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Successful Combination Therapy with Rituximab and Glucocorticoids for Autoimmune Optic Neuropathy

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Conflict of interest: None declared

Patient: Female, 77
Final Diagnosis: Autoimmune optic neuropathy
Symptoms: Vision loss in the left eye
Medication: —
Clinical Procedure: Treatment with Rituximab and Glucocortioids
Specialty: Ophthalmology and Internal Medicine

Objective: Unusual or unexpected effect of treatment

Background: Autoimmune optic neuropathy is optic neuropathy caused by an autoimmune mechanism. As treatment, steroid is usually used. If steroid is ineffective to improve visual function, other immunosuppressive agents are used as needed. Rituximab is one of molecular target agents and is now used as treatment for several types of autoimmune disorders.

Case Report: A 77-year-old woman presented with vision loss in her left eye. Her past medical history included disturbances of multiple organs. Laboratory tests revealed positive myeloperoxidase-anti-neutrophil cytoplasmic antibody. We assumed that her vision loss was caused by autoimmune optic neuropathy and put her on high-dose glucocorticoid therapy. Her visual function quickly re-deteriorated after high-dose glucocorticoid therapy discontinuation. To achieve vision improvement, we added rituximab to her treatment regimen. Her visual acuity recovered to almost 20/20 within a week later. She received other 3 rituximab-infusions and her visual acuity remained 20/20 while tapering glucocorticoid.

Conclusions: Autoimmune optic neuropathy may result in blindness if treatment fails. Rituximab may be a therapeutic option for autoimmune optic neuropathy and may produce immediate response.

MeSH Keywords: Antibodies, Monoclonal • Glucocorticoids • Optic Nerve Diseases

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/894064

Background

Autoimmune optic neuropathy is a broadly defined medical term for some types of optic nerve disorders involving an autoimmune mechanism [1]. Autoimmune disorders related to autoimmune optic neuropathy include multiple sclerosis, demyelinating disease, polyarteritis nodosa, anti-neutrophil cytoplasmic antibodies-associated vasculitis, cryoglobulinemic vasculitis, Henoch-Schönlein syndrome, and Grave's disease [2]. Glucocorticosteroid is the basis of treatment and other immunosuppressive agents are added as needed [2]. If treatment fails, autoimmune optic neuropathy results in blindness [3].

Rituximab, an anti-CD20 monoclonal antibody, is used as treatment for several types of autoimmune disorders. Especially in vasculitis syndrome, rituximab produces favorable outcomes even compared with classical cytotoxic agents [4,5]. Rituximab is also used for eye disorders and results in optic rescue [6,7].

Case Report

A 77-year-old Japanese woman presented with blurred vision in her left eye. She had history of proteinuria, interstitial pneumonia, numbness in her left arm, hypertrophic pachymeningitis, blindness in the right eye due to right optic neuropathy, chronic sinusitis, and bilateral sensory hearing loss. She had no history of smoking or substance abuse. She did not have diplopia, ptosis, abnormal eye movement, or lacrimal abnormalities. Visual acuity was no light perception in the right eye and light perception in the left eye. Funduscopy revealed a pale and atrophic optic disc and retina in the right eye and normal optic disc and retina in the left eye (Figures 1, 2). Direct papillary light reflex was absent in the right eye and sluggish in the left eye. Relative afferent papillary defect was positive in both eyes, especially in the right eye. No other abnormal findings were found on neurological, thoracic, or abdominal examinations except for bilateral sensory hearing loss. Her body weight was 37 kg.

Laboratory tests revealed the following results: elevated CRP (0.51, normal 0–0.4 mg/dL), erythrocyte sedimentation rate (23, normal 0–15 mm/hr), CH50 (49.7, normal 25.0–48.0 U/mL); decreased creatinine clearance (46, normal 80–140 mL/min); normal WBC (7700, normal 3500–8500 /μL), creatinine (0.61, normal 0.5–1.3 mg/dL), C3 (87, normal 65–135 mg/dL), C4 (31, normal 13–35 mg/dL), IgA (366, normal 110–410 mg/dL), IgG (1695, normal 870–1700 mg/dL), IgM (84, normal 35–220 mg/dL); positive myeloperoxidase-anti-neutrophil cytoplasmic antibody (30, normal <10 EU), anti-nucleolus antibodies titer (1:80, homogenous patters, normal 1:1–1:20); negative proteinase 3-anti-neutrophil cytoplasmic antibody (<1, normal <10 EU), anti-DNA antibody (2, normal <6.0 IU/mL), anti-ds-DNA antibody (10, normal <12.0 IU/mL), anti-SS-A/Ro antibody (7.0, normal <10.0 U/mL; negative anti-AQP4 antibody.

Cerebrospinal fluid analysis revealed the following results: consistency clear; elevated protein (83, normal 15-45 mg/dL), IgG index (0.71, normal <0.70); and normal cell count (2.4, 100% lymphocyte, normal <5 /μL).

Contrast-enhanced MRI showed normal optic nerve and no specific findings. CT images of chest and sinus revealed no signs of interstitial pneumonia or sinusitis, respectively (Figures 3, 4).

Biopsy was not performed because of the patient request.

According to her past medical histories, we assumed that her vision loss was due to an autoimmune mechanism. Her clinical course is summarized in Figure 5. The patient received a

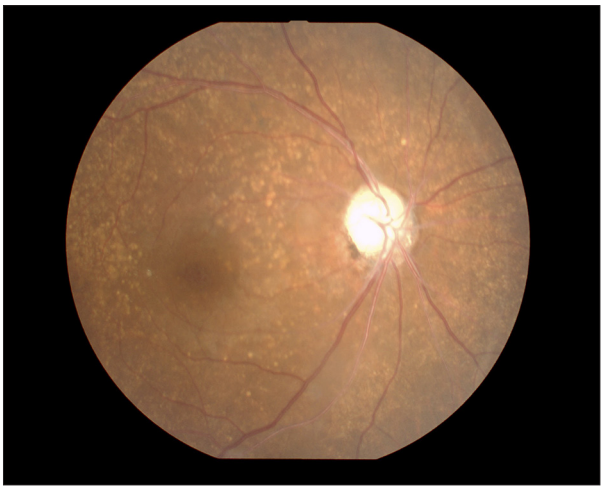

Figure 1. Retinal examination of the right eye revealed a pale and atrophic optic disc and retina.

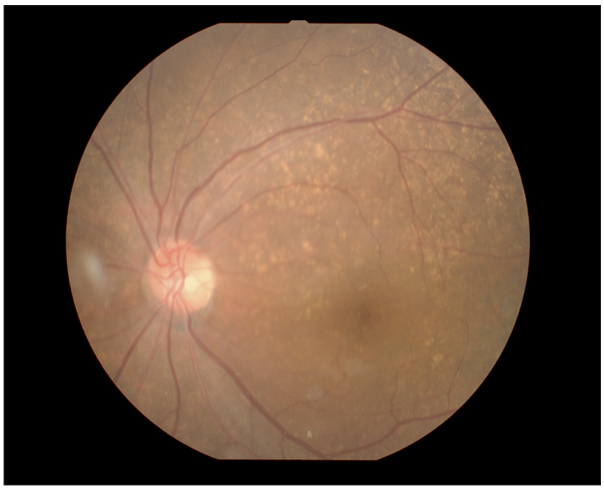

Figure 2. Retinal examination of the left eye revealed a normal optic disc and retina.

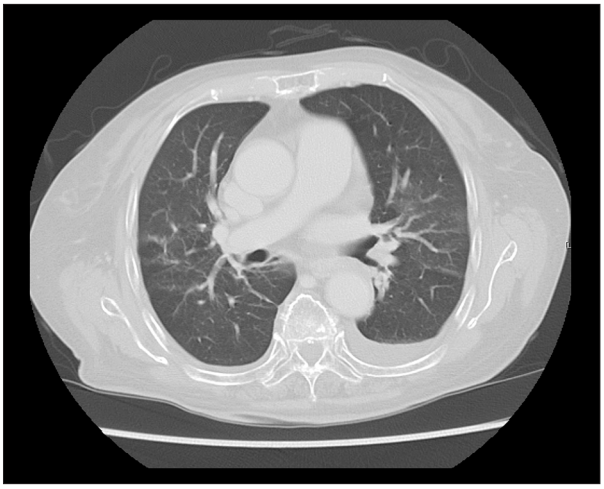

Figure 3. CT images of chest showed no findings compatible with interstitial pneumonia.

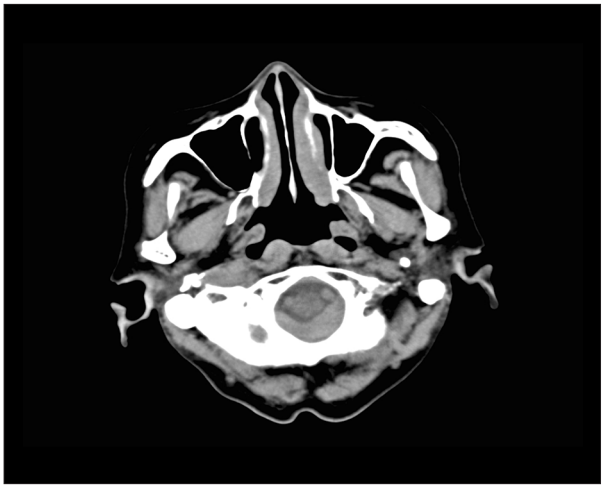

Figure 4. CT images of the sinus showed no findings compatible with sinusitis.

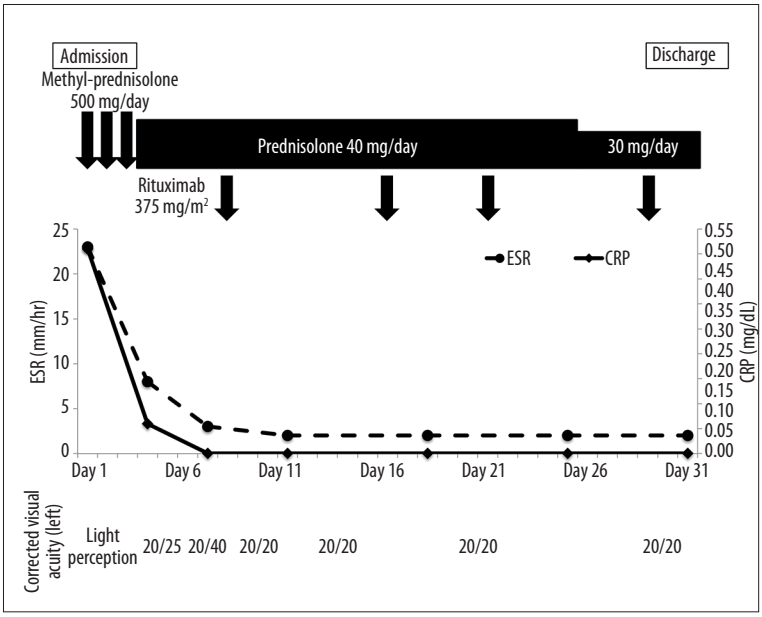

Figure 5. The clinical course of our patient.

3-day course of high-dose intravenous glucocorticoid (500 mg methyl-prednisolone/day) and following glucocorticoid therapy with oral prednisolone 40 mg daily. Immediately after high-dose intravenous glucocorticoid, her left corrected visual acuity recovered to 20/25 and deteriorated to 20/40 in a few days. To achieve vision improvement, rituximab therapy (rituximab 375 mg/m^2/week) was started. Within 1 week after the first rituximab-infusion, left corrected visual acuity recovered to 20/20 in the left eye and nasal and upper altitudinal quadrantanopsia was demonstrated. The patient received 3 additional rituximab-infusions and systemic glucocorticoid therapy was tapered while the patient remained free of ocular symptoms.

Discussion

We herein described the first case report of successful combination therapy with rituximab and glucocorticoid for autoimmune optic neuropathy. The broad definition of autoimmune optic neuropathy is optic neuropathy with an autoimmune nature [1].

Considering her past medical histories involving multiple organs and positive myeloperoxidase-anti-neutrophil cytoplasmic antibody, we first suspected our patient's vision loss was due to ischemic optic neuropathy secondary to granulomatous polyangiitis. Because of the absence of biopsy, the diagnosis of granulomatous polyangiitis was not confirmed. We considered whether our patient's symptomatic constellations met to the criteria of American

College of Rheumatology for granulomatous polyangiitis [8]. Our patient's symptomatic constellations were not sufficient to meet these criteria and we finally concluded that her vision loss was caused by autoimmune optic neuropathy secondary to vasculitis syndrome in which myeloperoxidase-anti-neutrophil cytoplasmic antibody played a major role. Anti-neutrophil cytoplasmic antibody-associated vasculitis is known to cause ocular surface manifestations such as episcleritis, scleritis, and peripheral keratitis. Ocular surface manifestations are the most common presentations of myeloperoxidase-anti-neutrophil cytoplasmic antibody-associated vasculitis. Posterior segment manifestations such as central/branch retinal vein occlusion, optic neuropathy, posterior scleritis, and anterior/posterior ischemic optic neuropathy are the second most common presentations [9].

Treatment for autoimmune optic neuropathy is based on glucocorticoid therapy. Immunosuppressive agents (e.g., azathioprine, chlorambucil, and cyclophosphamide) are added as needed to achieve and maintain vision improvement [2]. If the treatment fails, blindness is the consequence of autoimmune optic neuropathy [3]. In this case, we choose the combination therapy with rituximab and glucocorticoid because of the patient's age, the aim to achieve early steroid tapering, decreased creatinine clearance, and unilateral blindness due to history of failed treatment with immunosuppressive agent for right optic neuropathy. Immediate vision improvement was observed after the first rituximab infusion.

Rituximab, a monoclonal antibody targeting the B-cell antigen CD20, was initially used for CD20 positive malignant lymphoma and now is broadly used for several forms of autoimmune disorders [10]. The combination therapy of rituximab and glucocorticoid achieves outcomes equivalent to that of combination therapy with cyclophosphamide and glucocorticoid in induction of remission in severe anti-neutrophil cytoplasmic antibody-associated vasculitis [4,5]. Especially in relapsing cases of anti-neutrophil cytoplasmic antibody, re-treatment with rituximab and glucocorticoids is a safe and effective treatment, regardless of previous treatment [11]. Guerry et al. [12] recommends rituximab for refractory anti-neutrophil cytoplasmic antibody, relapsing anti-neutrophil cytoplasmic antibody, and granulomatous polyangiitis with head and neck manifestations. There is 1 case report demonstrating successful combination therapy with glucocorticoid, cyclophosphamide, and rituximab in a patient with refractory optic neuropathy secondary to granulomatous polyangiitis [6]. Rituximab was also used as treatment for idiopathic scleritis and produced good outcome [7].

As we observed in our patient, there is a report that demonstrated rapid regression in systemic autoimmune disorders after rituximab administration [13]. Antibody depletion does not occur within several hours after rituximab-infusion, but lymphocyte depletion does [14]. We believe our patient's immediate vision improvement could be explained by the hypothesis that rituximab decreases interactions between B-cell and T-cell (i.e., the effector cell) due to B-cell depletion rather than decreases antibody production by B-cell.

Conclusions

We herein reported a case of successful combination therapy with rituximab and glucocorticosteroid for autoimmune optic neuropathy. Autoimmune optic neuropathy may result in blindness and major disturbance in patient quality of life. This study is the first case report indicating that the combination therapy with rituximab and glucocorticoid is effective for autoimmune optic neuropathy.

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