Improvement of a Compressed Inferior Vena Cava due to IgG4-related Retroperitoneal Fibrosis with Steroid Therapy

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Abstract

A 79-year-old man had a 3.5-year history of edema of the lower extremities of unknown etiology. Abdominal computed tomography showed a soft tissue mass around the abdominal aorta, and the biopsy revealed dense fibrosis with abundant infiltration of IgG4-positive plasma cells. His serum IgG4 level was increased to 188 mg/dL. His lower extremity edema was induced by stenosis of the inferior vena cava (IVC) due to the mass. With a diagnosis of IgG4-related retroperitoneal fibrosis, he was treated with steroid, and the leg edema decreased with improvement of patency of the IVC and reduction of the soft tissue mass.

Key words: retroperitoneal fibrosis, IgG4, inferior vena cava, steroid


Introduction

IgG4-related disease is a new entity that has attracted much attention since our proposal in 2003 (1). It is a systemic disease histopathologically characterized by abundant infiltration of IgG4-positive plasma cells and lymphocytes, with fibrosis in various organs (1, 2). Idiopathic retroperitoneal fibrosis is a chronic inflammatory fibrosing condition of obscure origin usually involving the retroperitoneal spaces such as the abdominal aorta, kidneys, or ureters (3). Its common feature is hydronephrosis due to ureteral obstruction (3-5). Recently, it has become apparent that several patients with idiopathic retroperitoneal fibrosis are in fact occurring in the setting of IgG4-related disease (2, 6, 7). Here, we report the first case of IgG4-related retroperitoneal fibrosis causing marked stenosis of the inferior vena cava (IVC) resulting in edema of the lower extremities that improved after steroid therapy.

Case Report

A 79-year-old man noticed edema of the lower extremities in July 2007. He visited his doctor, but the cause of the edema of the lower extremities was unclear. He had a history of treated non-Hodgkin’s lymphoma (diffuse large B cell type, stage I) with CHOP therapy and radiotherapy to the neck in 2000. Abdominal computed tomography (CT), performed for follow-up of the edema of the lower extremities in February 2011, revealed a soft tissue mass around the abdominal aorta. On F-18 fluorodeoxyglucose (FDG)-positron emission tomography (PET) CT, accumulation of FDG was detected in the para-aortic area, whose maximum standardized uptake value (max SUV) was 5.4. Suspecting recurrence of lymphoma, a CT-guided needle biopsy of the para-aortic mass was performed. Histopathological examination revealed no neoplastic lesion, but dense fibrosis with abundant infiltration of IgG4-positive plasma cells and lymphocytes was present. IgG4-related retroperitoneal fibrosis was suspected, and he was referred to our hospital for fur-

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Received for publication January 22, 2012; Accepted for publication March 28, 2012
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The physical findings on admission included edema of both lower extremities, with greater edema of the right leg. No superficial lymphadenopathy, hepatomegaly, splenomegaly, or swelling of salivary glands was noted. There were no abnormal findings on laboratory examinations except for the elevation of serum IgG4 levels (188 mg/dL; normal range <135 mg/dL) and mildly decreased C4 (11 mg/dL; 17-45 mg/dL). The serum IgG level and IgE level was 1,590 mg/dL (870-1,700 mg/dL) and 132 IU/mL (0-250 IU/mL), and autoimmune antibodies such as antinuclear antibody and rheumatoid factor were negative. Blood coagulation parameters and D-dimer were within the normal ranges. Hydronephrosis was not detected on abdominal US, and leg vein ultrasonography and echocardiographic examination showed no thrombus. Although he could not undergo contrast-enhanced CT due to bronchial asthma, plain CT showed a soft tissue density area around bilateral renal hila and the abdominal aorta involving the IVC (Fig. 1a), with edematous change in the subcutaneous tissue and right leg dominance. Pelvic magnetic resonance imaging (MRI) showed a low-intensity area in the same regions as on CT. Venography of MRI showed marked stenosis of the IVC caudally from the renal vein (Fig. 2a). The retroperitoneal mass compressed the IVC, resulting in the development of collateral veins, such as the lumbar veins. Development of the left collateral veins was dominant. The pancreas was within normal size on CT and MRI, and the main pancreatic duct was normal on magnetic resonance cholangiopancreatography.

With a diagnosis of IgG4-related retroperitoneal fibrosis, the patient was begun on treatment with 30 mg prednisolone daily for 2 weeks. Two weeks after starting steroid therapy, his leg edema decreased, and he lost 6 kg of body weight. The dose was tapered by 2.5-5 mg every two weeks. Four weeks later, the soft tissue mass around the abdominal aorta decreased in size, and the patency of the IVC improved (Fig. 1b, 2b). The serum IgG4 level normalized to 52 mg/dL from 259 mg/dL.

**Discussion**

Autoimmune pancreatitis (AIP) is a peculiar form of pancreatitis with a presumed autoimmune etiology (1, 2, 8). In AIP patients, fibrosis and extensive infiltration of IgG4-positive plasma cells and T lymphocytes are detected in the
peripancreatic retroperitoneal tissue, bile duct wall, periportal area of the liver, gallbladder wall, and salivary glands, as well as in the pancreas. Various extrapancreatic lesions associated with AIP also show these peculiar histological findings. Serum IgG4 levels are significantly and frequently elevated in patients with AIP. Pancreatic and extrapancreatic lesions of AIP improve after steroid therapy. Therefore, we proposed a novel clinicopathological entity “IgG4-related sclerosing disease” (1). AIP and its extrapancreatic lesions are clinical manifestations reflecting this systemic disease (1, 2).

Idiopathic retroperitoneal fibrosis is a rare disease characterized by the presence of fibroinflammatory tissue around the abdominal aorta and the iliac arteries, which often entrap the ureters. The major clinical manifestations include abdominal or back pain and systemic symptoms such as fatigue or weight loss (3-5). Ureteral obstruction occurs in about 60-80% of cases and often causes acute renal failure (4, 5). In a study from the Mayo Clinic, lower extremity edema was reportedly detected in 13% of 183 cases of idiopathic retroperitoneal fibrosis, but there was no precise description regarding involvement of the IVC by idiopathic retroperitoneal fibrosis (9).

Retroperitoneal fibrosis is occasionally an extrapancreatic lesion of AIP, and some forms of retroperitoneal fibrosis belong to IgG4-related disease (2, 6, 7). In Stone’s review of 14 cases of IgG4-related retroperitoneal fibrosis, all patients were men, their mean age was 67 years, serum IgG4 levels were elevated in all 10 examined patients, AIP was present in 11 patients (while the mediastinum or salivary glands or lymph nodes were involved in the other 3 patients), and steroid therapy was effective in 11 of 11 treated patients (7). In the report of Zen et al., in their analysis of 10 cases of IgG4-related retroperitoneal fibrosis, the average age was 66.5 years, all were men, serum IgG4 levels were elevated in all 10 cases, and edema in the lower extremities was detected in 1 case clinically (6).

The present IgG4-related retroperitoneal fibrosis in a 79-year-old man with elevated serum IgG4 levels was histologically proven. He had a history of treated non-Hodgkin’s lymphoma with CHOP therapy and radiotherapy to the neck 11 years previously. Although lymphoma should be differentiated with IgG4-related lymphadenopathy (10), we considered the diagnosis of the lymphoma was correct as it was effectively treated with chemoradiotherapy. His chief complaint of edema of the lower extremities was induced by the compressed IVC involved in the retroperitoneal mass, although the shape of the retroperitoneal mass at onset of edema was unknown. After steroid therapy, the edema improved dramatically, with resolution of the compressed IVC and a decreased in the mass. This is the first case of improvement of a compressed IVC involved in IgG4-related retroperitoneal fibrosis with steroid therapy. The cause of his edema had been unclear for 3.5 years. Since IgG4-related disease responds well to steroid therapy, IgG4-related retroperitoneal fibrosis should be kept in mind in the differential diagnosis of edema of the lower extremities of unknown etiology.

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

Acknowledgement
This work was supported in part by the Research Committee of Intractable Pancreatic Diseases (Principal investigator: Tooru Shimosegawa) and the Research Committee of Intractable Diseases, provided by the Ministry of Health, Labour, and Welfare of Japan.

References