Original Contribution

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Complete Visual Recovery From Severe Outer Retinitis After Tonsillitis

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Background: To report a case of severe acute bilateral outer retinitis after tonsillitis and rapid morphologic and functional recovery after steroid treatment.
Methods: Observational case report.
Results: A 26-year-old woman with acute bilateral blurred vision that developed after tonsillitis underwent spectral-domain optical coherence tomography (SD-OCT) that showed photoreceptor outer segment damage. Full-field electroretinography (ERG) and multifocal ERG were non-recordable. The patient had a remarkable anatomic and functional recovery in response to steroid treatment; however, partial damage remained around the macula on SD-OCT, and an adaptive optics imaging system showed damaged cone photoreceptors.
Conclusions: Prednisolone is an effective treatment for a disease that is believed to be due to suspicious involvement of the autoimmune system. Even severe outer retinitis can recover completely with rapid diagnosis and treatment.

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The outer segment of the photoreceptors in the retina plays an important role in vision when severe damage causes severe visual loss and results in retinitis pigmentosa, autoimmune disorders, acute zonal occult outer retinopathy (AZOOR) complex, inflammation, infection, and others (1,2). The outer segment can recover spontaneously in diseases such as AZOOR (3); however, autoimmune retinopathies (AIRs), including cancer-associated retinopathy (CAR), melanoma-associated retinopathy, and nonparaneoplastic AIR (npAIR), cause rapid progressive visual loss. Although the pathogenicity and treatment for AIRs are not established, previous studies have reported that a preceding infection can trigger an AIR (4). Several reports have suggested that immunosuppressive therapy improves vision in cases of AIR (5); others have reported that patients with CAR and npAIR have progressive visual function damage despite immunosuppressive treatments (6,7). We report a case of severe outer retinitis, the rapid diagnosis and treatment of which resulted in recovery of the microstructures of the photoreceptor layer and retinal function.

CASE REPORT

In August 2016, a 26-year-old woman developed a sore throat and fever. An otolaryngologic evaluation resulted in diagnosis of acute tonsillitis, and the patient was treated with amoxicillin hydrates and ceftriaxone sodium hydrates. The acute tonsillitis resolved but bilateral blurred vision developed on September 7, 2016. Three days later, the patient reported bilateral visual loss and iritis. Because of the rapid visual deterioration, she visited our hospital. She had no relevant family history except for smoking. The initial examination showed best-corrected visual acuities (BCVAs) of 0.15 in the right eye and 0.09 in the left eye. Slit-lamp examination showed bilateral conjunctival injections, keratic precipitates, inflammatory cells (1+) in the anterior chamber, and anterior vitreous opacity (0.5+). Attenuation of the retinal vessels was seen in color fundus photographs.

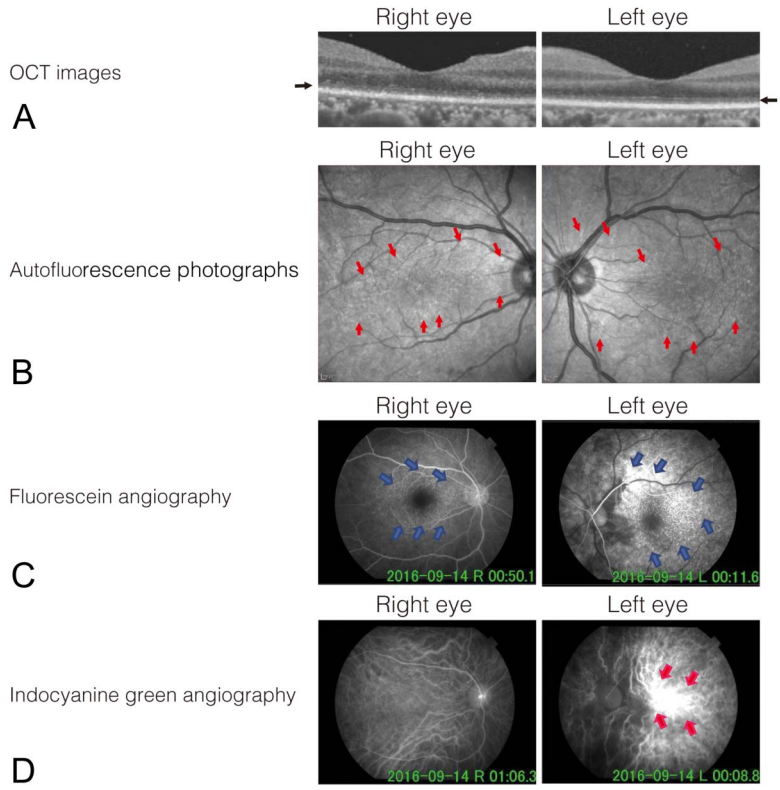

FIG. 1. Retinal damage at the initial examination. **A**. Optical coherence tomography (OCT) images. The *black arrows* indicate the blurred external limiting membrane and loss of the interdigitation zone and ellipsoidal zone lines. **B**. Autofluorescence photographs. The *red arrows* indicate the high-intensity spots. **C**. Fluorescein angiography. The *blue arrows* indicate the window defects. **D**. Indocyanine green angiography. The *red arrows* indicate hyperfluorescence.

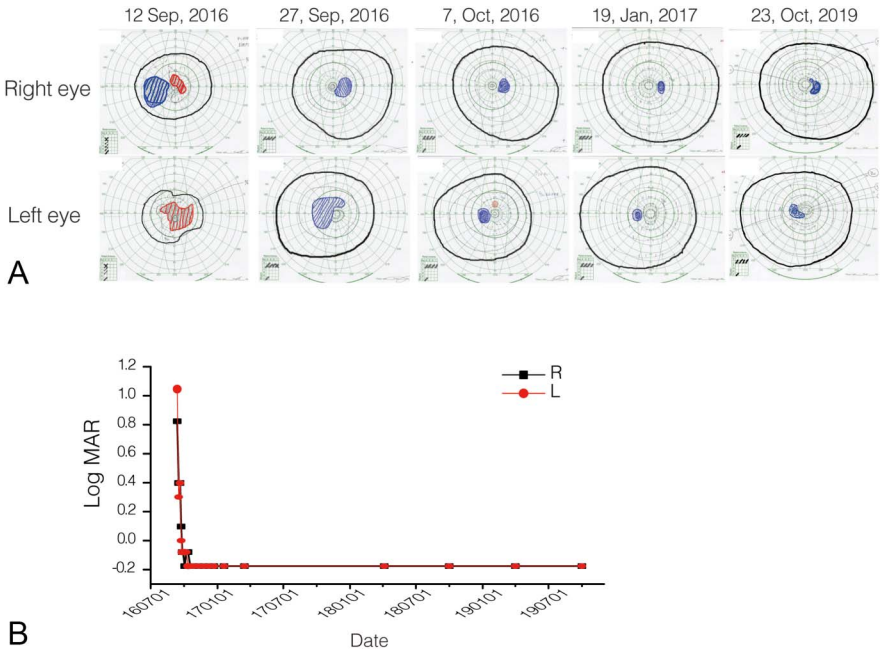

FIG. 2. Recovery of visual function. **A**. Recovery of the visual fields. *Red* indicates the central scotoma and *blue* the large Mariotte blind spot. **B**. Improvement of the visual acuity. *Black* indicates the right eye and *red* the left eye. logMAR, logarithm of the minimum angle of resolution; R, right eye; L, left eye.

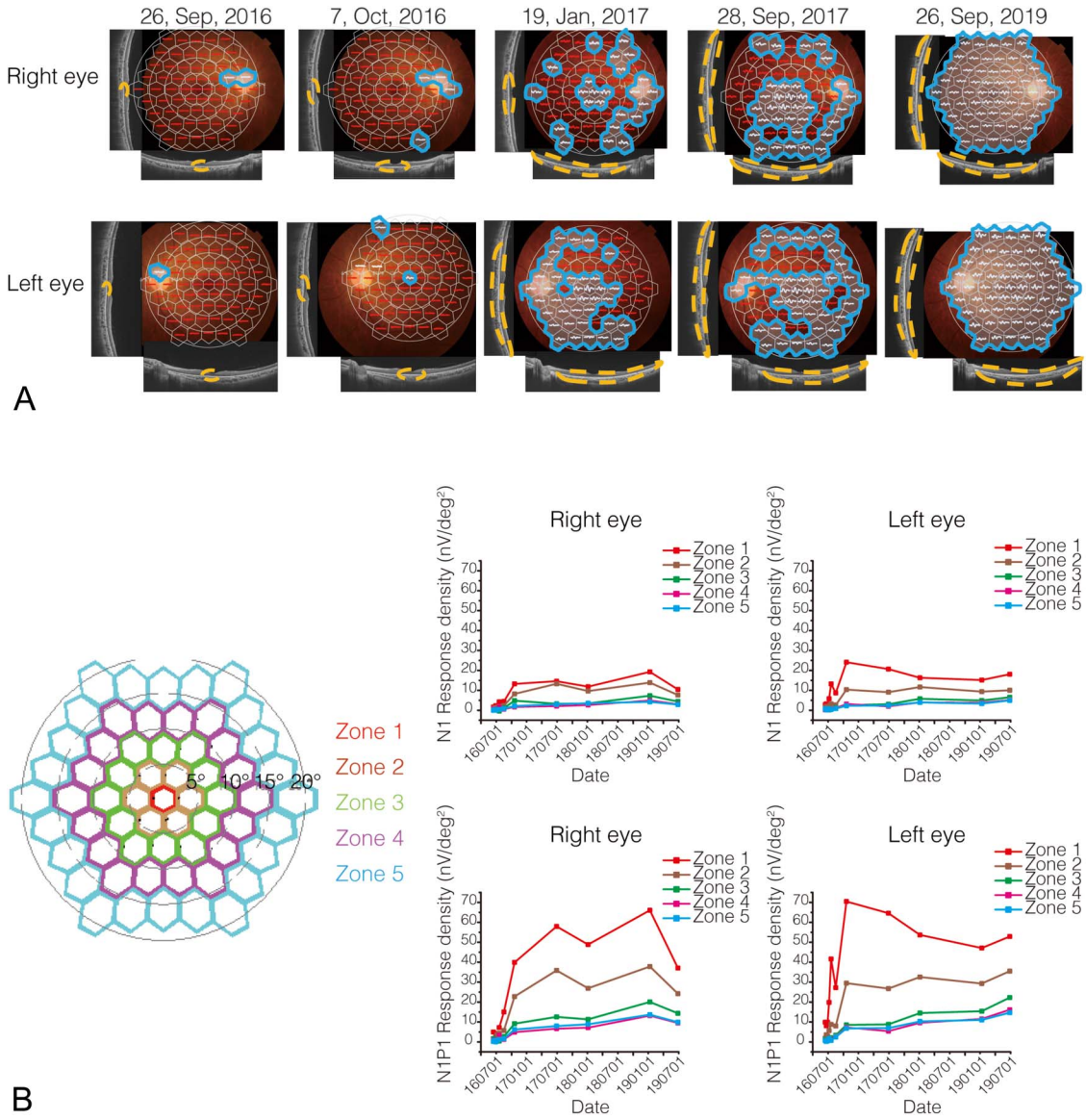

FIG. 3. The relationship between spectral-domain optical coherence tomography (SD-OCT) and multifocal electroretinography (mf-ERG) function. **A**. Improvement in the structures seen on OCT images. The *yellow lines* indicate the improvement of the external limiting membrane and ellipsoidal zone lines in the SD-OCT image; the *blue circles* indicate the improvement in the mf-ERG response. **B**. Improvement of the mf-ERG responses. N1, the first negative peak; P1, the first positive peak; N1P1, the corresponding amplitude.

Spectral-domain optical coherence tomography (SD-OCT) showed inflammation of the vitreous surface of the retina, a blurred external limiting membrane (ELM), and loss of the interdigitation zone (IZ) and ellipsoid zone (EZ) (Fig. 1A). Autofluorescence photographs showed high-intensity spots in the macula (Fig. 1B). Fluorescein angiography (FA) showed a window defect (Fig. 1C), and indocyanine green angiography showed hyperfluorescence in both maculas (Fig. 1D), indicating damage to the retinal pigment epithelium and chorioretinitis. Kinetic perimetry showed a central scotoma and large Mariotte blind spots bilaterally. Full-field electroretinography (ff-ERG) was nonrecordable. The cerebrospinal fluid had only an increased number of nucleated cells and no tumor cells, protein, or immunoglobulin G. Echocardiography, MRI, computed tomography, and positron emission tomography did not show significant findings, such as infection, malignancy, or vasculitis. The laboratory examination showed increased values for C-reactive protein, β-microglobulin, and soluble interleukin-2 receptor. The autoantibody test showed increased antinuclear antibody and complementary factor C3 values. No antibodies were found against herpes simplex virus, cytomegalovirus, *Toxoplasma gondii*, syphilis, streptolysin O, rubella virus, and recoverin antibody. Based on the clinical findings and examination results, we diagnosed an autoimmune disorder complicated by noninfectious aseptic

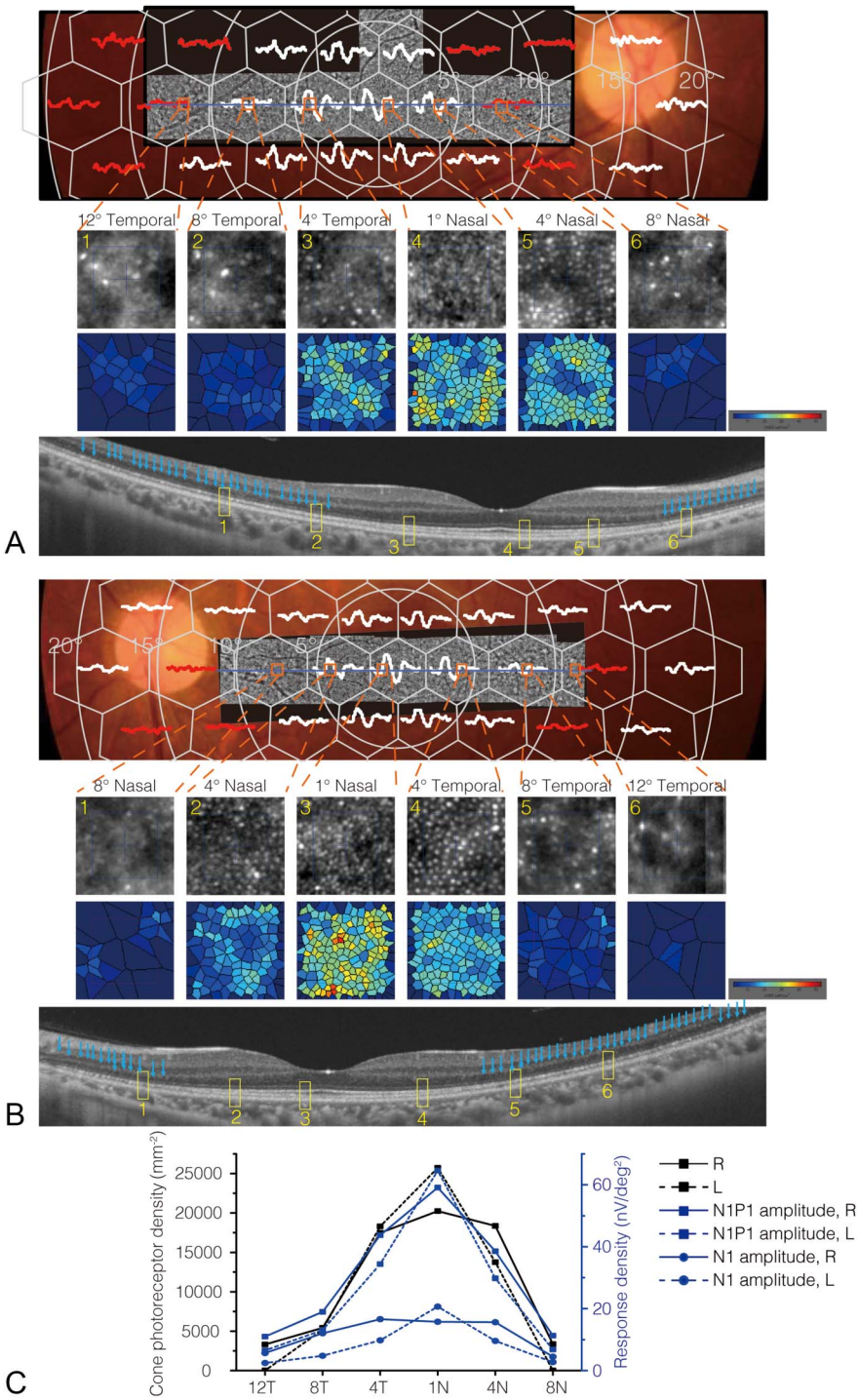

FIG. 4. The relationship among the adaptive optics (AO) image, spectral-domain optical coherence tomography (SD-OCT), and the multifocal electroretinography (mf-ERG) response. **A** and **B**. The relationship with the mf-ERG responses, AO image, and the structures in the SD-OCT image. **A**. Right eye. **B**. Left eye. The Voronoi segmentation obtained from AO images is color coded with the local cell density. **C**. The cone photoreceptor density calculated from the AO images compared with and by the mf-ERG response. The *black line* indicates the cone photoreceptor density; the *solid black line* indicates the right eye; the *dotted black line* indicates the left eye; the *blue line* indicates the mf-ERG response density; the *solid blue line* indicates the right eye; the *dotted blue line* indicates the left eye; the *squares* indicate the N1P1 response and the *circles* the N1 response. N1, the first negative peak; P1, the first positive peak; N1P1, the corresponding amplitude.

meningitis. We started intravenous methylprednisolone pulse therapy 5 days after the onset of visual loss. The vision improved rapidly, and inflammation in the anterior chamber and vitreous cavity decreased the next day. The central scotoma in kinetic perimetry recovered (Fig. 2A), and we detected the ELM and EZ lines in the fovea. However, the inflammation in the vitreous cavity and chorioretinitis remained. After we prescribed a second round of pulse therapy, the bilateral BCVA recovered to 1.2 (Fig. 2B). We started 45 mg of oral prednisolone and the inflammation in the vitreous cavity subsequently resolved. With tapering of the oral steroid, OCT detected the ELM and EZ lines in the macula, and the cone and oscillatory potential responses of the ff-ERG were recorded, followed by recovery of the IZ line in the fovea. The ELM and EZ lines in the posterior pole and the rod response of the ff-ERG then recovered. The recovery of the ff-ERG response might depend on the improvement of the ELM and EZ lines. The multifocal ERG (mf-ERG) response in the fovea recovered quickly, but the response in the posterior pole around the macula, where the ELM and EZ lines were still partially fragmented, remained low (Fig. 3A, B). The adaptive optics (AO) images obtained using the AO camera (rtx1; Imagine Eyes, Orsay, France) showed that the cone photoreceptor densities were more decreased and the cone mosaic was more disrupted in the peripheral retina (Fig. 4A, B), which indicated damage to the cone photoreceptors. The cone photoreceptor densities were associated with visualization of not only the EZ and IZ lines but also the ELM line and the mf-ERG response (Fig. 4C). After suspending the oral steroid medicine, the patient has not had a recurrence in 3 years.

DISCUSSION

Most outer segment damage remains despite treatment (6,7), but a few case reports have described recovery (8,9). The vision of this patient recovered completely from bilateral severe outer retinitis after acute tonsillitis.

We first suspected that this patient had an infectious disease such as syphilis or vasculitis, but the systemic findings were not significant. The patient had aseptic meningitis with an elevated soluble interleukin-2 receptor. Vogt–Koyanagi–Harada disease and neurologic Behçet disease are uveitic disorders complicated by aseptic meningitis. However, those diagnoses were ruled out because of the FA findings and the absence of HLA-B51. Ultimately, we diagnosed this patient as being suspicious for an AIR due to the clinical course, although we did not detect an anti-recoverin antibody or identify an association with any other antibodies reactive to retinal tissues or lysates, which meant not all clinical diagnostic criteria were met (10).

AIR, a rare disease that results initially in disordered photoreceptor cells, is a rapid and progressive disease that requires early diagnosis and treatment. Some autoantibodies for retinal antigens might be associated with the disease. However, the pathophysiology of npAIR is not understood, and the onset trigger and established treatment are unknown, which delays treatment. In a case series of patients with CAR and melanoma-associated retinopathy, 65% were positive for anti-retinal antibodies (11). In other case series of patients with npAIR, 41% and 43% had anti-retinal antibodies (6,12). Hence, autoantibodies to a retinal antigen are not identified in all patients with AIR (13) and might not be specific for the disorder (14). Cancer and antirecoverin antibody were not found in this case.

The clinical phenotype of AIR is heterogeneous. In one report, 5 of 6 patients with CAR and 8 of 16 patients with npAIR improved after immunosuppressive treatments (5). Other studies of patients with CAR reported improvements in visual acuity or visual fields after steroid, plasmapheresis, or immunoglobulin treatments (8,9). Some case series of patients with CAR and npAIR have reported a progressive decline in visual function despite immunosuppressive therapy (6,7). The treatment efficacy varies and is not established, and no cases have had complete improvement of the retinal function. In this case, the diagnosis was established and treatment with a steroid was administered 5 days after the onset of visual loss. We detected photoreceptor damage using AO images and showed that the cone photoreceptor densities are associated with visualization of not only the EZ and IZ lines (15,16) but also the ELM line and the mf-ERG response. We believed that early diagnosis and treatment might result in improved retinal function even after severe outer retinopathy. Although an anti-retinal antibody, other than the antirecoverin antibody, is not shown to be associated with this outer retinopathy, this case was strongly responsive to immunosuppressive treatment. Thus, this case report showed suspicious involvement of the autoimmune system.

STATEMENT OF AUTHORSHIP

Category 1: a. Conception and design: K. Matsushita; b. Acquisition of data: R. Kawashima; c. Analysis and interpretation of data: R. Kawashima, K. Matsushita, N. Hashida, and K. Kuniyoshi. Category 2: a. Drafting the manuscript: R. Kawashima, and K. Matsushita; b. Revising it for intellectual content: R. Kawashima, K. Matsushita, N. Hashida, K. Kuniyoshi, T. Fujikado, and K. Nishida. Category 3: a. Final approval of the completed manuscript: R. Kawashima, K. Matsushita, N. Hashida, K. Kuniyoshi, T. Fujikado, and K. Nishida.

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