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Case Report

A Case of Inflammatory Lung Disease and Retroperitoneal Fibrosis Attributed to Systemic IgG4-related Disease

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SUMMARY

Recently, immunoglobulin (Ig) G4-related diseases such as autoimmune pancreatitis (AIP), sclerosing sialadenitis, retroperitoneal fibrosis, and sclerosing cholangitis have been reported. IgG4-related diseases are characterized by high serum IgG4 concentrations, sclerosing inflammation with numerous IgG4-positive plasma cells, and steroid sensitivity, irrespective of their organ of origin. We describe a case of inflammatory lung disease and retroperitoneal fibrosis, suggested to involve IgG4. The patient was a 76-year-old man. A computed tomographic scan of the chest showed nodular air-space consolidation in the left upper lobe. The serum IgG4 concentration was abnormally elevated, but there was no evidence of AIP. Bilateral hydronephrosis associated with thickened soft tissue around the abdominal aorta had been diagnosed previously. He had undergone surgery, and retroperitoneal fibrosis was diagnosed histologically (hematoxylin and eosin stain). Histological examination of bronchoscopic specimens taken from the left S3 region showed mononuclear-cell infiltration of the fibrotic bronchial wall, including many IgG4-positive plasma cells. Specimens of the region affected by retroperitoneal fibrosis were retrospectively reanalyzed, and the cells were positive for IgG4 on immunostaining, similar to the lung tissue. The patient responded to treatment with corticosteroids. In conclusion, the present case shared many clinical and clinicopathological similarities with systemic IgG4-related autoimmune disease. To our knowledge, however, this is the first reported case of inflammatory lung disease with retroperitoneal fibrosis in a patient with systemic IgG4-related autoimmune disease.

Key Words : inflammatory lung disease, retroperitoneal fibrosis, IgG4-related disease, chest computed tomography, histopathological examination

Abbreviations Used

AIP : autoimmune pancreatitis, WBC : white blood cells, ANA : anti-nuclear antibody, SS : Sjögren's syndrome, KL-6 : Krebs von den lungen, CRP : C-reactive protein, CH50 : 50 % hemolytic unit of complement, C : complement, CT : computed tomography, H&E : hematoxylin and eosin

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A 76-year-old man presented with a 2-month history of dry cough on exertion in May, 2007. Chest radiography and computed tomography (CT) revealed nodular air-space consolidation in the left upper lobe (Figure 1, panels A and B). The patient had a past

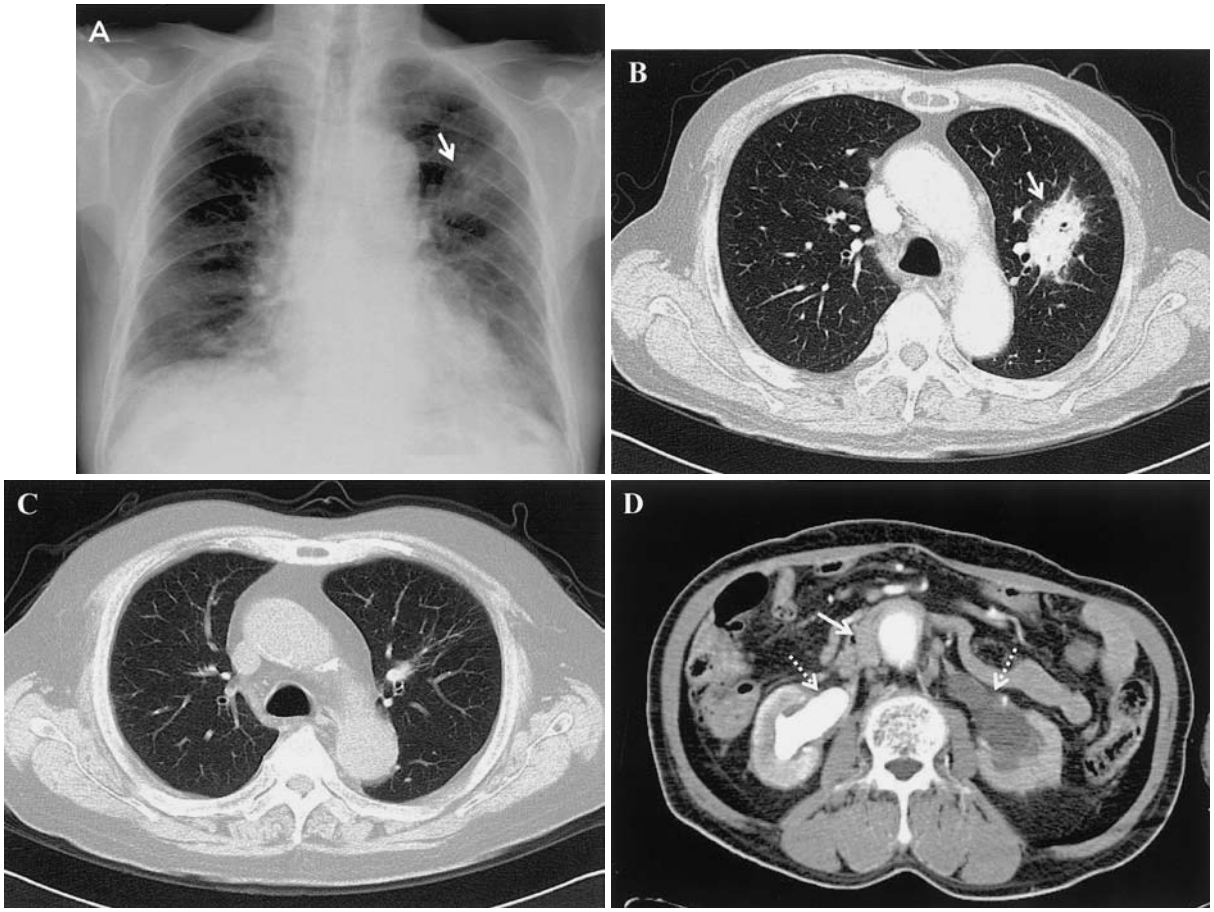

Figure 1

Chest x-ray films and CT scans obtained before and after treatment with corticosteroids. The chest x-ray film in Figure 1A and CT scan in Figure 1B were taken in May 2007. The chest CT scan in Figure 1C was taken in February 2008. The arrows indicate consolidation in the left upper lobe. Previously, in May 2004, thickening of soft tissue around the wall of the abdominal aorta (solid-line arrow) and bilateral hydronephrosis (dotted-line arrows) were seen on enhanced CT scans of the abdomen (Figure 1D).

history of bilateral hydronephrosis associated with retroperitoneal fibrosis and had undergone surgery in May, 2004. The results of physical examinations were normal. The oxygen saturation was 96 % while breathing room air. Laboratory test values were as follows : white blood cells (WBC) 15200/μl ; eosinophils 6.0 % ; serum C-reactive protein (CRP) 1.0 mg/dl (normal range, ≦0.3 mg/dl) ; amylase 130 IU/l ; IgG 3902 mg/dl (870-1700 mg/dl) ; IgG4 321 mg/dl (4.8-105 mg/dl) ; IgE 822 IU/ml (< 295 IU/ml) ; anti-nuclear antibody (ANA) positive (x80, speckled and homogeneous) ; both anti-Sjögren's syndrome (SS) A (anti-SSA/Ro) and anti-SSB/Ro negative (≦20 index and ≦25 index, respectively) ; complement (C) 3 91 mg/dl (44-102 mg/dl) ; C4 16 mg/dl (14-49 mg/dl) ; 50 % hemolytic unit of complement (CH50) 39 U/ml (33-48 U/ml) ; and Krebs von den lungen (KL)-6 3170 ng/ml (< 500 U/ml).

Bronchoscopy with bronchoalveolar lavage, performed through the left S3 bronchus, revealed macrophages (83 %), neutrophils (6 %), and lymphocytes (11 %). Histological examination of biopsy specimens obtained from the left S3 region, stained with hematoxylin and eosin (H&E), showed signs of severe inflammation and lymphoplasmacytic infiltration of the fibrotic bronchial wall (Figure 2, panels A). Infiltration by many IgG4-positive plasma cells was seen on immunostaining (Figure 2. panels B). IgG4 was apparently involved in the development of the lung lesions. Because of increasing consolidation in the left upper region on imaging studies, the patient was treated with oral prednisolone (0.4 mg/kg/day) in October,

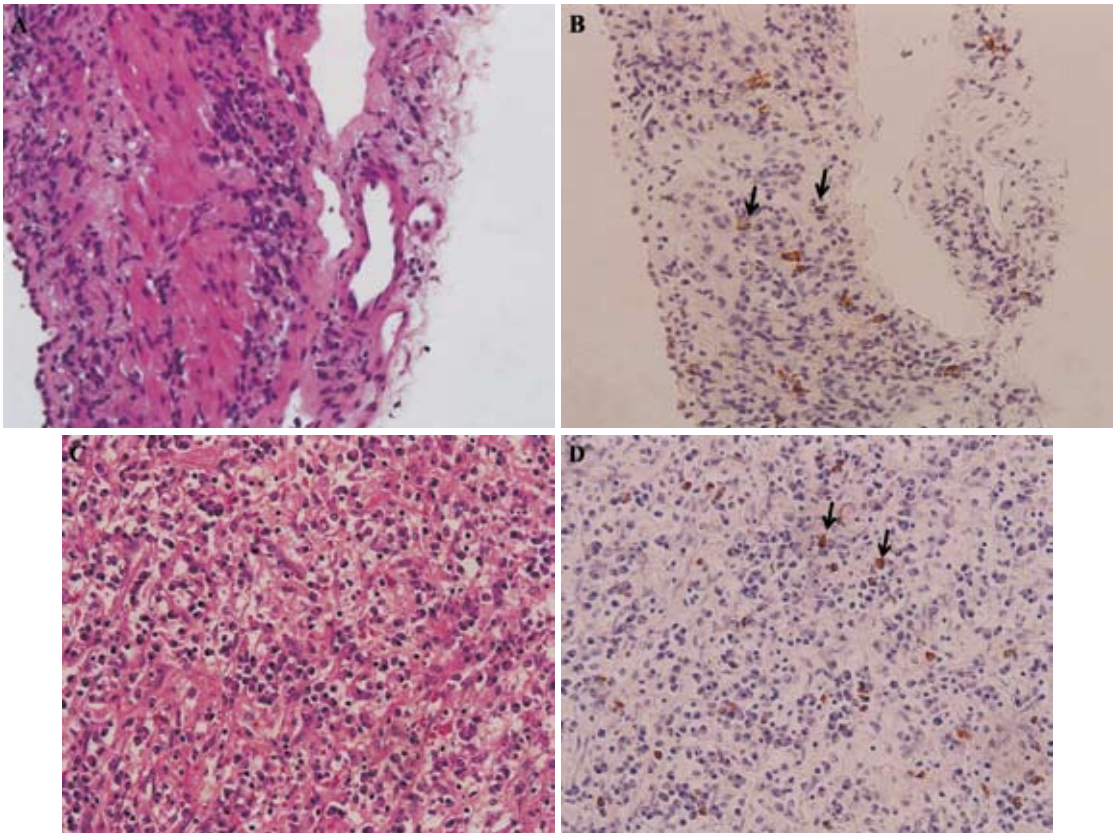

Figure 2

Histological photographs of specimens of the lung and the peritoneal fibrotic tissue around the abdominal aorta. Figure 2A shows H&E-stained biopsy specimens obtained from the left S3 region of the lung. Severe inflammation and lymphoplasmacytic infiltration of the fibrotic bronchial wall are evident (Figure 2A). Lymphoplasmacytic infiltration associated with fibrotic changes was also found in peritoneal fibrotic tissue around the abdominal aorta (Figure 2C). Immunostaining of the lung tissue and the peritoneal fibrotic tissue around the abdominal aorta showed infiltration by many IgG4-positive plasma cells (Figure 2B and Figure 2D, respectively). The arrows indicate IgG4-postive plasma cells. The original magnification is x200.

2007. The dose of prednisolone was gradually tapered, with no evidence of recurrence. In December, 2007, the laboratory data had improved. Notable laboratory values were as follows : CRP 0.38 mg/dl ; IgG 1072 mg/dl ; IgG4 73 mg/dl. In February, 2008, chest CT findings (Figure 1, panels C) dramatically improved, and the serum KL-6 value decreased to 1650 mg/dl. Previously in May, 2004, bilateral hydronephrosis had been caused by thickening of soft tissue around the wall of abdominal aorta as confirmed by abdominal enhanced CT (Figure 1, panels D). On retrospective reanalysis, the soft tissue stained positively for IgG4 on immunostaining, similar to the lung tissue (Figure 2, panels C and D, respectively).

DISCUSSION

Recently, IgG4-related diseases such as autoimmune pancreatitis (AIP), sclerosing sialadenitis, retroperitoneal fibrosis, and sclerosing cholangitis have been reported[1~3]. Some cases have been associated with pulmonary lesions[4]. Clinically and pathologically, IgG4-related diseases typically present with a high serum IgG4 concentration and infiltration of tissue by many IgG4-positive plasma cells[1~4].

The clinical features of IgG4-related pulmonary diseases include mass lesions, a pattern of interstitial pneumonia, and consolidation with air bronchograms on imaging studies. Other common features are inflammatory pseudotumors (plasma cell granulomas) and interstitial pneumonia associated with fibrotic changes

and infiltration by plasma cells, lymphocytes, and macrophages on histological examination[4~7]. Our case showed nodular air-space consolidation on chest CT. Severe inflammation and lymphoplasmacytic infiltration of the fibrotic bronchial wall were evident on tissue specimens stained with H&E. Immunostaining showed infiltration by many IgG4-positive plasma cells. The features of this case were consistent with those of previously reported cases of IgG4-related pulmonary diseases[4~7].

Retroperitoneal fibrosis is characterized by a thick retroperitoneal fibrotic mass that covers the abdominal aorta and compresses the ureters[8]. The development of fibrosis can obstruct the ureters and cause renal failure, or signs and symptoms may be related to the enhancement or entrapment of other structures by the inflammatory mass, causing conditions such as hydronephrosis. Retroperitoneal fibrosis with mononuclear-cell infiltration was also seen in our patient. When we retrospectively studied whether tissue specimens of the retroperitoneal fibrosis were positive for IgG4 on immunostaining, the results were similar to those for the lung tissue. Hirano et al reported pulmonary involvement in 4 of 30 patients with AIP during follow-up[9]. Furthermore, AIP with interstitial pneumonia was documented by Taniguchi et al in 2004[10]. These findings suggest that IgG4-related disorders can occur in both the lung and other organs. The inflammatory lung disease and retroperitoneal fibrosis in our patient were both apparently related to systemic IgG4-related autoimmune disease. As for the treatment of IgG4-related disease, corticosteroid therapy has been found to be effective[6]. Our case responded to corticosteroid therapy, and the pulmonary lesions disappeared, with no subsequent signs or symptoms of recurrence.

In conclusion, the present case had many clinical and clinicopathological similarities to systemic IgG4-related autoimmune disease. To our knowledge, however, this is the first reported case of inflammatory lung disease with retroperitoneal fibrosis in a patient with systemic IgG4-related autoimmune disease.

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