmune sensorineural hearing loss (ASHL): short-term glucocorticoid therapy improved hearing loss but she experienced six ASHL attacks within 4 years. (B) Hearing improvement after adalimumab (ADA) therapy: serial audiograms showing improvement of hearing levels in her bilateral ears 4 weeks after ADA initiation.



coma, secondary to BD panuveitis.

In February 2018, her ASHL relapsed and she was admitted to our department to establish a GC-free treatment strategy for relapsing ASHL. She had no symptoms except for hearing loss. Audiometry revealed sensorineural hearing loss at 33 dB and 67 dB in her right and left ear, respectively (Fig. 1B). Brain MRI and cerebrospinal fluid analysis showed no abnormalities and interleukin-6 levels in the cerebrospinal fluids were within normal range. For the relapsing ASHL concomitant with BD, ADA was subcutaneously administered at a starting dose of 80 mg, followed by ADA 40 mg biweekly. Subsequently, the patient was able to distinguish between several voice words in a few days. Four weeks after ADA initiation, audiogram demonstrated significant improvement of hearing loss: 27 dB in the right ear and 25 dB in the left ear (Fig. 1B). To date, there are no recurrences of ASHL and her glaucoma remains stable.

In the present case, ADA treatment improved ASHL in a BD patient who could not take GC because of its side effects. Although the pathogenesis of ASHL remains unclear, TNF- α is proposed to play an important role in inner ear inflammation of ASHL. In an animal model of immune-mediated labyrinthitis, numerous TNF- α -producing cells infiltrated the inner ear and etanercept improved hearing loss in immune-mediated labyrinthitis model mice (7, 8). In humans, available data are insufficient to provide significant evidence supporting TNF- α blockers for treating ASHL (3). However, TNF- α inhibitors have been used in refractory cases of ASHL, and some case reports showed the positive effects of ADA for ASHL (9, 10). TNF- α is one of the critical inflammatory cytokines in BD as well as in ASHL. Although the pathophysiological relationship between BD and ASHL is unclear, TNF- α

might be associated with the development of both diseases.

In conclusion, we successfully treated ASHL in a patient with BD using ADA monotherapy. Anti-TNF- α agents can be promising drugs for ASHL and for avoiding the adverse effects of GC.

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