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Case report

Improvements of visual function and outer retinal morphology following spontaneous regression of cancer in anti-recoverin cancer-associated retinopathy

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ABSTRACT

Purpose: To report an anti-recoverin antibody-positive cancer-associated retinopathy (anti-recoverin CAR) patient with remarkable improvements of visual function and outer retinal morphology following spontaneous regression of cancer.

Observations: A 65-year-old woman with small cell lung carcinoma developed progressive, bilateral vision loss with diffuse loss of the ellipsoid zone at the macula on optical coherence tomography and marked reduced responses of a- and b-waves on electroretinography. Western blot analysis led to a diagnosis of anti-recoverin CAR. The visual function and outer retinal morphology gradually improved following spontaneous regression of the cancer and the initiation of systemic corticosteroid. Subsequent intermittent chemotherapy and continuation of corticosteroid maintained reduction of the cancer and prevented the recurrence of CAR, with preservation of improvements of the visual function and macular outer retinal morphology.

Conclusions and importance: These results suggest that requirement for obtaining good visual prognosis in CAR patients is to make the cancer regress prior to falling into photoreceptor apotosis.

1. Introduction

Cancer-associated retinopathy (CAR) is an autoimmune retinopathy caused by antiretinal antibodies generated against aberrant expression of retinal antigen in cancer cells.[1,2] Of CAR patients, those with anti-recoverin antibody-positive (anti-recoverin) CAR often suffer from progressive visual and retinal dysfunction, having resistance to systemic immunosuppressive therapy,[2] and finally result in poor visual outcomes,[1,2] due to the apoptotic death of photoreceptor cells.[3] Spontaneous regression occurs in various types of cancer. However, spontaneous regression of small cell lung cancer is rare and has been previously reported in only less than twenty cases.[4] We describe the ophthalmological findings of an anti-recoverin CAR patient with spontaneous regression of lung cancer, as previously reported in the pneumology's literature.[5]

2. Case report

A 65-year-old woman presented with progressive blurred vision of both eyes for six days with night blindness, when the patient was admitted to the medicine for small cell lung carcinoma (SCLC, cT1aN3M0 stage IIIb). The patient had no medical or family history. The patient's best-corrected visual acuity (BCVA) was 0.01 OD and 0.5 OS. Slit-lamp biomicroscopy showed normal findings OU. Funduscopy and fluorescein angiography showed no abnormal appearance except for narrowed retinal arteries OU (Fig. 1A). Single-flash electroretinography (ERG) showed marked reduced responses of a- and b-waves OU (Fig. 1B). Goldmann perimetry showed a central scotoma OD and a ring scotoma OS, of 25 × 40° (Fig. 1C and D). Enhanced depth imaging optical coherence tomography through the fovea revealed diffuse loss of the ellipsoid zone at the macula OU (Fig. 1E and F, arrows). Systemic prednisolone (PSL) 40 mg/day was immediately initiated for a presumed diagnosis of CAR and thereafter tapered. Four days after the first visit, the results of chest computed tomography and serum tumor

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markers antecedent to chemotherapy revealed spontaneous regression of the SCLC.[5] Western blot analysis against recoverin protein using the patient's serum[6] led to a diagnosis of anti-recoverin CAR.[5] The patient subsequently received chemotherapy of four courses.

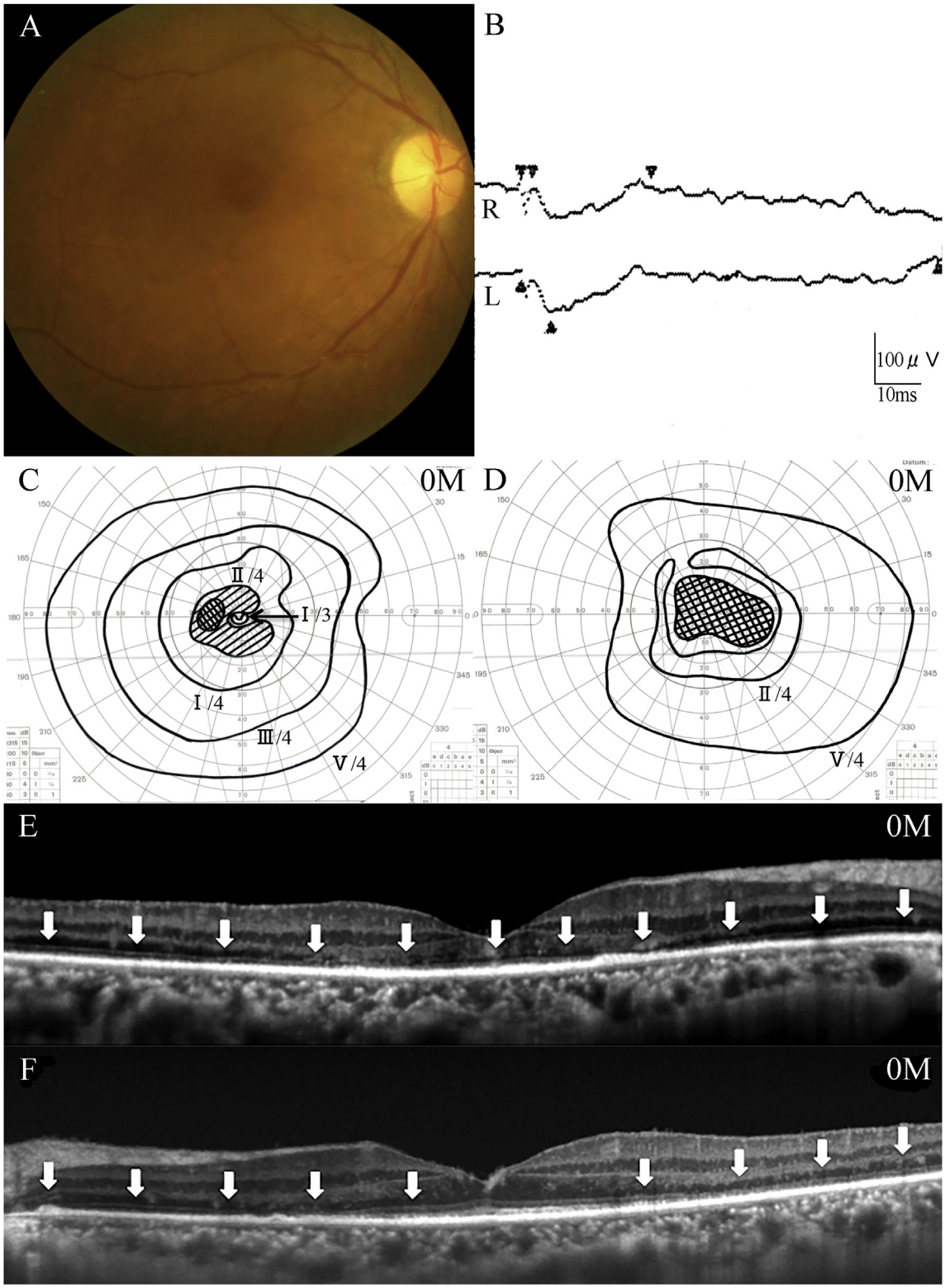

Fig. 1. Findings at the first visit in a 65-year-old patient with anti-recoverin antibody-positive cancer-associated retinopathy. A, Fundus photograph of right eye showing normal retinal appearance except for the attenuated retinal arteries. B, Single-flash electroretinography showing marked reduced a- and b-waves in both eyes. C, D, Goldmann perimetry revealing a ring scotoma in the left eye (C) and a central scotoma in the right eye (D), of 25 × 40°. E, F, Horizontal images of enhanced depth imaging optical coherence tomography through the fovea showing diffuse loss of the ellipsoid zone (arrows) at the macula (E, right eye, F, left eye).

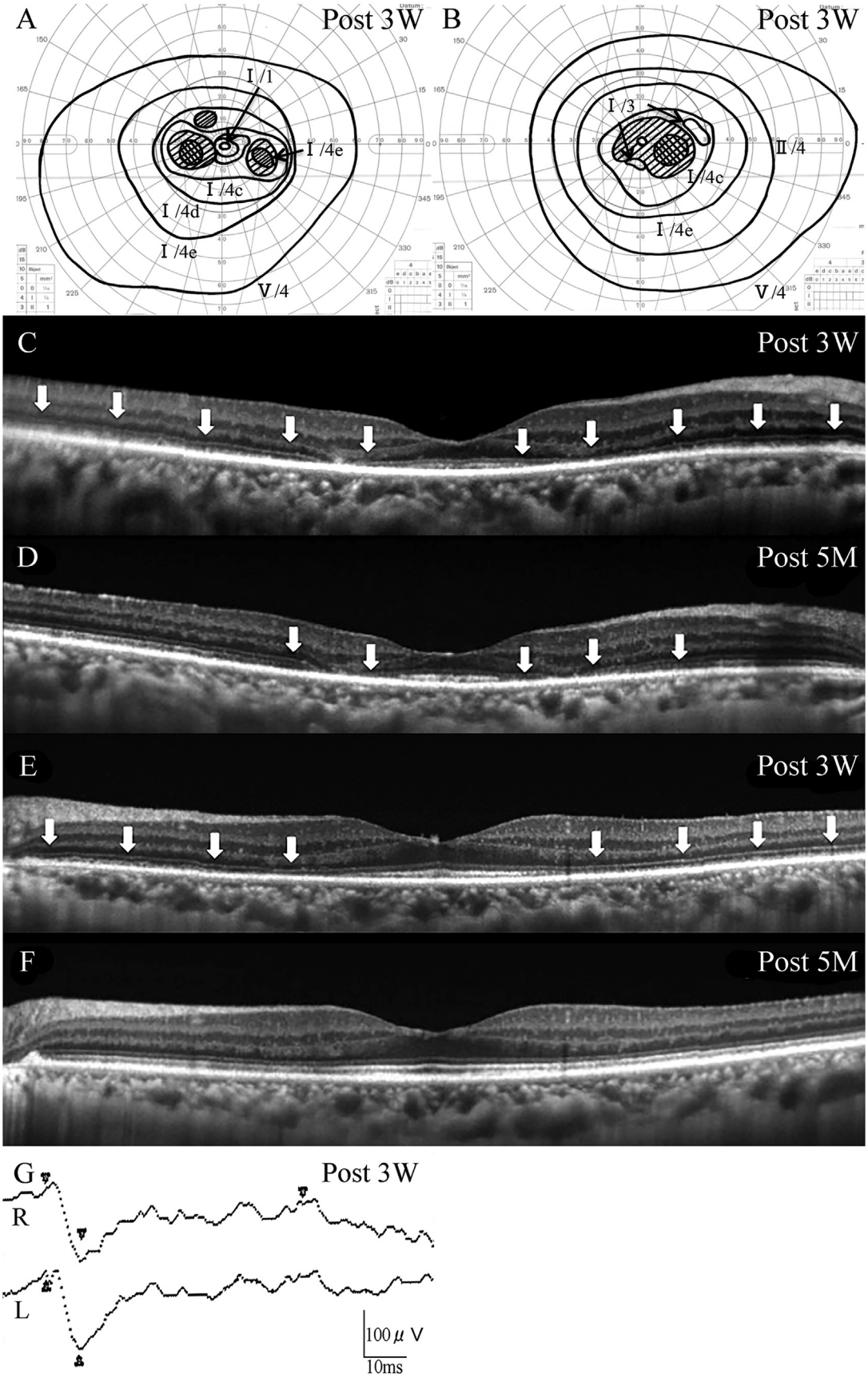

Fig. 2. Goldmann perimetry (A, B), enhanced depth imaging optical coherence tomography images (C—F), and single-flash electroretinography (G) after systemic corticosteroid and chemotherapy following spontaneous regression of cancer. A, B, Three weeks after the start of treatment, scotomata shrank with the improvements of central sensitivity (A, left eye, B, right eye). C, E, Three weeks after treatment, the ellipsoid zone at the fovea improved in both eyes (C, right eye, E, left eye). D, F, Five months after treatment, the macular ellipsoid zone further improved in the right eye (D) and was completely restored in the left eye (F). In C to F, arrows indicate the loss of the ellipsoid zone. G, Amplitudes of the a-wave improved 3 weeks after treatment compared to that at the initial visit.

Three weeks after the start of PSL, the BCVA improved to 0.1 OD and 0.8 OS. The scotomata shrunk OU (Fig. 2A and B) and the area of macular ellipsoid zone loss decreased OU (Fig. 2C, E). Amplitudes of a-wave on ERG increased (Fig. 2G). Five months after treatment (PSL10 mg/day), the BCVA further improved to 0.4 OD and 1.0 OS, with marked amelioration of macular outer retinal morphology (Fig. 2D, F). Ten months after treatment, since CAR recurred prior to the SCLC recurrence, the PSL dose was temporarily increased to 20 mg/day. Her BCVA improved again. Thereafter SCLC recurred two times and chemotherapy was performed each time. Forty-five months after treatment (PSL 10 mg/day), the BCVA was 0.8 OD and 1.0 OS, with preservation of improvement of the macular outer retinal morphology and further improvement of a-wave amplitudes on ERG. Reduction of the SCLC was maintained with no recurrence of CAR.

3. Discussion

Visual prognosis in patients with anti-recoverin CAR is generally poor despite the administration of various immunosuppressive therapies and the final BCVA resulted in less than 0.1 in approximately 70%.[1] We encountered an anti-recoverin CAR patient with marked improvements of visual function and outer retinal morphology following spontaneous regression of SCLC. In the present case, Kitai et al. reported the presence of recoverin in the tumor cells on immunohistochemistry.[5] Moreover, IFN-ELISPOT assay using the patient's peripheral blood mononuclear cells stimulated by recoverin peptide in vitro revealed activation of recoverin-specific antitumor cytotoxic T lymphocytes.[5] From these results, the mechanism why the SCLC spontaneously regressed in this case appeared to be due to the activation of recoverin-specific antitumor cytotoxic T lymphocytes following the aberrant expression of recoverin on the tumor cells.[5] We speculated the reason why the patient's visual function not only markedly improved but maintained the improvement for the long follow-up period as follows. First, aberrant expression of recoverin on cancer cells and the following serum anti-recoverin antibody production were suppressed owing to the spontaneous regression of the SCLC. Next, systemic corticosteroid therapy immediately administrated prior to falling into the apotosis of photoreceptor cells led the patient's visual and retinal dysfunction to the improvements. Subsequent intermittent chemotherapy and continuation of corticosteroid prevented the photoreceptor damage by maintaining suppression of the antigen-antibody reaction. Thus, our results suggest that requirement for obtaining good visual prognosis in CAR patients is to make the cancer regress prior to falling into photoreceptor apotosis.

Patient consent

Informed consent was obtained in writing from the patient for the use of their information and external photograph for the purpose of this report.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Conflict of interest

The following authors have no financial disclosures: US, WS, KH, AK, HK, JSK, and SI.

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