Visual Field Deficit: A Rare Initial Symptom of Autoimmune Pancreatitis

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Abstract

An autoimmune pancreatitis (AIP) patient with metachronous and multiple extrapancreatic lesions is reported. Initial symptoms were proptosis, oculomotor deficits, and a visual field deficit of the left eye, and swelling of bilateral lacrimal glands. Swelling of the right salivary gland and elevated serum levels of hepatobiliary enzymes were detected. AIP associated with IgG4-related orbital pseudotumor, IgG4-related sclerosing dacryoadenitis and sialadenitis, and IgG4-related sclerosing cholangitis was diagnosed. All symptoms and lesions improved with steroid therapy. Although an orbital pseudotumor is a rare extrapancreatic lesion of AIP, we should know that AIP patients may describe unusual symptoms such as abnormal visual field.

Key words: autoimmune pancreatitis, IgG4, orbital pseudotumor, sclerosing sialadenitis, sclerosing dacryoadenitis


Introduction

Autoimmune pancreatitis (AIP) is a peculiar type of pancreatitis of presumed autoimmune etiology. It is characterized clinically by a preponderance of elderly males, jaundice as a frequent initial symptom, and responsiveness to steroid therapy; serologically by elevation of serum IgG or IgG4 levels; radiologically by enlargement of the pancreas and irregular narrowing of the main pancreatic duct; and histopathologically by dense fibrosis with lymphoplasmacytic infiltration in the pancreas (1, 2). Other prominent features of this disease involve a variety of extrapancreatic complications (1-3).

We found dense fibrosis with abundant infiltration of T lymphocytes and IgG4-positive plasma cells and obliterate phlebitis in extrapancreatic lesions associated with AIP, such as sclerosing cholangitis, sclerosing cholecystitis, sclerosing sialadenitis, and retroperitoneal fibrosis. Furthermore, we also found dense infiltration of IgG4-positive plasma cells and T lymphocytes in various organs of AIP patients, such as the periportal area of the liver, gastric mucosa, colonic mucosa, dermis, lymph nodes, and bone marrow (1, 2, 4, 5). Therefore, we proposed the existence of a novel clinicopathological entity, “IgG4-related sclerosing disease” (1, 2, 4), which is a systemic disease characterized by extensive IgG4-positive plasma cell and T lymphocyte infiltration of various organs. In some cases, only 1 or 2 organs are clinically involved, while in others, 3 or 4 organs are affected (1, 2).

From this point of view, both AIP and the extrapancreatic lesions of AIP may occur randomly. We report an AIP patient who developed a visual field deficit of the left eye and swelling of bilateral salivary glands, which were metachronously associated with sclerosing sialadenitis and sclerosing cholangitis.

Case Report

A 76-year-old man noticed swelling in the left upper eyelid in October 2007 and visited another hospital. The patient was suspected to be having an allergic reaction at the initial...
visit, but the eyelid swelling gradually increased. In April 2009, the patient felt proptosis, oculomotor deficits, and a visual field deficit of the left eye, as well as swelling of bilateral lacrimal glands. The left orbital lesion was biopsied on suspicion of malignant tumor, but there was no malignancy, and he was followed without treatment. In June 2009, swelling of the right salivary glands and elevated serum levels of hepatobiliary enzymes were detected. He was referred to our hospital for further examination.

The physical findings on admission included proptosis and oculomotor deficits of the left eye and painless swelling of bilateral lacrimal glands and the right salivary gland. No superficial lymphadenopathy, hepatomegaly, or splenomegaly was noted. The visual acuity of the right eye was 1.2, left eye was 0.2. The ophthalmologic examinations showed a lower visual field deficit (Humphrey Field Analyzer, Carl Zeiss Meditec, Dublin, CA) (Fig. 1a) and an omnidirectional ocular motility disorder of the left eye.

Laboratory examinations showed elevation of serum hepatobiliary enzyme levels: alanine aminotransferase, 307 (normal range, 5-40) IU/L, aspartate aminotransferase, 319 (5-35) IU/L, alkaline phosphatase, 1191 (80-260) IU/L, γ-glutamyl transeptidase, 988 (5-70) IU/L, lactic dehydrogenase, 205 (115-245) IU/L, and leucine aminopeptidase 193 (<170) IU/L. Hepatitis B surface antigen and antibody to hepatic C virus were negative. Immunologically, the serum IgG level was 4,135 (<1,700) mg/dL and IgG4 level was 2,490 (<135) mg/dL; antinuclear antibody (ANA) was positive (×80). Anti-Ro antibody (SS-A), anti-La antibody (SS-B), anti-mitochondrial antibody, and anti-smooth muscle antibody were all negative.

Head magnetic resonance imaging (MRI) showed proptosis of the left eye due to an orbital tumor and swelling of bilateral lacrimal glands (Fig. 2a, b). There were no sites of involvement on head MRI. Re-examination of the biopsied piece of the orbital tumor in the previous hospital revealed abundant infiltration of IgG4-positive plasma cells and lymphocytes, and focally storiform-like fibrosis (Fig. 3a-d). There were no findings of obliterative phlebitis or MALT lymphoma.

Abdominal computed tomography (CT) and MRI revealed diffuse pancreatic enlargement and mild thickening of the gallbladder and bile duct wall (Fig. 4a). An endoscopic retrograde cholangiopancreatography indicated diffusely irregular narrowing of the main pancreatic duct and stenosis of the lower bile duct. The patient was diagnosed as having AIP according to the Japanese Clinical Diagnostic Criteria for Autoimmune Pancreatitis 2006 (6).

Percutaneous liver biopsy performed for liver dysfunction after admission to our hospital revealed dense infiltration of lymphocytes and IgG4-positive plasma cells and mild fibrosis in the periportal area of the liver (Fig. 5).

The patient was diagnosed as having AIP associated with IgG4-related sclerosing dacyrooadenitis, orbital pseudotumor, IgG4-related sialadenitis, and IgG4-related sclerosing cholangitis. He was begun on treatment for systemic IgG4-related disease with 30 mg prednisolone daily for 2 weeks. The dose was tapered by 2.5-5 mg every two weeks. Four weeks after starting steroid therapy, findings on abdominal CT/MRI (Fig. 4b) and blood tests improved. The visual acuity, lower visual field deficit, and omnidirectional ocular motility disorder of the left eye also improved significantly (Fig. 1b), along with improvement of proptosis and lacrimal gland swelling (Fig. 2c, d).

Discussion

AIP patients frequently have significantly elevated serum IgG4 levels and various extrapancreatic lesions. AIP and its extrapancreatic lesions show similar histopathological findings and good responsiveness to steroid therapy. Currently, they are recognized as organs clinically involved in IgG4-
Figure 2. Magnetic resonance imaging of orbit reveals swelling of bilateral lacrimal glands (short arrow) (a, axial T2-weighted imaging) and an orbital floor pseudotumor (long arrow) (b, coronal T1-weighted fat-suppressed imaging). (c, d) These lesions improved markedly after steroid therapy.

Figure 3. Histology of the biopsied orbital tumor showing lymphoplasmacytic infiltration and focally storiform-like fibrosis [(a) lower power view, Hematoxylin and Eosin staining; (b) high power view, Hematoxylin and Eosin staining; (c) Elastica Van Gienson staining]. (d) Immunohistochemically, abundant infiltration of IgG4-positive plasma cells was detected (IgG4-immunostaining).
related systemic sclerosing disease. In some cases, only 1 or 2 organs are clinically involved, while in others, 3 or 4 organs are affected (1, 2). Cases with significantly higher serum IgG4 levels, as in this patient, show higher AIP activity and frequently have associated extrapancreatic lesions (7). Extrapancreatic lesions with AIP sometimes appear metachronously. In our previous study, sclerosing sialadenitis, swelling of the lacrimal glands, lymphadenopathy, and retroperitoneal fibrosis were found to be the extrapancreatic lesions preceding AIP, while sclerosing cholangitis occurs synchronously (8). It is unclear why the onset period of each lesion differs in IgG4-related systemic sclerosing disease. AIP occurs most frequently with obstructive jaundice due to associated sclerosing cholangitis (1-3). Compared with AIP, swelling of the salivary or lacrimal glands can be easily noticed even without symptoms. AIP might exist subclinically when preceding salivary or lacrimal gland lesions are diagnosed.

In the present case, the visual acuity, lower visual field deficit, and omnidirectional ocular motility disorder of the left eye improved along with improvement of proptosis. There was no abnormality of the optic nerve and brain on head MRI. Therefore, these ophthalmic symptoms would have been caused by an orbital pseudotumor. Orbital pseudotumor is an idiopathic, benign, inflammatory condition that accounts for approximately 10% of all orbital mass lesions (9, 10). The etiology of orbital pseudotumor is unknown (11). The presentation may be acute or subacute and may occasionally exhibit chronic progression. Orbital pseudotumor may be unifocal or diffuse and may affect any part of the orbit (12). It is usually unilateral, but it may occasionally be bilateral. Chirapapaisan et al. reported that the presenting symptoms included proptosis (80%), oculomotor deficits (61%), pain (51%), lid swelling or a mass (45%), ptosis (25%), and chemosis (18%) in 49 patients with orbital pseudotumor (13). Some patients with orbital pseudotumor may have decreased visual acuity due to optic nerve compression (14). Orbital pseudotumor is sometimes difficult to differentiate from MALT-lymphoma, there was no finding of lymphoma in the biopsy specimen of this case. Multifocal fibrosclerosis is an uncommon fibroproliferative systemic disorder with multiple manifestations, including retroperitoneal fibrosis, sclerosing cholangitis, and salivary gland fibrosis. There are some reports that multifocal fibrosclerosis was complicated by fibrotic orbital pseudotumor (15-17). We have reported a close relationship between AIP and multifocal fibrosclerosis (5). Some orbital pseudotumors including the present case appear to be orbital lesions involved in IgG4-related systemic disease.

Lacrimal gland swelling is also a rare extrapancreatic lesion of AIP. Lacrimal gland swelling was detected in 3.6% of 56 cases in our study (8). Hamano et al (18) reported that lacrimal gland swelling was detected in 8 (12.5%) of 64 AIP patients, and 6 of them had salivary gland swelling. Recently, it was reported that serum IgG4 levels were elevated, and abundant infiltration of IgG4-positive plasma cells with fibrosis was detected in the lacrimal glands in patients with Mikulicz’s disease (19, 20), which is a unique condition that refers to bilateral, painless, symmetrical swelling of the lacrimal, parotid, and submandibular glands (21). Mikulicz’s disease is currently recognized as the lacrimal and salivary gland lesions of IgG4-related systemic disease (20).

IgG4-related sclerosing cholangitis is frequently associated with AIP, and the stenosis is usually located in the lower part of the common bile duct (1-3). In cases with stenosis of the lower bile duct, thickening of the bile duct
wall consists of fibrosis with infiltration of IgG4-positive plasma cells that sometimes spread extensively to the upper bile duct (1, 2). In the present patient, infiltration of mono-nuclear cells, including IgG4-positive plasma cells, and mild fibrosis were observed in the periportal area obtained by liver biopsy.

AIP sometimes develops with various symptoms due to associated extrapancreatic lesions. According to the classification (head and neck, thoracic, hepatic and pancreatobiliary, retroperitoneal, and systemic group) of IgG4-related disease by Zen and Nakanuma (22), the present case would be classified into systemic group with multiple lesions not restricted to 1 area. However, a visual field deficit due to orbital pseudotumor appears to be quite rare. An AIP patient who developed a visual field deficit of the left eye and swelling of bilateral salivary glands, which was metachronously associated with sclerosing sialadenitis and sclerosing cholangitis, was reported.

**The authors state that they have no Conflict of Interest (COI).**

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