Multifocal Fibrosclerosis Combined with Idiopathic Retroperitoneal and Pericardial Fibrosis

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Abstract

A 70-year-old man who had been diagnosed with retroperitoneal fibrosis (RPF) was admitted to our hospital complaining of dyspnea. Imaging studies showed massive pericardial effusion. His condition deteriorated and pericardiostomy was performed. A biopsy of the pericardium revealed marked fibrosis with infiltration of lymphocytes, which was identical to RPF findings. A diagnosis of multifocal fibrosclerosis was made. Despite aggressive treatment, he died with clinical signs of cardiovascular failure. The autopsy specimen revealed proliferation of fibrosis with infiltration of lymphocytes in multiple organs. Even after successful decompression of urinary obstruction for RPF, long-term follow-up is necessary in these patients because of the possibility of other fatal complications such as pericardial fibrosis.

Key words: retroperitoneal fibrosis, multifocal fibrosclerosis, pericarditis

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Introduction

Retroperitoneal fibrosis (RPF) was defined as a disease of unknown etiology by Ormond in 1948 (1). It is characterized by proliferation of periaortic fibrous tissue with subsequent ureteral compression, leading to hydronephrosis. Multifocal fibrosclerosis (MFS) is a term used to describe a combination of similar fibrous proliferation occurring at different anatomical sites, including mediastinal fibrosis (2), sclerosing cholangitis (3), Riedel’s thyroiditis (4), and pseudotumor of the orbit (5). However, involvement of the pericardium is quite rare and most cases are diagnosed at autopsy. Here, we report a case in which MFS was diagnosed by a biopsy of the pericardium during follow-up for RPF.

Case Report

A 70-year-old man was admitted to our hospital on June 11, 2003, complaining of dyspnea and anasarca. In 1978, he underwent right nephrectomy due to a renal stone. He had been in good health since then and had been taking no medication. In 1995, he was admitted to the urological floor complaining of back pain and anuria. His blood examination showed acute renal failure with hydrenephrosis; his blood urea nitrogen (BUN) concentration was 45.9 mg/dl and serum creatinine level was 3.1 mg/dl. Computed tomography of the abdomen revealed low density area around the left kidney (Fig. 1) and a biopsy of the mass revealed marked fibrosis with mild infiltration of lymphocytes (Fig. 2). However, granulomatous reaction was not observed. These findings were compatible with the diagnosis of RPF. Drainage using a ureteral stent was performed. After the drainage, the serum creatinine level was decreased (1.5 mg/dl) and he was discharged. In 2000, he was readmitted to the urological department complaining of dyspnea. Laboratory findings showed aggravation of renal function (serum creatinine level, 3.1 mg/dl), a chest X-ray revealed mild cardiomegaly. Echocardiography revealed normal cardiac function with mild pericardial effusion. A diagnosis of congestive heart failure secondary to chronic renal failure was made, and he was successfully treated with diuretics. High doses of methylprednisolone therapy (125 mg daily for 3 days) were initiated, followed by low-dose prednisolone (10 mg daily). Examination of upper gastrointestinal tract revealed no evi-

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Figure 1. Enhanced computed tomography revealed low density area around the left kidney (arrows).

Figure 2. Histopathology of the retroperitoneal mass showed marked fibrosis with mild infiltration of lymphocytes (HE stain, × 200).

dence of malignant tumor. After discharge, his serum creatinine level was maintained between 1 to 2 mg/dl on low-dose prednisolone (5 mg daily).

In May 2003, he became aware of swelling of the lower extremities, which was becoming progressively worse. On June 11, 2003, he visited an internist complaining of dyspnea. A chest X-ray revealed marked cardiomegaly (Fig. 3A), and he was immediately hospitalized. On admission, he was 157 cm in height and weighed 70 kg. His temperature was 35.8°C, pulse rate was 72/min, and blood pressure was 114/76 mmHg. Conjunctiva was anemic, but not icteric. The thyroid gland was not palpable. Heart sounds were decreased in intensity and a coarse crackle was heard bilaterally at the bases. The abdomen was soft and distended, and a mass was palpated in the left lower abdominal quadrant. There was marked edema in the extremities and face.

Laboratory findings showed aggravation of renal function: BUN was 80.2 mg/dl and serum creatinine was 3.1 mg/dl. Endocrine function tests revealed marked hypothyroidism: free T4<0.4 ng/ml, and TSH 126.6 ng/ml. C-reactive protein level was negative, and test for antinuclear antibody (ANA), rheumatoid factor, perinuclear antineutrophil cytoplasmic antibody (p-ANCA), cytoplasmic antineutrophil cytoplasmic antibody (c-ANCA) and anti-thyroid antibodies were all negative. Echocardiography revealed massive pericardial effusion without cardiac tamponade (Fig. 3B). Abdominal computed tomography revealed a retroperitoneal mass around the left kidney.

Although he was treated with diuretics and levothyroxine sodium, his condition deteriorated. Echocardiography revealed increments of pericardial effusion and was suggestive of cardiac tamponade. Unresponsiveness to treatment for hypothyroidism led us to suspect the likelihood of MFS. As a result, pericardioscopy was performed on July 11. A biopsy of the pericardium revealed marked fibrosis with marked infiltration of lymphocytes (Fig. 4). Histological findings of the pericardium were identical to those of the retroperitoneal biopsy and a diagnosis of MFS was made. Despite aggressive supportive treatment, including steroid pulse therapy, he died with clinical signs of heart failure on August 4, 2003, and an autopsy was performed. Macroscopic findings showed encasement of the kidney by fibrous tissue (Fig. 5). Fibrous mass was not found around the aorta. The autopsy specimen revealed proliferation of fibrosis with infiltration of lymphocytes in the pericardium, retroperitoneum, lung, pleura and left kidney. However, fibrosis was not found in the thyroid.

Discussion

Causes of the ureteral obstruction due to retroperitoneal mass include RPF and metastasis of malignant tumors. Recently, Freitas et al reported a rare case of granulomatous vasculitis leading to hydronephrosis (6). However, granulomatous vasculitis such as Wegener’s granulomatosis and Churg-Strauss syndrome was unlikely in the present case because test for ANA, p-ANCA and c-ANCA were all negative and the granulomatous reaction was not observed histologically. Approximately two-third of cases of RPF are considered idiopathic, and the remaining third are ascribed to other causes such as drug medication and malignant tumors. In our case, there was no history of drug medication. Furthermore, examination of upper gastrointestinal tract and whole body CT scan revealed no evidence of malignant tumor. Thus, the cause of RPF was considered idiopathic.

Although many cases of RPF have been reported since the first report in 1905, involvement of the pericardium is still rare. To our knowledge, only 8 cases of MFS with pericardial involvement have been reported in a review of the English literature (7-15). In most of the cases, pericarditis or constrictive pericarditis was the initial clinical manifestation of MFS, followed
by the diagnosis of RPF. It is because in RPF, symptoms related to the urinary tract are uncommon until obstructive uropathy has led to azotemia and other clinical manifestation of renal failure. However, in the present case, there was a past history of RPF 8 years previously, and pericardial involvement became apparent during the follow-up for RPF. Although the onset of pericardial involvement in this case is not clear, this is the first report in which RPF preceded pericardial involvement in MFS.

In most of the cases, a diagnosis of MFS with pericardial involvement is not suspected while a patient is alive and can only be made at autopsy. In the present case, echocardiography revealed massive pericardial effusion on admission. Although the possibility of MFS was considered, severe low free T4 levels associated with pericardial effusion were most suggestive of myxoedema. It is possible that hypothyroidism, which was coincidental in our case, contributed to the late diagnosis of MFS. Unresponsiveness to treatment for hypothyroidism led us to suspect the likelihood of MFS. However, the prognosis for such patients is poor and only one case has been reported to survive with bilateral ureteral stents and/or corticosteroid (14, 15). Although we could make a correct diagnosis while our patient was alive, we could not save him.

Although there may be more than one pathophysiological mechanism, growing evidence suggests that many cases of RPF are due to an autoallergic reaction to lipid material in the atheromatous aorta (16). In terms of treatment of RPF, in the past, surgery was the primary treatment method and...
corticosteroid treatment was an auxiliary measure. However, the efficacy of corticosteroid therapy has now been established (17) and corticosteroids should be administered before surgical treatment except for emergency cases such as those with bilateral hydronephrosis due to ureteral obstruction. After the diagnosis of MFS was made in our patient, we increased the corticosteroid dose but it had little effect. This is probably because the fibrosis of pericardium was too severe to respond to corticosteroid treatment. It is true that the prognosis for RPF itself is fairly good if urinary obstructions can be treated surgically. However, as in our case, it is possible that fibrosis of other organs may become apparent during the follow-up for RPF, leading to a fatal outcome. High-doses of corticosteroids should be administered early in the course of the RPF as the effectiveness of corticosteroid may be diminished by the progression of fibrosis.

In summary, we have reported a case in which MFS was diagnosed by a biopsy of the pericardium during the follow up for RPF. Even after successful decompression of urinary obstruction, long-term follow-up is required in these patients because of the possibility of other fatal complications such as pericardial fibrosis.

References