CASE REPORT

A rare clinical entity: Two cases of retroperitoneal fibrosis with different approach and consequences

Nadir bir klinik durum: Farklı yaklaşım ve sonlanımlarla iki retroperitoneal fibrozis olgusu

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Retroperitoneal fibrosis is a rare disease, characterized by the presence of a retroperitoneal tissue, consisting of chronic inflammation and marked fibrosis, which often entraps the ureters or other abdominal organs. Early symptoms are nonspecific as abdominal or lumbar discomfort. As the fibrosis progresses, the compressive effects determine the symptomatic evolution. Retroperitoneal fibrosis diagnosis is usually delayed, which can result in permanent organ failure and mortality. We present herein two cases of retroperitoneal fibrosis diagnosed in different stages of the disease and resulting in different outcomes. Our aim is to stress the importance of early diagnosis in preserving organ function.

Retroperitoneal fibroz, kronik inflamasyon ve belirgin fibroz içeren sıklıkla üreterleri ya da diğer intraabdominal organları çevreleyen retroperitoneal bir dokunun varlığı ile karakterize nadir bir hastalıktır. Erken dönem semptomları karında ve lumbar bölgede rahatsızlık şeklinde nonpesifik özelliktedir. Fibroz ilerledikçe oluşan bası etkisi septomlarda artışı belirler. Nadir bir klinik durum olması ve klinik ve fizik muayene bulgularının nonspesifik olması çoğu zaman teşhisi geciktirir ve kalıcı organ yetmezliği ve mortaliteye yol açar. Biz burada hastalığın farklı evrelerinde tanı almış ve farklı şekillerde sonuçlanmış iki retroperitoneal fibroz olgusunu sunduk. Amacımız erken teşhisin organ fonksiyonlarını korumadaki önemini vurgulamaktır.

Keywords: Retroperitoneal fibrosis, renal failure, retroperitoneal mass

Anahtar kelimeler: Retroperitoneal fibrozis, böbrek yetersizliği, retroperitoneal kütle

INTRODUCTION

Retroperitoneal fibrosis (RPF) is a rare disease, characterized by the presence of a retroperitoneal tissue, consisting of chronic inflammation and marked fibrosis, which often entraps the ureters or other abdominal organs (1). As it is a rare clinical entity, the diagnosis is often delayed, and permanent organ failure and mortality can occur. We present herein two cases of RPF diagnosed in different stages of the disease and resulting in different outcomes.

CASE REPORTS

CASE 1: A 34-year-old female patient was referred to the hospital in May 2010 with abdominal pain, which was belt-like and radiating to the inguinal regions and had increased progressively in last two months. It first started after her left nephrectomy operation in August 2008 due to hypertension caused by a nonfunctioning left kidney, in which grade 3 hydronephrosis was seen. She also defined nausea without vomiting, loss of appetite, fatigue, and a 10 kg weight loss in the last year. There was no known allergy or chronic medication history. On the physical examination, the thyroid was slightly palpable but not nodular, and there was generalized mild abdominal tenderness, which was felt more in the inguinal regions. There was a 3-5-fold increase in pancreatic enzyme levels and a mild normochromic, normocytic anemia. In abdominal ultrasonography (USG), together with normal pancreas, a 75x25 mm hypoechoic solid mass with lobulated contour was seen surrounding the left iliac artery. Ranson score was zero and pancreatic enzyme levels returned to normal in two days with conservative treatment. Contrasted abdominal and pelvic computed tomography (CT) scans were consistent with RPF (Figure 1A). Thyroid stimulating hormone level was found decreased (0.29 μIU/ml) with normal free T4 (1.1 ng/dl). The anti-thyroperoxidase antibodies were elevated (149 UI/ml). Thyroid USG was normal. Since RPF is highly associated with autoimmune diseases, immunological markers were requested. Only antinuclear antibodies (1/1000 titrated) and Ro-52 recombinant (1+) were detected positive, but she had no symptoms of dryness of the mouth or eyes. She was thought to have asymptomatic concomitant autoimmune thyroid and Sjögren diseases. The treatment of prednisolone 60 mg/day was started; her abdominal pain responded to

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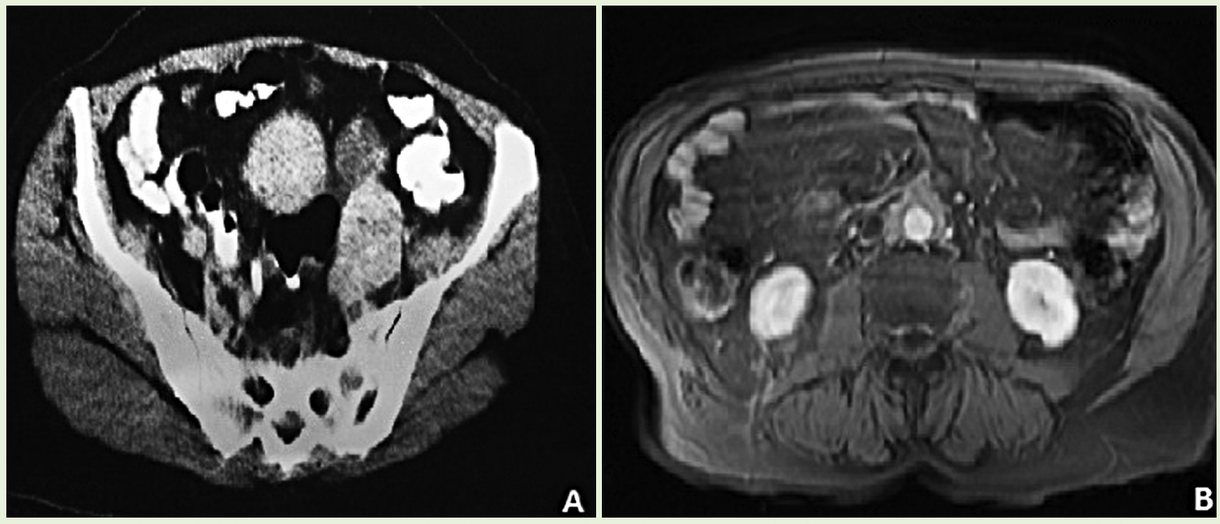
this treatment and progressively decreased during the follow-up.

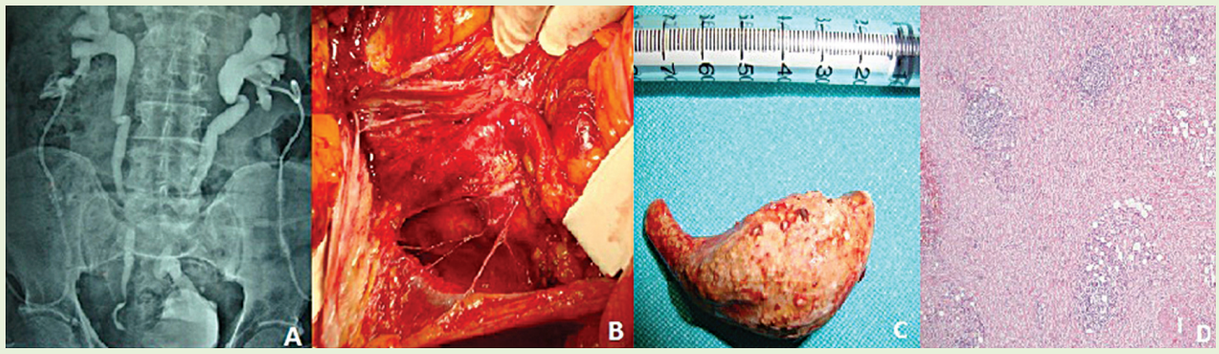
CASE 2: A 66-year-old male patient presented to the hospital with bilateral flank and low back pain in May 2010. It had started 10 days before with nausea and vomiting. He had a history of urolithiasis 10 years before and both prostate and ureterolithotomy operation four years ago. On the physical examination, only left-sided costovertebral angle tenderness was notable. His creatinine level was increased (4.86 mg/dl), and in the urinary system USG, the left renal pelvis and proximal ureter were detected as significantly dilated (13 mm at the most dilated part). Unenhanced abdominal and pelvic CT scans showed a retroperitoneal mass and left ureter calculus. After bilateral percutaneous nephrostomy catheter placement, creatinine levels decreased progressively. Both the abdominal magnetic resonance imaging (MRI) and intravenous urography confirmed the left ureter stone and diagnosis of extensive RPF (Figure 1B and 2A). Closure of nephrostomy catheters was attempted but creatinine levels started to increase, so laparotomy was done for ureterolysis, bilateral double J stent placement and ureterolithotomy. During the laparotomy, dense fibrous tissue was found in the retroperitoneal area, surrounding the aorta, inferior vena cava and both ureters (Figure 2B). The ureters were freed from the fibrous tissue, an approximately 2x1 cm ureteral stone was extracted, and the excised tissue was taken for histopathology (Figure 2C, 2D). Histopathology reported benign fibrous tissue with chronic inflammation without malignant changes. Thus, the histological diagnosis of RPF was also made. In the follow-up, subsequent improvement in serum creatinine concentration (1.2 mg/dl) was seen. Prednisolone 60 mg daily was started with the planning of dose tapering in the follow-up.

DISCUSSION

Retroperitoneal fibrosis (RPF) was first described by the French urologist Albarran in 1905, and the description of two cases by Ormond in 1948 established RPF as a clinical entity (2). Its true incidence is unknown, but its estimated incidence is 1:200,000 in the population and 1/10,000 in the autopsy series (3). It can be primary or secondary. Secondary RPF may be caused by malignancies, infections, medications, radiotherapy, or previous surgery; the primary RPF, named idiopathic RPF (IRF), is a diagnosis of exclusion (4). Most (>70%) cases are thought to be idiopathic. It is typically seen in people aged 40–60 years and is two to three times more likely in men (2). Hughes et al. (5) reported that IRF is a local immune reaction to lipid components of the atherosclerotic process in the abdominal aorta, resulting in a proximal fibrotic reaction, and this causes chronic periaortitis. However, findings of studies done during the past 10 years, with the systemic manifestations of the disease and its association with other autoimmune disorders, have challenged



Resim 1. A. Enhanced abdominal CT showing relatively contrast-enhanced retroperitoneal soft tissue mass, measuring 3 cm, which was seen surrounding the left iliac artery, starting from the proximal part of the left common iliac artery and extending to the uterus level, but with no aortic involvement. It does not demonstrate lymphadenopathy or invasion to adjacent tissues, and additionally, the mass had soft tissue density, excluding malignancy. **B.** T1-weighted MRI showing retroperitoneal soft tissue mass surrounding the aorta (1.5 cm in size on the anterior of the aorta), starting from the infrarenal level and extending to the iliac chains, inducing bilateral ureteral dilatation and hydronephrosis. There was also a 2.5x1.5 cm hyperdense calculus image in the left ureterocystic junction.



Resim 2. A. Intravenous urography showing bilateral dilatation of ureters and hydronephrosis, narrowing of the ureters at the L4/5 level and medial deviation of the ureters. **B.** Operation image of dense fibrous tissue in the retroperitoneal area surrounding the aorta, inferior vena cava and both ureters. **C.** Postoperative image of the ureteral stone, measuring approximately 2x1 cm in size. **D.** Hematoxylin and eosin staining of the retroperitoneal tissue biopsy showing benign extensive fibrotic tissue with chronic inflammatory cells.

this theory and lend support to the underlying systemic autoimmune process (6). Associated autoimmune diseases include primary sclerosing cholangitis, autoimmune pancreatitis and systemic lupus erythematosus (7). Pathologically, RPF manifests as progressive inflammation and fibrous proliferation of connective tissue, and its degree varies according to the stage and activity of the disease (8,9). RPF secondary to malignancy is indistinguishable from IRF histologically (9). In some cases, atypical localizations such as periduodenal, peripancreatic, pelvic, periureteral, or close to the renal hilum can be seen, and those are not characterized by aortic involvement (6). Early symptoms are nonspecific as abdominal or lumbar discomfort. As the fibrosis progresses, the compressive effects determine the symptomatic evolution. Severe pain in the lower back, abdomen, and flank areas and unilateral or bilateral lower extremity swelling are most common. A decrease in urinary excretion may show renal or ureteral involvement (80–100% of cases) (2). Systemic symptoms, which include fatigue, low-grade fever, nausea, anorexia, weight loss, and myalgias, can be seen insidiously and of varying duration (10). The physical examination is usually unremarkable except for the presence of hypertension, probably of renal origin. Occasionally, an abdominal or pelvic mass is present (9). Because of the non-specificity of the clinical manifestations and physical findings, diagnosis is often delayed, which leads to the late complications of advanced RPF (6). Mostly, there is significant morbidity due to progressive renal failure resulting from ureteral entrapment (8). Laboratory investigation shows elevated erythrocyte sedimentation rate (ESR) and/or impairment of renal function, commonly with a normochromic, normocytic anemia and to a lesser extent polyclonal gammopathy or mild thrombocytosis (9). Imaging studies are essential in the diagnosis and management of RPF. Sensitivity and specificity of intravenous urography are limited (11). Although its overall sensitivity is poor (25%) in the diagnosis of RPF, sonography should be done as a first-line study, especially when renal involvement is present. In USG, RPF is identified as a hypoechoic or anechoic mass, which can involve the ureters (2,6). In the CT scan, RPF appears as a peritoneal soft tissue that in most patients encases the surrounding vessels and ureters (12). MRI is the gold standard in the diagnosis of RPF, because it allows both better anatomical definition of soft tissues and detection of fibrosis than CT and uses non-iodinated contrast medium (13). It may also be valuable in assessing the response to treatment (11). Fluorodeoxyglucose-positron emission tomography, although not useful for the diagnosis of RPF because of low specificity, may be useful in assessing the disease activity and remote RPF origins and in monitoring the response to treatment, without helping in benign or malignant discrimination [2]. Thus, CT and MRI both show the extent and complications of the disease process, although they fare poorly in the differentiation of benign from malignant causes. Therefore, biopsy with histopathologic evaluation remains the most reliable diagnostic tool (12).

Management of RPF is mainly based on corticosteroids (CS) and immunosuppressive drugs. CS are usually effective in suppressing the inflammatory process in RPF, particularly in its early stages. Although there is no consensus in the literature regarding both steroid dose and therapy duration, the preferred regimen is prednisone at 40-60 mg/day tapered to 10 mg/day within 2-3 months and gradually discontinued after 1-2 years (14). The clinical and radiographic improvement is seen mostly after

therapy (9). Unfortunately, some patients are resistant to steroids, so in those patients, immunosuppressive drugs such as cyclophosphamide and azathioprine can induce disease remissions and regression of the mass, although they can be very toxic (6,14). The successful use of methotrexate, cyclosporin, and mycophenolate mofetil has also been reported. Finally, successful use of tamoxifen has also been reported, but its real effectiveness is uncertain (6). Ureterolysis or stents can be performed for ureteral obstruction (15). Long-term follow-up is mandatory because of late relapses (9). No predictors of response to therapy, CS requirement, or disease relapse have been identified (6). After the initiation of therapy, patients with RPF are usually monitored by subjective symptoms and regular assessment of ESR and C-reactive protein (CRP) (9).

We herein presented two cases of RPF, both of whom had an abdominal surgical history, so their RPF may be considered secondary. However, in Case 1, there was no identified reason for unilateral grade 3 hydronephrosis. Thus, the previous left-sided hydronephrosis was because of the same-sided fibrotic mass compression effect. In Case 2, unilateral urolithiasis did not explain the renal function impairment, and as a result, he was diagnosed as RPF, and his renal functions could be preserved with the early diagnosis and treatment. Therefore, in Case 1, perhaps because of the delayed diagnosis, the patient lost her left kidney and during this period experienced the discomforting abdominal pain. We want to emphasize with this report that although RPF is a rare clinical entity, it must be considered as one of the etiological factors in the presence of hydronephrosis of unknown cause or of persistent abdominal pain with chronic fatigue.

REFERENCES

1. Gilkeson GS, Allen NB. Retroperitoneal fibrosis: a true connective tissue disease. Rheum Dis Clin North Am 1996; 22: 23-38.
2. Cronin CG, Lohan DG, Blake MA, Roche C, McCarthy P, Murphy JM. Retroperitoneal fibrosis: a review of clinical features and imaging findings. AJR Am J Roentgenol 2008; 191: 423-31.
3. Bouhabel A, Takoucht F, Meier P. Idiopathic retroperitoneal fibrosis revealed by renal colic. Saudi J Kidney Dis Transplant 2005; 16: 78-80.
4. Pizzini AM, Corrado S, Radighieri E, Ferretti G, Carani C, Papi G. Hashimoto's thyroiditis associated with idiopathic retroperitoneal fibrosis: case report and review of the literature. Int J Clin Pract 2007; 61: 162-4.
5. Hughes D, Buckley PJ. Idiopathic retroperitoneal fibrosis is a macrophage-rich process. Implications for its pathogenesis and treatment. Am J Surg Pathol 1993; 17: 482-90.
6. Vaglio A, Salvarani C, Buzio C. Retroperitoneal fibrosis. Lancet 2006; 367: 241-51.
7. Lee JE, Han SH, Kim DK, et al. Idiopathic retroperitoneal fibrosis associated with Hashimoto's thyroiditis in an old-aged man. Yonsei Med J 2008; 49: 1032-5.
8. Takashima T, Onoda N, Ishikawa T, et al. Tumor forming idiopathic retroperitoneal fibrosis: Report of a case. Surg Today 2004; 34: 374-8.
9. Van Bommel EF. Retroperitoneal fibrosis. Neth J Med 2002; 60: 231-42.
10. Vaglio A, Corradi D, Manenti L, et al. Evidence of autoimmunity in chronic periaortitis: a prospective study. Am J Med 2003; 114: 454-62.
11. Vivas I, Nicolas AI, Velazquez P, et al. Retroperitoneal fibrosis: typical and atypical manifestations. Br J Radiol 2000; 73: 214-22.
12. Kottra JJ, Dunnick NR. Retroperitoneal fibrosis. Radiol Clin North Am 1996; 43: 1259-75.
13. Burn PR, Singh S, Barbar S, et al. Role of gadolinium-enhanced magnetic resonance imaging in retroperitoneal fibrosis. Can Assoc Radiol J 2002; 53: 168-70.
14. Monev S. Idiopathic retroperitoneal fibrosis: prompt diagnosis preserves organ function. Cleve Clin J Med 2002; 69: 160-6.
15. Warakulle DR, Prematilleke I, Moore NR. Retroperitoneal fibrosis mimicking retrocrural lymphadenopathy. Clin Radiol 2004; 59: 292-3.