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Original article

Retroperitoneal fibrosis: case series of five patients and review of the literature



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ABSTRACT

Chronic periaortitis (CP) is an umbrella term used to describe a group of nosologically allied conditions that include idiopathic retroperitoneal fibrosis (Ormond's disease), inflammatory abdominal aortic aneurysm, and perianeurysmal retroperitoneal fibrosis. Retroperitoneal fibrosis encompasses a range of diseases characterized by the presence of a fibro-inflammatory tissue, which usually surrounds the abdominal aorta and the iliac arteries and extends into the retroperitoneum to envelop neighboring structures-ureters. Retroperitoneal fibrosis is generally idiopathic, but can also be secondary to the use of certain drugs, malignant diseases, infections, and surgery. Here we describe a 5 years follow-up (2006–2011) of 5 patients admitted to our hospital with symptoms, laboratory, imaging and pathologic finding compatible with retroperitoneal fibrosis. We review our clinical course of our patient with respect to the literature.

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Fibrose retroperitoneal: série de cinco casos e revisão da literatura

RESUMO

Periaortite crônica (PC) é um termo genérico usado para descrever um grupo de condições nosologicamente ligadas que incluem a fibrose idiopática retroperitoneal (doença de Ormond), o aneurisma da aorta abdominal inflamatório e a fibrose retroperitoneal perianeurismática. O termo fibrose retroperitoneal engloba uma gama de doenças que se caracterizam pela presença de um tecido fibroinflamatório que geralmente envolve a aorta abdominal e as artérias ilíacas, se estende ao retroperitônio e envolve estruturas ureterais vizinhas. A fibrose retroperitoneal geralmente é idiopática, mas pode também ser secundária ao uso de determinados fármacos, doenças malignas, infecções e cirurgia. Este

Palavras-chave:

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estudo descreve o seguimento por cinco anos (2006–2011) de cinco pacientes internados em nosso hospital que apresentavam sintomas e achados laboratoriais, de imagem e patológicos compatíveis com a fibrose retroperitoneal. Revisou-se a evolução clínica dos pacientes, que foi comparada com os achados da literatura.

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Introduction

Chronic periaortitis encompasses a group of rare abdominal aorta diseases, including idiopathic (nonaneurysmal) retroperitoneal fibrosis, inflammatory abdominal aortic aneurysm (IAAA), and perianeurysmal retroperitoneal fibrosis.¹ Some cases involve the thoracic aorta, leading to mediastinal fibrosis. The idiopathic form accounts for over 70% of cases of retroperitoneal fibrosis.² According to a Finnish study, the estimated incidence of idiopathic retroperitoneal fibrosis is 0.1 per 100,000 person-years.³ Men are affected twice to three times more often than women, the mean age at presentation is 50–60 years, although reports of the condition in children and older adults are not uncommon.

This report reviews the literature and describes clinical and laboratory characteristics, treatment, and outcome of a series of patients with retroperitoneal fibrosis.

Results

Five patients with retroperitoneal fibrosis were identified reviewing all rheumatology clinic inpatients records (2006–2011). The mean (\pm SD) age was 62.6 ± 5.7 years and mean (\pm SD) duration of disease at diagnosis was 3.2 ± 2.16 years. Abdominal and groin pain were the most common clinical manifestations (all patients).

All patients had normocytic anemia and a high C-reactive protein (CRP) and ESR levels. Three patients were found to have renal failure. Treatment in all cases consisted of steroids and tamoxifen. One patient did not improve after treatment, two patients had partial response, and two patients had full response (complete remission).

Case reports

Patient 1

A 64-year-old man with a history of dyslipidemia presented with chief complaint of groin pain during the preceding two months. Physical examination was normal, laboratory tests revealed elevated ESR (101 mm/h), mild anemia with hemoglobin of 11.6 g/dL, and mildly elevated creatinine (1.29 mg/dL). Anti-nuclear antibody (ANA) titer was negative. Imaging included a computed tomography (CT) scan, which showed bilateral moderate hydronephrosis and a mass surrounding the abdominal aorta from the level of the renal arteries through the iliac bifurcation. The patient underwent bilateral ureterolysis and omentopexy. Biopsy of the retroperitoneal mass disclosed collagenous tissue with inflammatory

cells, compatible with retroperitoneal fibrosis. The patient was first prescribed prednisone 1 mg/kg/day with tapering therapy down for three months then maintenance therapy with azathioprine 2 mg/kg/day and tamoxifen 20 mg bid. At a 6-month follow-up, an increment in the retroperitoneal process was noted and the dose of azathioprine was increased. Repeated CT scan one year later revealed a stable retroperitoneal lesion. The patient continued tamoxifen and azathioprine.

Patient 2

A 55-year-old man, a smoker and with a history of diabetes mellitus type 2, presented with abdominal pain and weight loss during the preceding 6 months. Physical examination was remarkable for abdominal tenderness. Laboratory tests revealed elevated inflammatory markers (CRP 138 mg/L, ESR 77 mm/h), mild anemia and normal creatinine. A CT scan, revealed hard tissue surrounding the abdominal aorta with hydronephrosis, and signs of atherosclerosis within the large arteries. The biopsy revealed fibrous tissue and inflammatory cells.

Treatment with high-dose steroids (1 g methylprednisolone for 3 days) and cyclophosphamide (500–1000 mg/m² IV monthly for 6 doses) led to resolution of the symptoms. Thereafter, the patient was prescribed tamoxifen and azathioprine 2 mg/kg/day. Under treatment, repeated imaging of magnetic resonance (MR) angiography study, one year later at follow up, disclosed minor tissue surrounding the aorta and inflammatory markers normalized. Treatment with cyclophosphamide was stopped after 6 months and the patient continued tamoxifen and azathioprine.

Patient 3

A 57 year-old man with a 3 year history of Etanercept treated sacroiliitis presented with pelvic pain and burning sensation in the groin. Physical examination was positive for bilateral flank tenderness, laboratory tests revealed elevated inflammatory markers (CRP 126 mg/L, ESR 113 mm/h), mild anemia with hemoglobin of 11.5 g/dL, and mildly elevated creatinine of 1.28 mg/dL. ANA was negative. IgG4 isotype level was elevated (243 mg/dL; normal 1–112). A CT scan, revealed a retroperitoneal mass encompassing the inferior vena cava and abdominal aorta with hydronephrosis. The sacroiliac joints appeared normal. Laparoscopic biopsy disclosed fibrotic tissue with chronic inflammatory aggregation and a few macrophages. Treatment consisted of prednisone 60 mg qd and tamoxifen 20 mg bid. Etanercept was discontinued. Repeated CT scan at follow up, one year later, showed marked regression of the retroperitoneal mass. Prednisone was tapered down and the patient continues tamoxifen only.

Patient 4

A 59 year-old woman with history of hypothyroidism was hospitalized for abdominal pain and evidence of bilateral hydronephrosis on abdominal ultrasound study. Physical examination was remarkable for diffuse abdominal tenderness with no rebound or peritoneal signs. Laboratory tests revealed elevated creatinine level of 2.4 mg/dL with elevated inflammatory markers (CRP 57 mg/L), and anemia with hemoglobin level of 9.5 g/dL. Imaging during hospitalization included positron emission tomography PET-CT scan, which revealed fibrotic tissue surrounding the abdominal aorta at the level of L3 to the iliac bifurcation. The patient underwent bilateral robotic ureterolysis followed by administration of prednisone 60 mg/day. No biopsy of the lesion was performed, and treatment was initiated on clinical and radiological grounds. Creatinine level at the last follow-up (2 years later) was greatly improved (1.26 mg/dL). Prednisone was tapered down and currently the patient is under no treatment, due to uncontrolled glucose level under prednisone treatment. Repeated PET-CT imaging showed no evidence of the retroperitoneal mass.

Patient 5

A 57-year-old woman with a history of dyslipidemia presented with the chief complaint of groin pain and general weakness. Physical test was normal, laboratory tests revealed elevated inflammatory markers (ESR 105 mm/h, CRP 57 mg/L), normal renal function with creatinine of 0.9 mg/dL. ANA titer was positive (1:160) with Homogenous (diffuse) pattern. Imaging included PET-CT uptake, which showed a mass surrounding the abdominal aorta from the level of the superior mesenteric artery through the iliac bifurcation without hydronephrosis. The patient was diagnosed with retroperitoneal fibrosis and treated with prednisone 60 mg/day and tamoxifen 20 mg bid. At one-year follow-up, symptoms resolved, inflammatory markers normalized and repeated PET-CT imaging 2 years later showed no evidence of the retroperitoneal mass. Prednisone was tapered down to 5 mg/d and tamoxifen continued.

Discussion

Retroperitoneal fibrosis can involve any organ proximate to the retroperitoneum. Ureteral obstruction occurs in up to 80–100% of cases.³ Intestinal or biliary-pancreatic involvement, lower-extremity venous obstruction, aortic or branch arterial compression, and other pelvic organ and peripheral nerve involvement have all been reported, as have more distant inflammatory and fibrotic complications of the mediastinum, pericardium or pleura, and even the thyroid, sinuses, or orbit, though these are uncommon.^{4,5} In four of our five patients hydronephrosis was a presenting manifestation, in resemblance to the literature.

Patients 4 and 5 diagnosed with retroperitoneal fibrosis based only on PET-CT imaging without biopsy. A few studies showed that retroperitoneal fibrosis can be diagnosed base only on PET-CT alone. In 2010, Jansen et al.⁶ evaluated whether PET-CT was useful for the diagnosis of retroperitoneal fibrosis. At baseline, the test was positive in 20/26 of patients

with positive predictive value of 0.63. Systematic review published in 2013,⁷ evaluated the role of PET-CT in the diagnosis of retroperitoneal fibrosis. The authors concluded that the test is useful in the diagnosis and in evaluating treatment response.

The results of routine laboratory tests are consistent with inflammatory diseases. In a large cohort of 58 patients with retroperitoneal fibrosis,⁸ Elevations in acute-phase reactants, such as ESR and CRP was found in 66.7% and in 64.9%, respectively and in all of our patients. Positive antinuclear antibodies detected in up to 27% of the cohort and in one patient of this case series.

IgG4 antibodies are dynamic molecules that can exchange Fab arms by swapping a heavy chain and attached light chain, IgG4 can form bispecific antibodies, as well as functioning as a monovalent molecule.⁹

IgG4 predominance in male patients with retroperitoneal fibrosis was reported recently, like patient 3 of our series.¹⁰ IgG4-related disease (IgG4RD) is a novel clinical disease entity characterized by elevated serum IgG4 concentration tissue infiltration by IgG4-positive plasma cells.

In the absence of randomized trials, the treatment of idiopathic retroperitoneal fibrosis is empirical. Spontaneous resolution has been reported in some cases,¹¹ and patients with indolent disease not affecting adjacent structures might need only monitoring. However, patients with active disease usually require medication. Glucocorticoids are the mainstay of therapy and all our patients received this treatment, other immunosuppressive drugs (e.g., mycophenolate mofetil, azathioprine)¹² have been used successfully together with glucocorticoids, but the superiority of these combinations over glucocorticoids alone is still unproven.¹³ Tamoxifen has become an attractive therapeutic option. However, in 2011, Vaglio et al.¹⁴ enrolled 40 patients with newly diagnosed idiopathic retroperitoneal fibrosis in a treatment trial. The 36 patients who achieved remission after induction therapy with 1 mg/kg prednisone daily were randomly assigned to receive either tapering prednisone (initial dose 0.5 mg/kg daily) or tamoxifen (fixed dose 0.5 mg/kg daily) for 8 months. Evaluation at termination of treatment revealed relapse rates of 6% in the prednisone group and 39% in the tamoxifen group, suggesting an advantage of prednisone.

Conclusion

We presented a series of 5 patients with retroperitoneal fibrosis. We emphasize that an abdominal and groin pain with elevated acute phase reactants should prompt an evaluation for retroperitoneal fibrosis.

One patient in our series with elevated serum IgG4 level developed this syndrome after being treated with Etanercept. This is the second report¹⁵ published concerned the development of retroperitoneal fibrosis after TNF inhibitors treatment, and further studies are needed.

Conflicts of interest

The authors declare no conflicts of interest.

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