

*Case Report*

## **Retroperitoneal fibrosis, sclerosing pancreatitis and bronchiolitis obliterans with organizing pneumonia**

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### **Introduction**

Multifocal idiopathic fibrosclerosis is an uncommon systemic illness characterized by exuberant fibrosis involving diverse organs. Association between retroperitoneal fibrosis and pancreatic fibrosis is rare, but has been described previously. Here, we report a case of multifocal idiopathic fibrosclerosis with retroperitoneal fibrosis, pancreatic fibrosis and bronchiolitis obliterans with organizing pneumonia (BOOP). This association has not been reported before.

### **Case**

A 38-year-old, non-smoking black man was admitted in May 2000 with weight loss of 6 kg in 3 months, anorexia, nocturnal sweats, dry cough, flank pain and oliguria. He had sickle-cell trait (Hb S: 36.4%). He denied alcohol abuse and had not taken any medications recently.

His clinical examination was unremarkable.

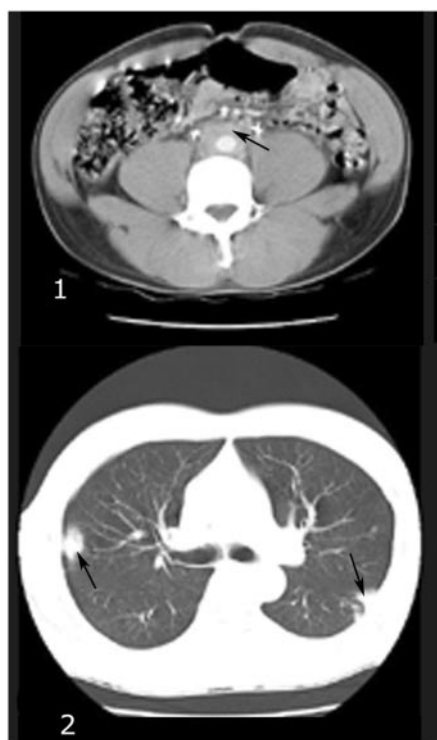
The main blood tests revealed the following: serum creatinine 647 µmol/l; an inflammatory syndrome (erythrocyte sedimentation rate 100 mm/h, fibrinogen 6.5 g/l, C-reactive protein 120 mg/l) associated with an aregenerative (reticulocytes 22180/mm<sup>3</sup>) normocytic anaemia (haemoglobin 8.5 g/dl); white blood cell count 6200/mm<sup>3</sup> with a normal differential; platelet count 257 000/mm<sup>3</sup>; glucose 5 mmol/l; alkaline phosphatase 183 IU/l (normal range 50–150); γ-glutamyl-transpeptidase 330 IU/l (normal range 25–70); lipase

378 IU/l (normal <250); amylase 142 IU/l (normal <82); and normal total bilirubin, aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Serological tests for hepatitis, rheumatoid factor, antimitochondrial, smooth muscle or antineutrophilic cytoplasmic antibodies were negative. Anti-DNA antibodies were positive with a titre of 1:160. Complement levels were normal. Serum protein electrophoresis revealed an increase in IgG at 18 g/l (normal range 7.5–15.6) with IgG4 at 1.1 g/l (normal range 0.039–0.865) without the discrete bands compatible with chronic inflammation. Urinalysis, and its cytology, acid-fast smear and culture were unremarkable. A skin test was negative.

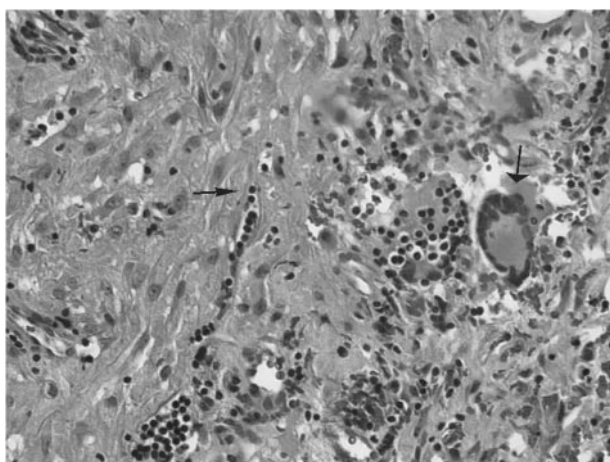
Renal ultrasonography and retrograde pyelography showed bilateral hydro-uretero-nephrosis, a medial deviation of the ureters and no masses or calculi. Bilateral ureteral stents were inserted, and serum creatinine returned to 92 µmol/l in 3 weeks. An abdominal contrast-enhanced computed tomography (CT) demonstrated extensive soft tissue infiltration concentrically around the aorta, inferior vena cava and both ureters, a diffuse swollen and irregular pancreas without dilatation of the Wirsung and common bile ducts, and no calcifications on plain CT films (Figure 1). No adenopathy or tumour was noted. Magnetic resonance cholangiography was normal. A laparotomy was performed. Intra-operative findings revealed normal-appearing ureters in a dense fibrotic retroperitoneal mass. Biopsies of the retroperitoneal mass and pancreas showed dense connective tissue infiltrated with macrophages, lymphocytes, plasma cells, myofibroblasts and no histiocytes—consistent with the diagnosis of retroperitoneal fibrosis and sclerosing pancreatitis (Figure 2). The result of an intra-operative liver biopsy was normal.

A chest X-ray showed peripheral reticulo-nodular opacities in the right lung. CT scan showed nodules in both lungs (Figure 1). Bronchoscopy was normal, but 37% of the cells in the bronchoalveolar lavage fluid were lymphocytes. An open lung biopsy was performed, which showed multiple fibroblast plugs filling

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**Figs. 1 and 2.** Retroperitoneal fibrosis around the aorta, inferior vena cava and ureters. (1) Bronchiolitis obliterans with organizing pneumonia. (2)



**Fig. 3.** Histology of the retroperitoneal fibrosis with macrophages and lymphocytes.

airspace, typical pathological features of BOOP. Sputum and blood cultures were negative. Human immunodeficiency virus, cytomegalovirus, adenovirus and mycoplasma serologies were negative.

Prednisone was started in July 2000, at 1 mg/kg per day for 2 months, and then the dose was slowly tapered. The patient's respiratory symptoms disappeared rapidly, in 2 weeks. Liver and pancreatic functions normalized, and the inflammatory syndrome disappeared in 4 weeks. Anaemia and antinuclear antibodies disappeared in 2 months. After 4 months,

the pulmonary nodules disappeared, and the pancreatic pseudotumour and retroperitoneal mass had regressed. The double J catheters were removed. Corticotherapy was stopped after 18 months with complete remission of the retroperitoneal mass, pancreatic pseudotumour and pulmonary nodules. The patient has done well for the past 2 years.

## Discussion

Retroperitoneal fibrosis is an uncommon entity characterized by chronic inflammation of connective tissue. In two-thirds of patients with retroperitoneal fibrosis, no aetiological factor can be identified. Although its pathogenesis is still unknown, most authors postulate an immunological process. This is suggested by its association with various inflammatory diseases; elevated inflammatory indices, sometimes autoantibodies and immune complexes; tissue infiltrated by inflammatory cells (including macrophages, T and B lymphocytes, plasma cells); and response to immunosuppressive therapy. Retroperitoneal fibrosis may be associated with other sclerosing diseases such as fibrous pseudotumour of the orbit, Riedel's thyroiditis, mediastinal fibrosis, constrictive pericarditis and primary biliary cirrhosis.

A few reports have mentioned the involvement of the pancreas. Twelve cases of retroperitoneal fibrosis associated with sclerosing pancreatitis (three-quarters with pseudotumour) have been reported [1,2]. High concentrations of serum IgG and IgG4 and similar histological lesions (infiltration of IgG4-bearing plasma cells) suggest that IgG4 may have a pathological role in the systemic fibrosing process [3,4]. In our patient, we observed a high concentration of IgG with elevation of IgG4. The elevated alkaline phosphatase may suggest an association with sclerosing cholangitis [2], but radiological, biological and histological data are not consistent with this hypothesis. We can hypothesize a slight intrapancreatic common bile duct stricture, reversed with corticosteroid therapy.

BOOP is a pulmonary lesion characterized histologically by varying degrees of obliteration of the lumina of the respiratory bronchioles by organizing connective tissue, often extending into the alveoli. BOOP is associated with various clinical conditions including infection and connective tissue disease, use of certain drugs and incidentally detected lesions associated with neoplasms [5,6]. However, there are only two cases of BOOP associated with a sclerosing disease, in this instance primary biliary cirrhosis [6].

The concurrent occurrence of retroperitoneal fibrosis, sclerosing pancreatitis and BOOP in one patient, as in ours, has not been reported previously. Our finding lends support to the concept of a broad-spectrum systemic or multifocal fibrosclerosing disease [7]. Its histopathological features include a generalized fibrocollagenous stroma, with various degrees of fibroblastic activity, and a mixed-cell type of inflammatory

infiltrate consisting predominantly of lymphocytes. These disparate entities might represent local manifestations of the same systemic disease affecting connective tissue, possibly mediated by an autoimmune process, and called systemic idiopathic fibrosis. A likely autoimmune aetiology justifies immunosuppressive therapy. Corticosteroids are classic first-line therapy, which is often successful in the early, active inflammatory stages of retroperitoneal fibrosis and BOOP. The possibility of recurrence requires regular surveillance.

*Conflict of interest statement.* None declared.

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