CASE REPORT

The Case of IgG4-Related Ophthalmic Disease with Perivascular Lesions of Superior Ophthalmic Vein Associated with Optic Nerve Disturbance

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ABSTRACT

A 61-year-old man with hyperthyroidism had exophthalmos with dilated conjunctival vessels in both eyes. Magnetic resonance imaging showed that the superior ophthalmic veins had a funicular-like appearance. Cerebral angiography showed no blood flow from both internal carotid arteries to the cavernous sinus, thus excluding a carotid-cavernous fistula. Blood tests showed an elevation of IgG4 (281 mg/dl), and a IgG4-related ophthalmic disease was considered. Steroid pulse therapy was performed, and all of the abnormal findings were improved. We concluded that this was a rare case of IgG4-related ophthalmic disease with perivascular lesions of the superior ophthalmic vein associated with optic nerve disturbance.

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Introduction

Immunoglobulin G4-related ophthalmic disease (IgG4-ROD) is a new clinical entity characterized by infiltration of IgG4-positive plasmacytes into various tissues such as the lacrimal glands, extraocular muscles, and trigeminal nerve.¹ A recent multicentre survey in Japan found that among the 1014 cases of orbital lymphoproliferative disease, 21.6% were IgG4-ROD.²

The major location of the lesions in patients with IgG4-ROD is the lacrimal gland. A recent study found that 87.7% of 65 patients had lesions in the lacrimal glands.³ Other major lesions were in a trigeminal nerve branch (38.5%), extracellular muscle (24.6%), diffuse orbital fat (23.1%), orbital mass (16.9%), eyelids (12.3%), and nasolacrimal duct (1.5%).³

We report our findings in a very rare case of IgG4-ROD in which magnetic resonance imaging (MRI) showed a funicular-like mass along the superior ophthalmic veins associated with optic nerve disturbance.

Case report

A 61-year-old man had hyperthyroidism and had been followed with thyroid-associated orbitopathy

for 5 years. The exophthalmos gradually worsened, and he was referred to Chiba University Hospital in 2016. Our initial examination showed that he had exophthalmos with dilated conjunctival vessels in both eyes (Figure 1). His visual acuities were 1.2 OD and 1.2 OS, and the intraocular pressures were 18 mmHg OD and 20 mmHg OS. The proptosis was 23 mm in the right and 25 mm in the left eyes. His ocular movements were limited, and MRI showed funicular-like appearance of the superior ophthalmic veins (Figure 2). Because, the extraocular muscles were not enlarged, the perivascular lesions of the superior veins may cause disturbance of the ocular movement.

Because it was difficult to differentiate the MRI findings from that of carotid-cavernous fistula (CCF), cerebral angiography was performed. The cerebral angiography showed no flow from both internal carotid arteries to the cavernous sinus, and CCF was excluded.

Blood tests showed high levels of IgG4 (281 mg/dl), and the cut-off value for serum IgG4 concentration is about 135 mg/dl. Thus, IgG4-related ophthalmic disease was considered. The interleukin-2 receptor was 400 U/ml, thyroid-stimulating hormone (TSH) receptor

Figure 1. Ocular findings at the initial examination. The patient had exophthalmos with dilated conjunctival vessels in both eyes. Ocular movements were also limited.

Figure 2. MRI findings before (left panels) and after steroid pulse therapy (right panels). Upper panels show T1 images, and lower panels show Short-T1 Inversion Recovery (STIR) images. The lesions surround the upper ophthalmic vein before treatment (left yellow arrows). After steroid pulse therapy, the lesions were significantly improved (right yellow arrows).

antibody was 13.0 U/ml, and C-reactive protein was 0.1 mg/dl. Systemic examinations showed no other lesions. Histopathological examinations of biopsy specimens could not be performed because the lesion was surrounding the superior ophthalmic veins. Although his visual acuities were good in both eyes, the critical fusion frequency (CFF) was 28 Hz in the right and 28.3 Hz in the left, and lower visual field defects were detected in both eyes (Figure 3). Because compressive optic neuropathy due to IgG4-ROD

was suspected, we treated the patient with 30 mg prednisolone for 14 days for a possible IgG4-ROD (Figure 4). However, the CFF and exophthalmos were not improved. Then, we switched to steroid pulse therapy (1 g of methylprednisolone for 3 days), and all of the findings including the MRI images and visual field defects were improved (Figures 2, 4, and 5). Oral prednisolone was tapered from 30 mg to 8 mg for 5 months. The patient is being followed continuously to detect any recurrences.

Figure 3. Humphrey visual fields before steroid pulse therapy. Lower visual field defects are present in both eyes which were fitted with the place of the lesions.

Figure 4. Diagram of the time course of the case. After steroid pulse therapy, the degrees of proptosis and CFF were significantly improved in both eyes.

Figure 5. Humphrey visual fields after steroid pulse therapy. After steroid pulse therapy, visual field defects were improved in both eyes.

Discussion

This case might possibly be the first case of IgG4-ROD surrounding the superior ophthalmic veins associated with optic nerve disturbance.^{4,5} The major sites for the IgG4-ROD lesions are the lacrimal glands, extraocular muscles, and branches of the trigeminal nerve.^{1,3} Lesions that have funicular-like appearance along the superior ophthalmic veins are very rare. Our initial findings showed that conjunctival vascular dilation was clinically noticed. The perivascular lesions of the superior ophthalmic veins may induce venous stasis.

According to the Comprehensive Diagnostic Criteria for IgG4-RD,⁶ there are three criterions: (1) clinical examination shows characteristic diffuse/localize swelling or mass in single or multiple organs; (2) haematological examination shows elevated serum IgG4 concentrations (135 mg/dl); and (3) histopathological examination shows (a) marked lymphocyte and plasmacyte infiltration and fibrosis, and (b) infiltration of IgG4+ plasma cells: ratio of IgG4+/IgG+ cells >40% and 10 IgG4+ plasma cells/HPF. Diagnosis is classified as “definitive” when (1)–(3) are satisfied; “probable” when (1) and (2) are satisfied; and “possible” when (1) and (3) are satisfied. Because biopsies could not be performed due to potential of bleeding, the diagnosis was “possible” IgG4-ROD according to the recent criteria of IgG4-ROD.^{1,6}

The previous study indicates that the serum IgG4 concentrations had a sensitivity of 90% and specificity of 60%.⁷ There were no signs of infectious diseases such as tuberculosis and other signs of malignancy in the systemic examination. Because we could not perform biopsy, malignant lymphoma could not be denied completely. However, the good response to steroid pulse therapy suggested that the lesions were associated with IgG4-ROD.

The patient had hyperthyroidism, and thus thyroid-associated orbitopathy was also considered. The extraocular muscles were not enlarged but thyroid-associated orbitopathy may be accompanied because the upper eyelid swelling could not be improved completely after steroid pulse therapy. Evidence supporting an association of serum IgG4 and thyroid-associated orbitopathy is increasing. Thus, Bozkirli et al. reported that the

serum IgG4 level in patients with Graves' disease was significantly higher in patients with thyroid-associated orbitopathy than without thyroid-associated orbitopathy.⁸ Sy et al. reported that 8.3% of patients with thyroid-associated orbitopathy had high levels of serum IgG4.⁹ Bozkirli et al. reported that IgG4 may be responsible for increasing the production of the TSH receptor antibody in the orbital tissues, and that serum IgG4 levels may be an early indicator of the acute inflammatory stage of thyroid-associated orbitopathy.⁸ These findings indicate that IgG4-ROD can be masked by thyroid-associated orbitopathy.

In conclusion, we report our findings in a very rare case of IgG4-ROD with funicular-like appearance along the superior ophthalmic veins associated with optic nerve compression. Ophthalmologists should consider that IgG4-ROD surrounding the superior ophthalmic veins can cause optic nerve disturbance.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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