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Case Report

A case of IgG4-related retroperitoneal fibrosis with multiple involvement

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Abstract: To increase awareness of IgG4-related retroperitoneal fibrosis (IgG4-RRPF) and reduce clinical misdiagnosis. We report a 79-year-old man with multiple organs involvement of IgG4-RRPF, who developed right lower extremity edema, hemoptysis and fever. The abdomen computed tomography (CT) scan image showed lymph nodes enlargement. The positron emission tomography/CT scan image showed pancreatic malignancy with multiple nodal lymph node metastasis, lung fibroblast proliferation, and right lung apex bullae. The chest CT scan image showed pulmonary multiple lymph nodes with calcification in the mediastinum. Posterior peritoneum magnetic resonance imaging showed the body and tail of the pancreas parenchymatous mass. The serum IgG4 concentration was high. The fibrous connective tissue with IgG4-positive plasma cells infiltration in the left supraclavicular lymph node biopsy was found. Fiberoptic bronchoscopy showed diffuse alveolar hemorrhage, and the transbronchial lung biopsy found no cancer cells. The patient was treated with glucocorticoids and immunosuppressive agents. After 2 months treatment, the patient showed rapid improvement. This is a case of IgG4-RRPF with multiple organs involvement. Glucocorticoid is the first-line treatment.

Key words: Multiple organs involvement; IgG4-related retroperitoneal fibrosis.

Introduction

Retroperitoneal fibrosis (RPF) was first reported in France in 1905 Albrran (1). In 1948 Ormond proposed RPF as an independent disease, RPF is also known as Ormond disease. RPF includes idiopathic RPF and secondary RPF, the former is about 70%, the latter about 30%, which often is secondary to cancer, inflammation, trauma, radiation therapy and certain drug applications. Recent studies have fou Idiopathic RPF nd that Idiopathic RPF biopsy has a large number of IgG4 + plasma cells. Therefore, idiopathic RPF is thought to be an IgG4-related disease (IgG4-RD). Because of the development of IgG4-RD, idiopathic retroperitoneal fibrosis has been re-recognized and evaluated, and a group of RPF subtypes with better homogeneity in pathological and therapeutic has been proposed, which is IgG4-related retroperitoneal fibrosis (IgG4-RRPF).

Case report

A 79-year-old man was admitted with a 2-day history of right lower extremity edema. The patient had no history of smoking, habitual drinking, allergy, bronchial asthma, or atopic disorder. On physical examination, his body temperature was 36.9 ℃, blood pressure was 160/87 mmHg, and pulse was 71 bpm. Laboratory findings revealed the following: leukocytes, 5.1×109/L; percentage of neutrophils, 69.4%; percentage of lymphocytes, 20.4%; hemoglobin, 119 g/L; platelet, 196×109/L; C-reactive protein, <1mg/L (normal <0.10 mg/L); C3, 0.608 g/L (normal 63–134 mg/dl); C4, 0.178 g/L (normal 13–36 mg/dl); IgA, 2.16 g/L (normal\300 IU/ml); IgG, 26.1 g/L (normal 870–1,700 mg/dl); IgM, 0.676 g/L. The serum concentration of the IgG4 was 22 g/L. Serum protein electrophoresis: serum γ-globulin, more than 32%. Test results for urine routine, biochemistry, coagulation function, tumor markers, and antinuclear antibody were all negative.

A chest X-ray showed bilateral infiltration. The abdomen ultrasound showed left upper quadrant parenchymatous mass in posterior peritoneum. The abdomen computed tomography (CT) scan image showed liver multiple cysts, left renal cyst, right hydronephrosis and ureteral dilatation, lymph nodes enlargement in left obturator nodule (Fig.1). The right lower extremity vein CT showed that the middle of the right common iliac vein was narrow. Posterior peritoneum magnetic resonance imaging showed the body and tail of the pancreas parenchymatous mass (Fig.2). The positron emission tomography/CT scan image mainly showed pancreatic malignancy with multiple nodal lymph node metastasis, lung fibroblast proliferation, and right lung apex bullae (Fig.3). Gastroscopy showed that the external body of the stomach was compressed. The histopathological findings of left supraclavicular lymph node biopsy were fibrous connective tissue with IgG4-positive plasma

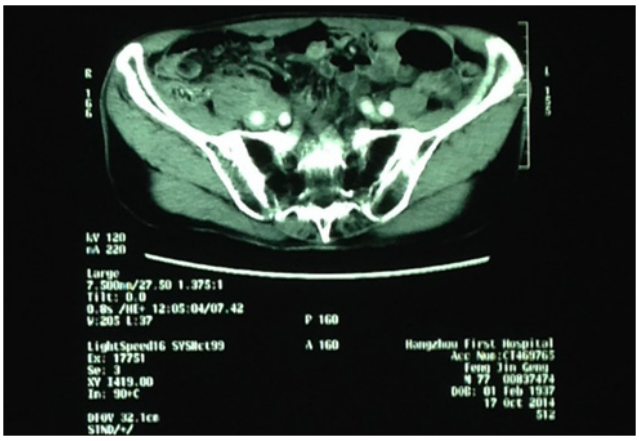

Figure 1. Abdomen computed tomography (CT) scan image.

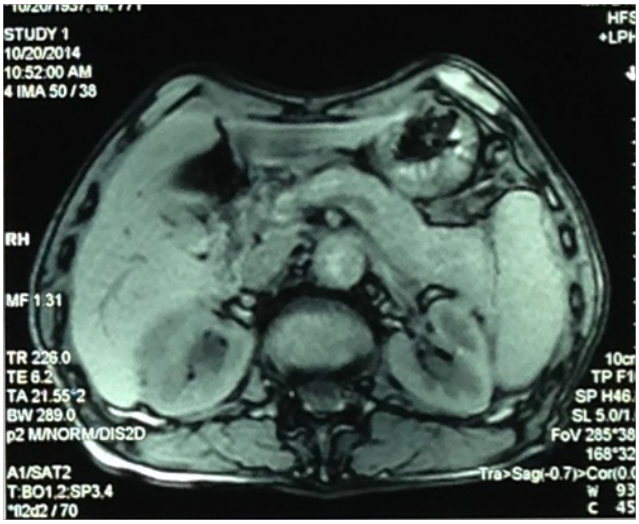

Figure 2. Posterior peritoneum magnetic resonance imaging.

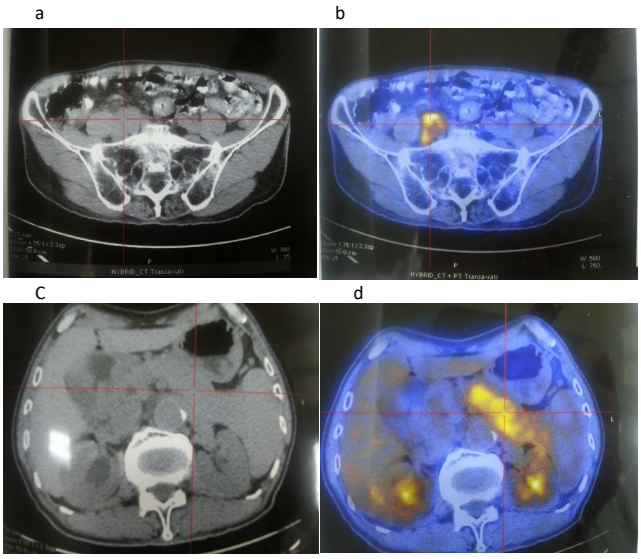

Figure 3. (a-d): Positron emission tomography/CT scan image.

cells infiltration (Fig.4). Immunohistochemical staining showed IgG +, IgG4+, CD3+, CD5+, CD20+, CD79+, CD68+, CD138+, CD21+, K+, Bc12+, Ki67+. (Fig.5) We made a diagnosis of IgG4-RRPF according to retroperitoneal involvement and the serum IgG4 level. The patient was treated with 16 mg prednisolone daily, 7.5mg methotrexate weekly, and 10 mg tripterygium wilfordii polyglycoside tables three times daily. At 2 months after treatment initiation, there was a marked improvement in pancreas mass, and the serum concentration of IgG4 had decreased from 22 to 12.4g/L.

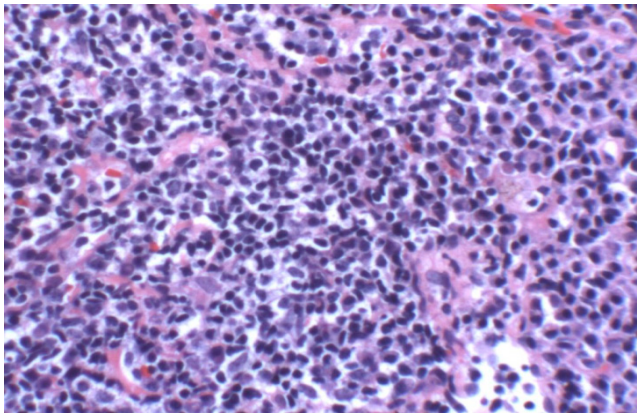

Figure 4. Histopathological finding of the left supraclavicular lymph node biopsy.

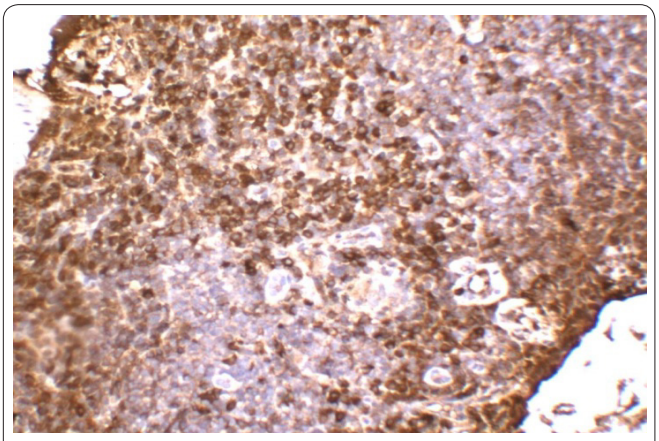

Figure 5. Immunohistochemical staining of the left supraclavicular lymph node biopsy.

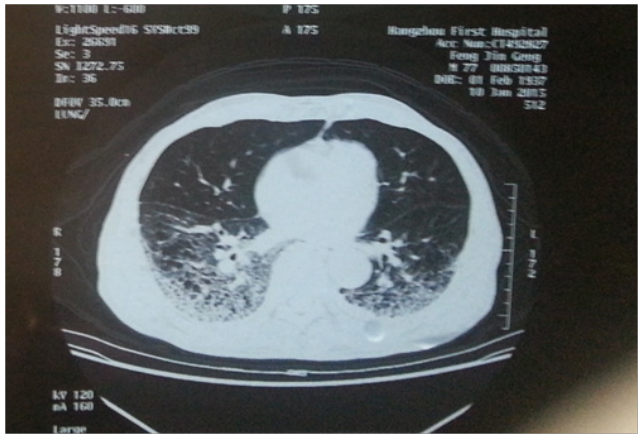

Figure 2. Chest CT scan image.

The patient was admitted to the department of respiratory with hemoptysis and fever after a week. Main laboratory findings were as following: C-reactive protein, 67mg/L. Test results for blood routine, biochemistry, coagulation function, procalcitonin and other makers were all negative. The chest CT scan image showed pulmonary infection, emphysema, and multiple lymph nodes with calcification in the mediastinum (Fig.6). Fiberoptic bronchoscopy showed diffuse alveolar hemorrhage, and the transbronchial lung biopsy found no cancer cells. The patient was treated with methylprednisolone at an initial dose of 40 mg daily besides antibiotic therapy. At 3 weeks after treatment, his respiratory symptoms and chest CT image had improved, and C-reactive protein was normal. The serum concentration

of IgG4 was 3.77g/L.

Discussion

RPF is one of the unexplained rare collagen vascular disease(2). RPF mainly confined to the retroperitoneum early, which is often manifested as symptoms of ureteral obstruction and intestinal obstruction, lower extremity edema and other symptoms. At present, the diagnosis of RPF relies mainly on CT or MRI image, which shows the soft tissue mass around retroperitoneal or abdominal organs, that includes abdominal aorta, ureter, and pancreas. In terms of treatment, Surgery relieve obstruction, or hormones control the condition. Recently, more reports suggested that RPF was a high IgG4-associated disease.

Kamisawa et al. first proposed the concept of IgG4-RD in 2003 (3). Recent investigation showed that the incidence of this disease throughout Japan would be 0.28–1.08/100,000 population, with 336–1,300 patients newly diagnosed per year. Most patients are male and the median age of onset of IgG4RD is 58 year(4). The recent consensus statement provided some definitions of histopathological features: dense lymphoplasmacytic infiltrate, storiform-type fibrosis and obliterative phlebitis(5). In addition, eosinophil infiltration and phlebitis with unobstructed lumens are also helpful in the diagnosis of IgG4-related disease. In that, they were considered to be secondary pathologic features. The diagnosis of IgG4-related diseases relies mainly on the above pathological features, while the IgG4 plasma cell count and IgG4 + / IgG + plasma cell ratio in the tissue were secondary but essential.

IgG4-RD is a newly recognized inflammatory and fibrotic disease that may be involved in multiple organs and systems. It is usually characterized by a single or multiple organ enlargement, with or without serum elevated serum IgG4. IgG4-RD includes autoimmune pancreatitis, sclerosing cholangitis, retroperitoneal fibrosis, mikulich disease, IgG4-related nephropathy, IgG4-associated lung disease and other diseases(6).

Increased serum IgG4 is more common in patients with multiple organ involvement of IgG4-RD(7). However, patients with Connective tissue disease, pemphigus, bronchial asthma, systemic sclerosis, chronic hepatitis, allergic dermatitis and other diseases may also have high lever in serum IgG4(8). Therefore, blood IgG4 is not the evaluation of disease activity, severe Degree or a reliable indicator of response to treatment. Histopathology and immunohistochemical staining of IgG4-RD are the most valuable diagnostic criteria. In our case, the patient could be diagnosed with IgG4-RD according to comprehensive clinical diagnostic criteria in 2011(9).

IgG4-RRPF is common in elder males. There was no radiological correlation between IgG4-related RPF and non-IgG4-RRPF. IgG4-RRPF is characterized by storiform-type fibrosis, but non-IgG4-RRPF is a nonspecific fibrosis transparent layer with occlusive phlebitis. Eosinophilia, lymphoplasmosis, IgG4-positive plasma cells and IgG4-RD characteristic organ involvement contribute to the identification of both. In the late stages of organ involvement, as the lesions (like retroperitoneal tissue) are fibrosis and plasma cells decrease, the diagnosis of IgG4-RD become difficult.

IgG4-ralated lung disease mainly includes IgG4-related interstitial lung disease, pulmonary inflammatory pseudotumor and lymphomatoid granulomatosis(10-11). IgG4-related lung disease manifested as four major categories of CT features: solid nodular type, round-shaped ground-glass opacity, alveolar interstitial type, and bronchovascular type(12). Pancreatic lesions of IgG4-RD are also known as autoimmune pancreatitis, which is characterized by diffuse enlargement of the pancreas, pancreatic duct extensive stenosis. Attention should be paid to that the Clinical manifestations and imaging performances of AIP are similar to pancreatic cancer. The diagnosis of AIP including IgG4 + plasma cells infiltration, fibrosis, and high serum IgG4 level in pancreatic.At present, there is no uniform treatment in patients with IgG4-RD, but these patients are generally sensitive to glucocorticoid response, glucocorticoid is recognized as IgG4-RD first-line treatment. Therefore, glucocorticoid is first-line treatment of IgG4-RD, and efficacy depends on the ease of organ involvement according to the rating scale(13). Some studies reported that most patients respond well to glucocorticoid, but recurrence is common(14-16). Hormones can also be combined with methotrexate, azathioprine, and tamoxifen, which can effectively reduce the dependence on glucocorticoid and recurrence, but the complications of hormone should be prevented(14). Negative test results in Hepatitis B, hepatitis C antibody are also indispensable before combination between hormone and cytotoxic drugs. In addition, biological agents such as anti-CD20 monoclonal antibody, anti-TNF-α and other treatment can be used for recurrent refractory RPF. According to our case, hormone use ought to be individualized treatment, but hormone dosage is relatively large when multiple systems are involved.

IgG4-RD and IgG4-RRPF are new concepts in China. Because of the low incidence of RPF and the lack of large sample test, the pathogenesis, clinical features and differences of non-IgG4-related retroperitoneal fibrosis are still unclear. In summary, for multi-system involvement diseases or abdominal and (or) retroperitoneal soft tissue mass and pancreatic mass, parotid gland enlargement in CT/MRI, serum IgG4 levels should be noted.

Disclosure of conflict of interest

The authors have declared that no competing interests exist.

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