

Refractory Bilateral Sudden Sensorineural Hearing Loss Associated with Systemic Lupus Erythematosus : Clinical Implication of Plasmapheresis

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– ABSTRACT –

Sudden sensorineural hearing loss (SNHL) is a rare manifestation of systemic lupus erythematosus (SLE). A 38-year-old female presented headache followed by bilateral SNHL. The hearing threshold level was 75dB in the right and 45dB in the left ear. In spite of high dose steroid treatment, the hearing of both ears became profound hearing loss in several days. Serologic tests showed positive autoimmune markers corresponding to SLE with suspicious antiphospholipid (antibody) syndrome (APS). Follow up hearing tests showed no improvement in spite of anticoagulant, intravenous immunoglobulin and high dose steroid treatment. The patient underwent two cycles of plasmapheresis followed by immunosuppressant, and the hearing level in left side improved to 60dB after plasmapheresis. We presume that elevated blood viscosity and vasculitis due to immune deposits can cause cochlear vessel occlusion, which is responsible for the hearing loss. Prompt immunosuppressive treatment and, in refractory case, plasmapheresis can possibly reverse the hearing loss. (*J Clinical Otolaryngol* 2015;26:257-262)

KEY WORDS : Sudden deafness · Antiphospholipid syndrome · Lupus anticoagulant.

Introduction

Sudden sensorineural hearing loss (SNHL) is an uncommonly reported manifestation of systemic lupus erythematosus (SLE).^{1,2,16} Especially, in undiagnosed SLE patients, sudden SNHL is rarely detected as a first symptom. Immune complex infiltration, hyperviscosity, autoimmune deposit can be suggested as possible mechanisms of SNHL in patients with SLE. Also, this condition has been reported to be related to concomitant antiphospholipid (antibody) syndrome (APS).³⁾

We report a case of a 38 year-old female with severe

headache followed by bilateral sudden SNHL. She was initially diagnosed as bilateral SNHL due to aseptic meningitis by the cerebrospinal fluid (CSF) study. Later, she was diagnosed as SLE with suspicious APS through serologic investigation including autoimmune antibody test.

We reviewed the relationship of SLE concomitant APS with sudden SNHL, and treatment modality is discussed.

Case Report

A 38-year-old female with 2 week-history of severe headache was referred from neurology department for the evaluation of sudden onset bilateral hearing loss in January 2013. Her past medical history revealed frequent fetal loss during early pregnancy. Physical examination was unremarkable. The initial evaluation of pure tone audiometry showed four frequency average (500, 1,000, 2,000 and 3,000 Hz) of 75 dB in the right ear and

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45 dB in the left ear (Fig. 1). Speech test showed no speech recognition in the right ear, and a speech reception threshold of 45dB and a word discrimination score of 60 percent in the left ear. During admission, she complained gradually aggravating imbalance without spinning vertigo. Videonystagmography (VNG) caloric test taken on the admission day 5 showed right canal paresis of 78%, but the total response of bithermal stimulations was 7.6°/sec, which was consistent with bilateral vestibulopathy. Weak spontaneous nystagmus to left side was detected (Fig. 2). Laboratory test showed lymphopenia (681/mm³) and an elevated inflammatory markers including erythrocyte sedimentation rate (ESR) (83 mm/hr), and C-reactive protein (7.16 mg/dL). CSF study conducted for the evaluation of headache showed an elevated leukocyte count of 25/μL, which was consistent with aseptic meningitis.

Antinuclear antibody (ANA) test routinely done in sudden deafness, showed positive result in cytoplasmic type (titer 1 : 160), so further work-up for autoimmune disease proceeded after rheumatologic consultation. Additional autoimmune serologic test results showed positive tests for anti-double strand DNA(anti-dsDNA) IgG (15 IU/mL) (normal range : 0.00–5.30 IU/mL), anti-

cardiolipin (aCL) IgG (30.0 U/mL) and IgM (4.0 IU), positive lupus anticoagulant, and low complement (C3/ C4 81/9) (normal range, C3 : 90–180, C4 : 10–40). With the impression of sudden SNHL associated with SLE based on the satisfaction of 2 clinical criteria and 6 immunologic criteria out of the Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) classification criteria⁴) and suspicious anti-phospholipid syndrome (APS),⁵) she was treated with steroid pulse therapy of methylprednisolone (500 mg twice a day for 3 days) and maintenance of high dose steroid (1 mg/kg/day).

Despite of steroid treatment, her hearing was deteriorated and at the admission day 12, the audiogram showed total hearing loss in her both ears. Based on the consultation to Rheumatology department, intravenous immunoglobulin (IVIG) 400 mg/kg/day and anticoagulant medication (Enoxaparin Sodium, 40 mg/0.4 mL twice a day, subcutaneously) for suspicious APS were added to high dose steroid therapy, but it did not work. As an immunologic process was strongly suspected to be responsible for her pathologic process and a conventional steroid pulse/sequential high dose steroid and IVIG treatment showed no response, plasmapheresis was started at the admission day 18, which continued for 4 days. The audiogram taken on the 4th day of plasmapheresis showed a partial improvement in the left ear to 95 dB, and on 7 days after plasmapheresis, the four frequency pure tone average had improved to 60 dB, in addition, the speech reception threshold to 65 dB and word recognition scores to 30 percent. However, a sharp, sloping, and high frequency hearing loss persisted above 2,000 Hz. Her blood test for ANA, anti-dsDNA and anti-cardiolipin IgG became negative and C3/C4 level had been normalized as well since 2 days after 1st plasmapheresis, which implied reduced disease activity.

She had a continuous nausea after taking oral steroid pills, so for steroid sparing, azathioprine (1.5 mg/kg/day) was added, and she received second series of plasmapheresis from the admission day 33 to 36. At 7 months post-presentation, the patient is under maintenance dose of steroid medication, Aspirin® 100mg and

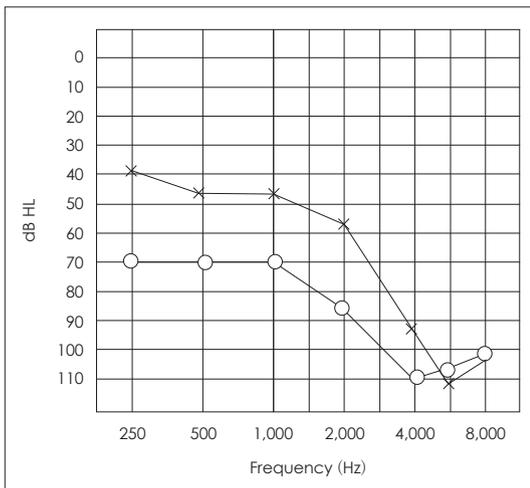


Fig. 1. Initial audiogram. The patient had been treated to fit the aseptic meningitis for 5 days. The audiogram showed four frequency average (500, 1,000, 2,000 and 3,000 Hz) of 75 dB in the right ear (—o—) and 45dB in the left ear (—x—).

Warfarin® 5 mg, but follow up audiogram did not reveal any more improvement in hearing (Fig. 3). The laboratory result shows normal blood cell count with negative autoimmune markers and she has persistent disequilibrium without rotating vertigo.

Discussion

SLE is characterized by immune complex deposits along the vascular walls, thus causes a vasculitis. Audi-

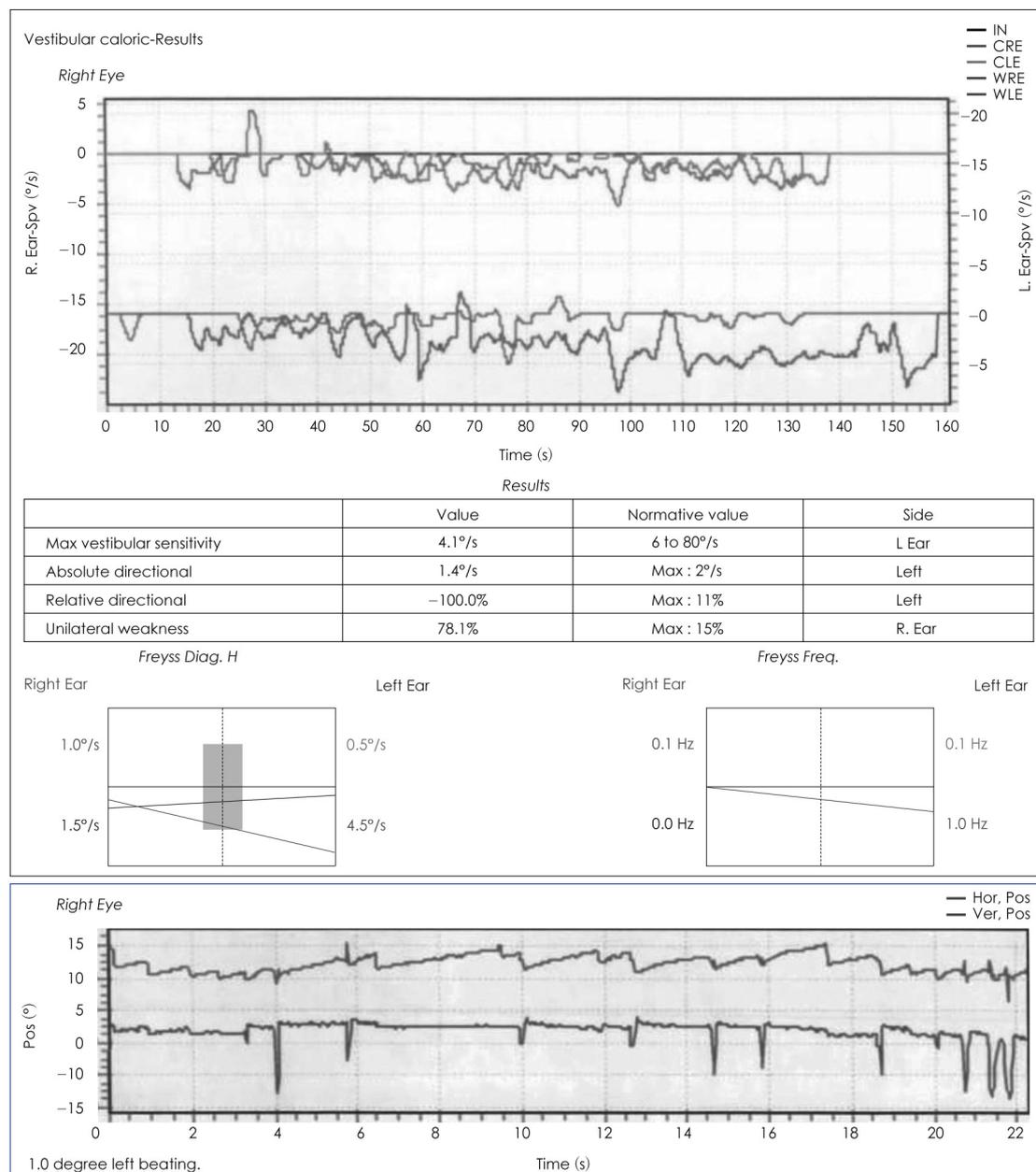


Fig. 2. The result of vestibular function test. The caloric test taken on admission day 5 showed right canal paresis of 78%, but the total response of each side showed bilateral vestibulopathy with weak spontaneous nystagmus to left side.

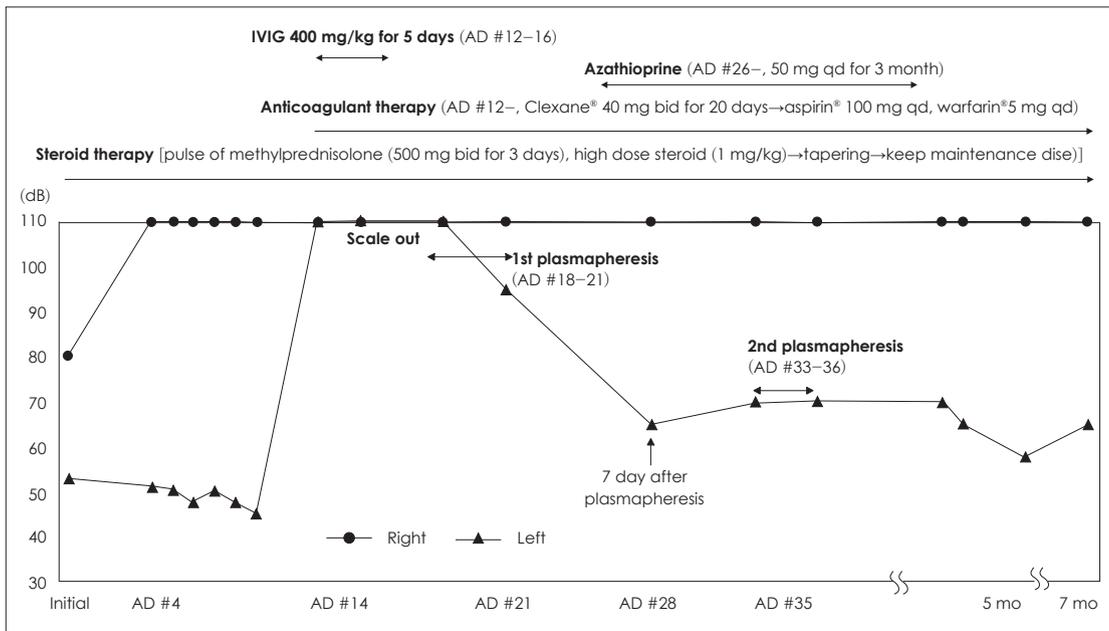


Fig. 3. The flow sheet of audiometry and treatment regimen. The patient showed a rapid deterioration of hearing function despite of high dose steroid, IVIG therapy, and anticoagulant, which urged us to do plasmapheresis. After plasmapheresis, the patient showed partial improvement in the left ear. She has been under maintenance dose of steroid and anticoagulant, but no more improvement in hearing was noted. IVIG : intravenous immunoglobulin, qd : once a day, bid : twice a day, AD : admission, mo : month.

ologic complication is explained by either a vasculitis within the cochlea or microinfarctions in cochlea by circulating immune complexes.^{1,6)} Although the pathogenesis of sudden SNHL in patients with SLE is not clear, several reports suggest an association with the aCL antibody.^{3,6-8)}

SLE patient with aCL antibody has higher chance of thrombotic symptoms, so called antiphospholipid (antibody) syndrome (APS).^{5,9)} In the 1980s, Graham Hughes first described it as “anticardiolipin syndrome”, but subsequently renamed it as APS.¹⁰⁾

SLE patients with aCL have higher tendency of having pregnancy related disorder (recurrent abortion), stroke and deep vein thrombosis. Due to the relatively frequent co-occurrence with aCL antibodies, some authors think sudden SNHL as one of the neurologic manifestations of SLE and aCL antibodies.^{3,5,7)} Hisashi had described an association between SNHL in SLE and the APS, and he postulated a thrombotic mechanism as the cause of the hearing loss.¹¹⁾ Also, a majority of cases suggest a positive therapeutic benefit from anticoagulant therapy, thereby reinforcing a

likely thrombotic aetiology of SNHL in these patients.^{3,8,9,12)}

However, as the bilaterality and unresponsiveness to anticoagulant treatment, thrombosis can be a less plausible mechanism in this patient. The neurological complications in APS is mainly an ischemic-thrombotic origin, but a possible cellular involvement by antiphospholipid antibodies and/ or direct neural/neuronal tissue damage by antibody-mediated interactions, and circulatory disturbance in cochlea by high blood viscosity could not be excluded.⁵⁾

Treatment can be directed towards preventing thromboembolic events using antithrombotic medications or towards modulating the immune response with immunotherapy in APS.^{5,7)} So far, no consensus about the intensity of anticoagulant therapy has not been achieved, but in acute onset of SNHL in the presence of aCL antibodies, anticoagulation treatment is generally recommended.^{5,9)}

Also, in autoimmune mediated inner ear disease, significant number of patients have response failure to steroids due to steroid dependant or unacceptable side effects. In these cases, alternative immunosuppressive approaches

and steroid sparing agents such as cyclophosphamide, azathioprine, IVIG can be recommended.¹³⁾ In this patient, she had a continuous nausea after taking oral steroid pills, so for steroid sparing, azathioprine (1.5 mg/kg/day) was added. Even though her symptom didn't show an improvement after steroid and steroid sparing agents, her stable serologic test showed reduced disease activity.

In this patient, although there is no direct evidence of relationship between the presence of aCL antibodies and the hearing loss, considering the rapid course of hearing deterioration and unresponsiveness to conventional steroid treatment, this patient doesn't fit the regular autoimmune inner ear disease criteria.¹³⁾ Vasculitis and high blood viscosity due to immune mediated responses including aCL antibody can be the possible mechanism of hearing loss in this patient.

The improvement in the hearing level after plasmapheresis treatment supports the theory that macromolecules, including aCL antibodies, might play a pathological role in micro-circulation in the inner ear and impairment of hearing in this patient.¹⁴⁾ The hypothesis is supported by the partial reversal of symptoms that occurred with plasmapheresis.

Considering the possibility that vasculitis and hyperviscosity is a prelude to infarction, early diagnosis and treatment would be paramount in lowering the incidence of deafness to prevent the ischemic change in cochlea.¹⁴⁾ Plasmapheresis is one of the most powerful immune suppressive method, furthermore, it can reduce blood viscosity by removing immune complexes from plasma substantially.^{12,14,15)} It will take at most several weeks to reduce immune complex by immunosuppressive medication, on the other hands, plasmapheresis can reduce it promptly. In this patient, the serologic markers to indicate the disease activity of SLE, that is, ESR, CRP, anti-dsDNA Ab, C3, C4 were within normal range immediately after the plasmapheresis, which implied the fast effectiveness of plasmapheresis.

For the invasiveness and high expenses, plasmapheresis would not be the choice in most sudden SNHL in SLE patient. However, when an immunologic process is strongly suspected to be responsible for the hearing loss but unresponsive to conventional treatment, plasmapheresis should

be considered promptly not to proceed to irreversible damage of cochlea.¹⁵⁾

Due to the rarity of sudden SNHL in SLE, it is difficult to clarify the possible association with aCL through the performance of sufficiently sized studies. Therefore, otorhinolaryngologists, rheumatologists and other clinicians who treat these individuals need to be aware of the possible treatment modalities from each reported cases.

In case of unusual presentation of sudden SNHL, a heightened index of suspicion and more discriminating diagnostic tools including in-depth analysis of autoimmune markers is necessary to get the well-directed medical therapy in proper time.²⁾ Even though her audiologic status is frustrating for doctors, it is noteworthy that plasmapheresis could reverse the hearing level of the left ear partially. Even though the role of plasmapheresis in lupus is still controversial, plasmapheresis can be considered when the disease is refractory to the conventional treatment.

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