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Case report

Electroretinographic improvement after rituximab therapy in a patient with autoimmune retinopathy

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ABSTRACT

Purpose: To describe the effect of rituximab on full-field electroretinography (ERG) in a patient with nonparaneoplastic autoimmune retinopathy (npAIR).

Observations: A 58-year-old male patient with visual complaints, positive anti-retinal antibodies and negative work-up for cancer was diagnosed with npAIR. Visual acuity and ancillary tests were normal except abnormal ERG in both eyes. The patient was given one course of rituximab 375 mg/m^2/week for 4 weeks and cyclophosphamide 1 gr/m^2/month for 6 months. A second course of rituximab was necessary as autoantibody titers showed no change and as new antibodies were noted after treatment with rituximab and cyclophosphamide. Electroretinography was repeated after the first course of rituximab, after cyclophosphamide, and the second course of rituximab therapy.

Conclusions and importance: Rituximab therapy led to marked improvement in full-field ERG readings and regression of symptoms was reported by the patient after rituximab infusions. The effect of rituximab in npAIR was objectively demonstrated with ERG.

1. Introduction

Autoimmune retinopathy (AIR) is an immune-mediated retinal degeneration characterized by progressive vision loss, abnormal electroretinography (ERG), visual field deficits, and presence of circulating anti-retinal autoantibodies. Two forms of AIR exists: paraneoplastic (pAIR) and nonparaneoplastic (npAIR). Paraneoplastic AIR is further subdivided into cancer-associated retinopathy (CAR) and melanoma-associated retinopathy (MAR) [1–5]. Lymphoma associated retinopathy (LAR) has also been described [6–8]. Nonparaneoplastic AIR is more common than pAIR [1,3,4]. Patients with npAIR are mostly female and have a history and/or family history of autoimmune disease [1–4].

The diagnosis of AIR should be considered in patients with subacute vision loss, photopsias, nyctalopia, scotomas, photoaversion, dyschromatopsia and/or visual field loss [1–5]. Some patients may also have diminished central vision and loss of contrast sensitivity [4]. Symptoms are usually bilateral, but can be asymmetric between the eyes [1–5]. Visual acuity may be deceivingly good in the early stages of the disease [1]. The fundus can appear unremarkable initially and demonstrate retinal vascular attenuation, diffuse retinal atrophy, retinal pigment epithelium abnormalities, and/or disc pallor later in the disease course [1–5]. Usually, there is no or minimal intraocular inflammation [1–5]. The mean age of onset ranges between 55 and 65 years, with npAIR having a younger age of onset than pAIR [2].

Because of the presumed autoimmune nature of AIRs immunomodulatory agents have been used in an attempt to treat the disease. It is uncertain whether treatment significantly alters the natural course of the disease [1]. More favorable treatment results are achieved in pAIR, particularly CAR [1]. An early attempt to treat AIRs is suggested to end-up with a beneficial outcome [1,9].

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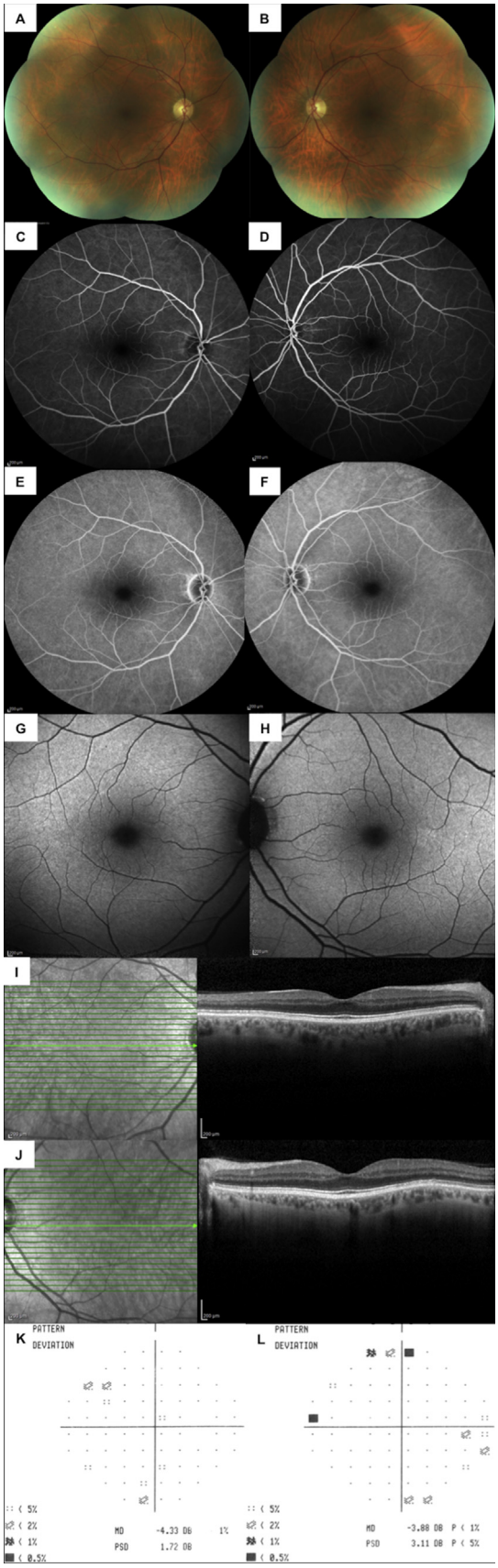

Fig. 1. Color fundus photograph of the right (A) and left eye (B) show attenuated retinal vessels more prominent in the retinal arteries than in retinal veins. Fluorescein angiography shows no abnormal fluorescence in the early (C, D) and late frames (E, F) in the right and left eye. Fundus autofluorescence shows normal autofluorescence in the right (G) and left eye (H). Spectral-domain optical coherence tomography of the right (I) and left eye (J) shows normal inner and outer retinal architecture. Pattern deviation plot of visual field testing with 30-2 Swedish Interactive Thresholding Algorithm (SITA) Fast program of the Humphrey Field Analyzer is within normal limits in the right (K) and left eye (L).

2. Case report

A 58-year-old male patient was referred to the oncology department in August 2014 with a preliminary diagnosis of CAR due to abnormal full-field ERG and elevated cancer antigen (CA) 15-3. The patient was complaining of seeing a peripheral white halo when passing from dark to light and vision fading of colors more prominent in his right eye, for 5 months. He had systemic hypertension and liver hemangiomas. He denied smoking and family history of cancer and autoimmune disease.

Work-up revealed microangiopathic gliosis on cranial magnetic resonance imaging (MRI), hepatic hemangiomas on abdominal MRI (stable when compared with the abdominal MRI taken in 2012), and a normal esophagogastroduedenoscopy and colonoscopy. Complete blood count, serum biochemistry, free/total prostate specific antigen, CA 19-9, carcinoembriogenic antigen, and alpha-fetoprotein were normal. Repeat CA15-3 was positive at 30.4 U/mL (normal: 0–25 U/mL). Ultrasound of subareolar breast tissue was normal. Positron emission tomography/computed tomography showed no hypermetabolic activity.

Ophthalmologic examination showed a best-corrected visual acuity of 1.0 in both eyes. Pupils were equal and reactive to light; there was no relative afferent pupillary defect. Biomicroscopy was unremarkable in both eyes. Intraocular pressures were 16 mmHg in both eyes. Fundus examination showed attenuated retinal vessels more prominent in the retinal arteries than in retinal veins bilaterally (Fig. 1A, B). Fluorescein angiography, fundus autofluorescence, spectral-domain optical coherence tomography (SD OCT), and computerized perimetry were normal in both eyes (Fig. 1C–L). Full-field ERG and pattern visual evoked potentials (VEP) and ERG were conducted in October 2014 (Table 1). Western blot analyses at Casey Eye Institute Ocular Immunology Laboratory showed anti-retinal autoantibodies against 23-kDa (not reactive to recoverin), 42-kDa, and 70-kDa proteins and anti-optic nerve autoantibody against 35-kDa protein. A diagnosis of npAIR was established based on the patient's visual symptoms, abnormal full-field ERG, and the presence of anti-retinal autoantibodies. A treatment protocol consisting of 4 cycles of rituximab 375 mg/m^2/week, followed by 6 cycles of cyclophosphamide 1 gr/m^2/month was planed. Electroretinography was repeated after 4 cycles of rituximab infusions before cyclophosphamide was begun and after the 6 cycles of cyclophosphamide therapy. Despite remaining subnormal a marked improvement in full-field ERG parameters was recorded 3 weeks after the course of rituximab and before cyclophosphamide treatment in February 2015 (Table 1). The patient reported recovery in visual symptoms after the third cycle of rituximab infusion.

After completion of 6 cycles of intravenous pulse cyclophosphamide therapy full-field ERG was repeated in August 2015 (Table 1) and blood was send to Casey Eye Institute Ocular Immunology Laboratory for re-evaluation. Although full-field ERG readings showed a decline when compared to post-rituximab, readings were still better than baseline. Anti-retinal antibody testing showed positivity of 23-kDa (not reactive to recoverin), 36-kDa (GADPH), 40-kDa (aldolase), and 42-kDa with no significant change in previous antibody titers and presence of new autoantibodies. Also were noted new anti-optic nerve antibodies against 19-kDa, 21-kDa, 23-kDa, 35-kDa and 136-kDa proteins.