Retroperitoneal Fibrosis in a Patient with Rheumatoid Arthritis

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A 54-year-old male diagnosed with rheumatoid arthritis (RA) was effectively treated with methotrexate and adalimumab. He was admitted with fatigue and right lower back pain which had persisted for 1 month. An enhanced abdominal computed tomography scan showed an ill-defined mass with soft tissue attenuation surrounding the right common iliac artery involving the right middle portion of the ureter. Laparoscopic ureterolysis and biopsy were performed. Microscopic evaluation confirmed the presence of fibroblastic proliferation, with a pleomorphic inflammatory cell infiltrate consisting predominantly of lymphocytes, macrophages, and vascular endothelial cells, without granuloma or neoplastic cells. Therefore, our diagnosis was retroperitoneal fibrosis (RPF)-associated RA. Clinicians should consider the possibility of RPF in patients with RA who experience lower back pain, abdominal pain, or dysuria, and order suitable imaging studies.

Key Words. Retroperitoneal fibrosis, Rheumatoid arthritis

INTRODUCTION

Retroperitoneal fibrosis (RPF) is an uncommon disease characterized by the presence of retroperitoneal tissue consisting of chronic inflammation and marked fibrosis that often entraps the ureters or other abdominal organs [1]. Histological examination revealed a collagen-rich background and fibroblasts admixed with an inflammatory infiltrate consisting of lymphocytes, plasma cells, macrophages, and eosinophils [2]. RPF has many causes; however, in approximately 70% of cases, the cause is unknown [3]. Several reports have described the association between RPF and spondyloarthritis [4], whereas other types of arthritis appear to be rare. Here we report a case of RPF-associated rheumatoid arthritis (RA) and review the literature about the association between RPF and RA.

CASE REPORT

A 54-year-old man diagnosed with RA at the age of 48 (the duration of illness was 6 years) was treated with methotrexate and adalimumab. He had no history of smoking, surgery, or radiation therapy. In January 2012, he was admitted to our department with fatigue and right lower back pain that had persisted for 1 month. No aggravation of joint symptoms was noted.

Laboratory findings showed rheumatoid factor and anti-cyclic citrullinated protein antibody levels of 53.5 IU/mL and 73.76 IU/mL, respectively. An elevated erythrocyte sedimentation rate (ESR) of 33 mm/h (normal, 0 to 9 mm/h) and an increased C-reactive protein (CRP) level of 10.25 mg/L (normal, 0 to 5 mg/L) were noted. There was no renal dysfunction (creatinine, 0.92 mg/dL; modification of diet in renal disease clearance, 90 mL/min). Immunoglobulin G4 (IgG4) level was normal at 100 mg/dL (upper limit of normal, 135 mg/dL).

An enhanced abdominal computed tomography (CT) scan showed an ill-defined mass with soft tissue attenuation surrounding the right common iliac artery that involved the right middle portion of the ureter. The obstructed ureter induced right kidney hydronephrosis (Figure 1A and 1B). Laparoscopic ureterolysis and biopsy...
Figure 1. (A) A computed tomography (CT) scan showing a retroperitoneal mass encircling the right common iliac artery, encasing the middle portion of the right ureter (arrow), (B) and resulting in hydronephrosis (arrow). (C) A CT scan after 3 months showing a decreased mass of retroperitoneal fibrosis encircling the right common iliac artery and ureter (arrow). (D) In addition, hydronephrosis has been relieved (arrow).

Figure 2. A biopsy specimen from the affected area demonstrating extensive fibrosis with lymphocytes and plasma cell infiltrates (arrow) arranged in a diffuse and nodular pattern. The white open spaces are entrapped fat cells (H&E, ×200).

were performed. Microscopic evaluation confirmed the presence of fibroblastic proliferation, with a pleomorphic inflammatory cell infiltrate consisting predominantly of lymphocytes, macrophages, and vascular endothelial cells without granuloma or neoplastic cells (Figure 2). An immunohistochemical study showed negative staining for plasma cells with IgG4, a hallmark of IgG4-related retroperitoneal disease. Therefore, our diagnosis was RPF-associated RA.

The patient was started on oral prednisolone 1 mg/kg/d for 2 weeks that was slowly tapered to 10 mg/d over the following 3 months. The methotrexate and adalimumab therapy was maintained. Follow-up laboratory findings showed that the ESR was 5 mm/h and the CRP level was 3.15 mg/L.

Follow-up CT scanning performed 3, 12, and 24 months after onset showed greatly reduced RPF volume and re-
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DISCUSSION

RPF is a rare (prevalence 1/100,000 persons), chronic, and progressive disorder of unknown etiology that involves the proliferation of fibrous tissue in the retroperitoneum as well as the body compartment containing the kidneys, aorta, renal tract, and various other structures [5]. Its association with various immune-related conditions and response to immunosuppression has led to the autoimmune etiology of idiopathic RPF. Additionally, some studies have reported that secondary RPF can be caused by malignant disease or certain infections and medications. However, in our patient with RPF and RA, there was no evidence of malignancy or infection. In addition, there was no history of surgery or smoking.

Many studies have reported the active nature of aortic adventitial chronic inflammation associated with human advanced atherosclerosis, i.e., chronic periaortitis (CP), and they have indicated the potential to progress to the clinically important disease idiopathic RPF [6]. Our patient presented with right lower back pain, and he was diagnosed with RPF. In a recent study, circulating autoantibodies such as antinuclear antibody (ANA) are detected in patients with CP. This shows that RPF may have an autoimmune origin and suggests that RPF and RA share common pathophysiological mechanisms [7]. Other reports suggested that systemic lupus erythematosus, Wegener’s granulomatosis, and microscopic polyangiitis might be associated with RPF [8]. In addition, 14 reported cases of CP that CP is possibly associated with spondyloarthritis. In that study, human leukocyte antigen-DRB1*03 was found in patients with CP which supports the hypothesis that autoimmune diseases including RA are closely related to RPF [9].

Additionally, one case report demonstrated IgG4-related RPF with concomitant RA [10]. In that report, a 67-year-old Japanese man presented with left flank pain and he was diagnosed with pathologically confirmed RPF. He had experienced symptoms of Reynaud’s disease and arthralgia for several months, and he was diagnosed with RA, with high serum levels of rheumatoid factor (113 IU/mL) and ANA positivity (80-fold). His symptoms improved and the retroperitoneal mass decreased in size after he received oral prednisolone. This shows that IgG4-related RPF is a recognized immune-mediated condition and supports the view that autoimmune diseases such as RA may be closely associated with RPF. However, the clinical significance of this finding requires further study.

From another perspective, RPF can be induced by medication. Couderc et al. [11] reported a case of aortitis, which may favor the occurrence of subsequent RPF during etanercept treatment for ankylosing spondylitis. This suggests that a tumor necrosis factor-α (TNF-α) inhibitor such as etanercept can play a role in RPF formation. However, in our patient, RPF did not recur during the 3-year period of adalimumab therapy following laparoscopic ureterolysis. As such, it is difficult to clearly state that TNF-α inhibitors cause RPF, and more studies are needed to determine whether RPF can be induced by drugs such as TNF-α inhibitors [11].

The treatment for RPF aims to relieve symptoms, decrease the retroperitoneal mass size, reverse ureteral obstructions, and prevent relapses once remission is achieved. As shown in our case, in the presence of severe obstruction, ureterolysis followed by omental wrapping of the ureters may be required. Medical treatment should also be initiated as soon as possible. There is evidence that treatment with glucocorticoids, sometimes associated with immunosuppressive agents, is highly effective in most patients for curbing disease activity and preserving renal function [12,13].

SUMMARY

With increasing awareness, RPF can be identified in patients with RA to enable its early diagnosis and treatment. Therefore, clinicians should consider the possibility of RPF in patients with RA who experience lower back pain, abdominal pain, or dysuria and then order suitable imaging studies such as CT and magnetic resonance imaging. Laboratory testing for ESR, CRP, urea, and creatinine level is also needed, and histologic confirmation is helpful in making a diagnosis.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES