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Susac Syndrome With Good Response to Intravenous Immunoglobulin: A Case Report

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Dear Editor,

Susac syndrome (SuS) is a rare disorder presumed to be immune-mediated endotheliopathy. It is characterized by a clinical triad of acute/subacute encephalopathy, branch retinal arterial occlusions, and sensorineural hearing loss, which are caused by microvessel occlusions in the brain, retina, and inner ear.[1] Since the first report by John Susac in the 1970s, approximately 450 cases have been reported worldwide and only two cases in Korea.[2-4] Here we report a SuS case that was well controlled after regular treatment with high-dose intravenous immunoglobulin (IVIg).

A previously healthy 32-year-old male presented with transient aphasia and numbness on the right face and arm that lasted 15 minutes. He had experienced occasional migraine-like headaches and blurry vision 3 months before symptom onset. Brain magnetic resonance imaging (MRI) revealed T2-weighted hyperintense lesions in the corpus callosum, basal ganglia, periventricular, subcortical white matter, or cerebellum, some of which exhibited abnormal diffusion restriction. Numerous leptomeningeal foci of enhancement were observed on contrast-enhanced fluid-attenuated inversion recovery (FLAIR) sequences (Fig. 1A). The characteristic MRI finding of SuS is a snowball-like lesion in the corpus callosum, which was present in our patient (Fig. 1A).[1] A cerebrospinal fluid examination revealed elevated protein (171.6 mg/dL) without pleocytosis. Oligoclonal bands were absent in the cerebrospinal fluid and serum. Anti-aquaporin-4 antibody and anti-myelin oligodendrocyte glycoprotein antibody were negative. Recurrent episodes of weakness and numbness in the right arm had developed by 6 days from aphasia onset. Brain MRI revealed several new diffusion-restriction lesions in the corpus callosum. An ophthalmologic examination was performed due to the suspicion of SuS. Retinal fluorescein angiography revealed branch retinal artery occlusion (Fig. 1B) and fundoscopy did not reveal the Gass plaque. He was treated using intravenous (IV) methylprednisolone (1 g/day for 5 days) followed by oral prednisolone (60 mg/day). The patient experienced extremely severe headache, dysarthria, and right-arm numbness approximately 1 month after the steroid pulse therapy, and soon after developed behavioral changes and alteration of consciousness. New diffusion-restriction lesions in the corpus callosum and periventricular area were demonstrated on MRI, but some of the previous lesions had disappeared. He was treated using IV methylprednisolone and IVIg (2 g/kg body weight over 2 days), followed by oral prednisolone and azathioprine (150 mg/day).[5] He improved almost completely over 1 week. Azathioprine was discontinued due to pancytopenia. The patient experienced vertigo and hearing loss in the left ear about 1 month after the IVIg infusion. Pure-tone audiometry revealed low-frequency sensorineural hearing loss in the left ear (Fig. 1C). Definite SuS was diagnosed based on the diagnostic criteria proposed by the European Susac Consortium.[6] He was treated using IVIg and IV cyclophosphamide. Cyclophosphamide was discontinued due to pancytopenia. The patient experienced severe headache and multiple new diffusion-restricting lesions with

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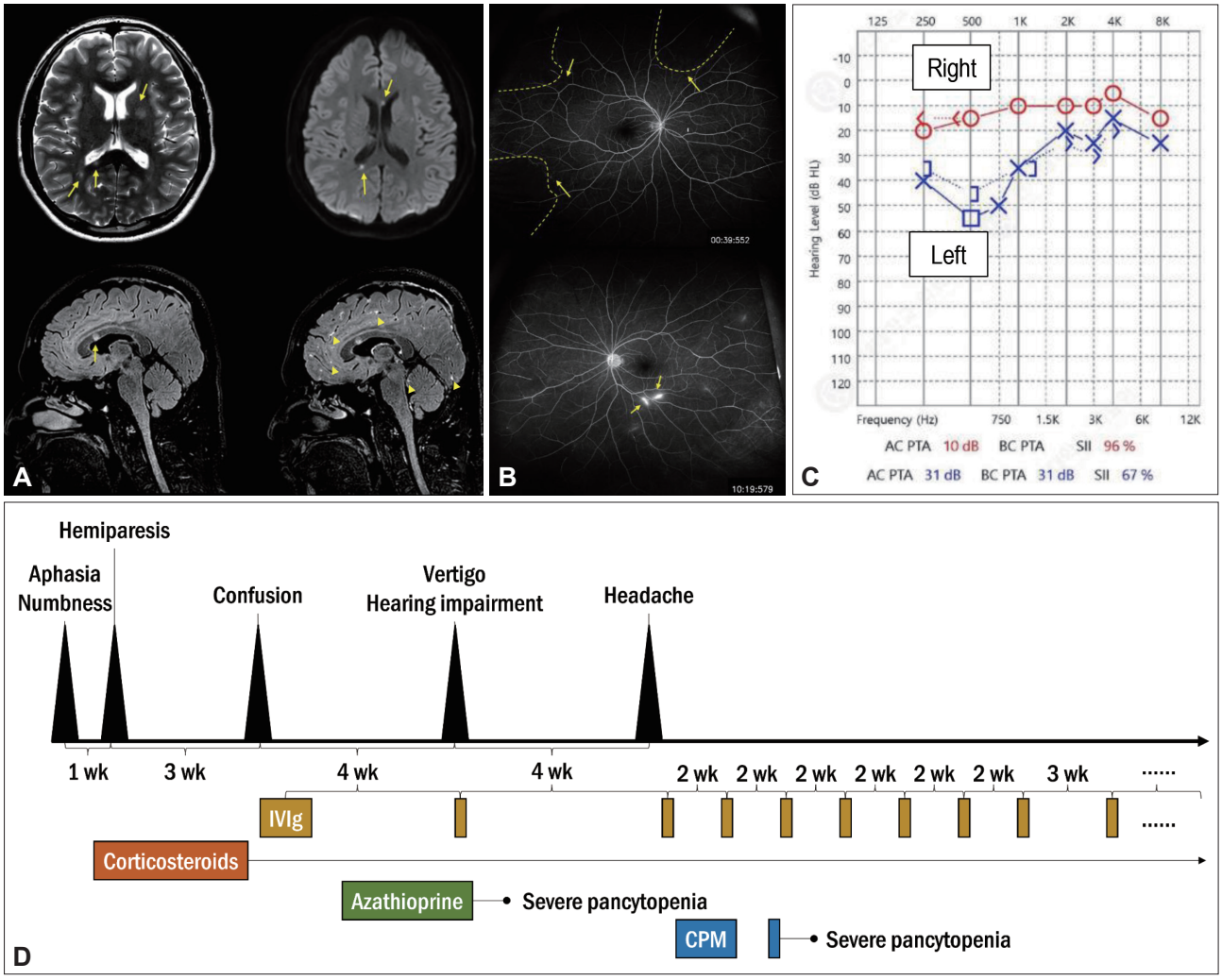

Fig. 1. Clinical manifestation of SuS and timeline of the clinical course. A: Findings of brain MRI. Axial T2-weighted sequence (upper left image) reveals hyperintense lesions (arrows) in the corpus callosum, deep white matter, and basal ganglia; axial diffusion-weighted image sequence (upper right image) reveals diffusion-restricted lesions (arrows) in the genu and splenium of the corpus callosum; sagittal T2-weighted FLAIR sequence (lower left image) reveals a characteristic snowball-like lesion (arrow) in the corpus callosum; and gadolinium-enhanced sagittal T2-weighted FLAIR sequence (lower right image) reveals numerous leptomeningeal foci of enhancement (arrowheads). B: Findings of FA. Upper image reveals branch retinal artery occlusion (arrows) and areas with decreased arterial blood flow (dashed lines). Follow-up FA (lower image) reveals arterial-wall hyperfluorescence (arrows). C: PTA reveals a low-frequency sensorineural hearing loss in the left ear. AC is plotted using an 'O' for the right ear and 'X' for the left ear. BC is plotted using a '<' for the unmasked right ear, '>' for the unmasked left ear, '[' for the masked right ear, and ']' for the masked left ear. D: Simplified clinical timeline of the patient. AC, air conduction; BC, bone conduction; CPM, cyclophosphamide; FA, fluorescein angiography; IVIg, intravenous immunoglobulin; PTA, pure-tone audiometry; SII, speech intelligibility index; SuS, Susac syndrome; wk, weeks.

T2-weighted hyperintensity on brain MRI about 1 month after the second IVIg infusion. He was treated with IVIg again, followed by IVIg infusion (1 g/kg body weight) every 2 weeks for about 3 months. There were no more clinical relapses or new lesions on MRI after shortening the IVIg infusion interval to 2 weeks (Fig. 1D). The IVIg infusion interval was gradually increased, and the patient remained stable for 15 months without relapse.

Multiple sclerosis was one of the initial differential diagnoses based on multiple T2-weighted hyperintense lesions on brain MRI in this patient. However, snowball-like lesions in the corpus callosum and numerous leptomeningeal foci of enhancement on contrast-enhanced FLAIR sequences suggested SuS rather than multiple sclerosis.[7] SuS was controlled after administering an IVIg infusion every 2 weeks in this patient. Treatment with corticosteroids alone was insufficient because severe encephalopathy developed while the patient was undergoing treatment with high-dose prednisolone (60 mg/day). This patient presented a good response to acute therapy using IVIg. However, relapses repeatedly occurred 1 month after the IVIg infusion. Although there have been no randomized controlled trials on SuS treatment, early, aggressive, and

sustained immunotherapy is highly recommended for its treatment, especially in the encephalopathic form.[5,8,9] IVIg is the mainstay of SuS treatment, and IV methylprednisolone, cyclophosphamide, rituximab, mycophenolate mofetil, and tacrolimus can be added.[5] In the practice of SuS treatment, some patients undergoing IVIg infusion every 4 weeks experience symptom relapse during the third or fourth weeks after IVIg infusion, which does not occur when the interval is changed to 2 weeks.[5] In patients with SuS, it should be considered to shorten the interval of IVIg infusion when relapses occur after IVIg treatment. Further studies are necessary to obtain systematic data on therapeutic strategies for SuS.

Ethics Statement

This study followed the tenets of the Declaration of Helsinki. Written informed consent was obtained from the patient.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

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Conflicts of Interest

Ha Young Shin, a contributing editor of the Journal of Clinical Neurology, was not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

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REFERENCES

1. Dörr J, Krautwald S, Wildemann B, Jarius S, Ringelstein M, Duning T, et al. Characteristics of Susac syndrome: a review of all reported cases. *Nat Rev Neurol* 2013;9:307-316.
2. David C, Sacré K, Henri-Feugeas MC, Klein I, Doan S, Cohen FA, et al. Susac syndrome: a scoping review. *Autoimmun Rev* 2022;21:103097.
3. Joe SG, Kim JG, Kwon SU, Lee CW, Lim HW, Yoon YH. Recurrent bilateral branch retinal artery occlusion with hearing loss and encephalopathy: the first case report of Susac syndrome in Korea. *J Korean Med Sci* 2011;26:1518-1521.
4. Cho HJ, Kim CG, Cho SW, Kim JW. A case of Susac syndrome. *Korean J Ophthalmol* 2013;27:381-383.
5. Rennebohm RM, Asdaghi N, Srivastava S, Gertner E. Guidelines for treatment of Susac syndrome – an update. *Int J Stroke* 2020;15:484-494.
6. Kleffner I, Dörr J, Ringelstein M, Gross CC, Böckenfeld Y, Schwindt W, et al. Diagnostic criteria for Susac syndrome. *J Neurol Neurosurg Psychiatry* 2016;87:1287-1295.
7. Triplett JD, Qiu J, O'Brien B, Gopinath S, Trewin B, Spring PJ, et al. Diagnosis, differential diagnosis and misdiagnosis of Susac syndrome. *Eur J Neurol* 2022;29:1771-1781.
8. London F, Pothalil D, Duprez TP, Sindic CJ. Potential benefits of early aggressive immunotherapy in Susac syndrome. *Acta Neurol Belg* 2016;116:451-460.
9. Fox RJ, Costello F, Judkins AR, Galetta SL, Maguire AM, Leonard B, et al. Treatment of Susac syndrome with gamma globulin and corticosteroids. *J Neurol Sci* 2006;251:17-22.