INTRODUCTION

Retroperitoneal fibrosis, also known as Ormond’s disease, was described as a clinical entity in 1948 [1]. It is a rare collagen vascular disease, characterized by the formation of plaque-like fibrosis in the retroperitoneal tissue, mainly on the anterior surface of the fourth and fifth lumbar vertebrae. As a result, the structures are entrapped retroperitoneally, namely the ureters; other involved organs may be compromised, such as the small bowel, colon and spinal cord.

Also known as retroperitoneal fasciitis or chronic retroperitoneal fibroplasias, it affects one patient per 200,000 to 500,000 individuals, with no racial predilection, but males being twice to three times more affected than females [2-3].

Retroperitoneal fibrosis may be primary (Ormond’s disease) or secondary to malignancy [4-5], medications [3] or contiguity to inflammation (Table I). It has been described in 5% of abdominal aortic aneurysm cases as well, and called “inflammatory aortic aneurysm” [6].

The etiology of the disease is unknown, though it has been suggested to be immunologically-mediated, due to association with autoimmune diseases, and the response to corticosteroids as well as immunosuppressive therapy [7]. In addition, up to 15% of patients have extra-retroperitoneal fibrotic processes including sclerosing cholangitis, mediastinal fibrosis, fibrosing thyroiditis (Riedl’s thyroiditis), and fibrotic orbital pseudotumors [8-9].

Here we describe a case of a patient that presented for...
recurrent scrotal edema that was misdiagnosed as inguinal hernia and was found to have retroperitoneal fibrosis.

CASE REPORT

A 56-year-old male patient presented to our hospital for a hernia repair.

He had been complaining of intermittent scrotal edema, without erythema or pain. He presented to his general practitioner who found no palpable masses upon examination, and was diagnosed with an inguinal hernia, for which a non-steroidal anti-inflammatory drug was prescribed, without improvement. He presented for a pre-operative examination. Upon evaluation, a hernia could not be found. A general workup was ordered.

Laboratory results showed renal failure with creatinine of 3.11 mg/dl (0.50-1.20), urea: 61 mg/dl (10-50), phosphorus: 5.9 mg/dl (2.6-5), magnesium: 2.8 (1.6-2.6), hemoglobin: 10.8 g/dl (13-18), hematocrit: 33.5% (38-50%) and C-reactive protein: 77 mg/l (negative at < 5 mg/l).

An abdomen-pelvis ultrasound was done, showing bilateral increase in kidney size of 13 cm on the right, and 13.4 cm on the left with no parenchymal disease; bilateral pelvicalyceal dilatation was noted, without nephrolithiasis. Doppler ultrasound of the renal vessels was normal.

A CT scan followed (Fig. 1a), revealing the same bilateral moderate hydronephrosis, with diffuse infiltration of the retroperitoneal fat surrounding the aorta and inferior vena cava. There was thickening of the peritoneal reflections at the level of the renal arteries, reaching the bifurcation; this infiltration could be responsible for the bilateral renal dilatation. There were no perivascular adenopathies.

Urgent bilateral double J ureteral stents were inserted with subsequent normalization of the creatinine within six days.

Retroperitoneal fibrosis was suspected. A tuberculin skin test was positive at 15 mm. HIV, hepatitis B and hepatitis C studies were negative. ANA profile was found negative, with C3 and C4 levels being normal. RA test for rheumatoid arthritis was also done, with negative results (< 8 IU/ml).

Erythroid sedimentation rate (ESR) was elevated, at 117 mm (1-13), in addition to a B2 microglobulin level elevated at 3.96 mg/l (0.8-1.2). Protein electrophoresis

<table>
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<th>ACQUIRED ETIOLOGIES</th>
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<td>Malignancy</td>
<td>Metastatic colon and breast cancer, lymphomas, sarcomas, carcinomas of the lung, cervix, prostate and bladder. Malignant retroperitoneal fibrosis is distinguished radiologically from retroperitoneal lymph nodes metastasis by medial displacement of the ureters.</td>
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<td>Irradiation</td>
<td>Treatment of pelvic tumors</td>
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<td>Trauma</td>
<td>Peritoneal injury</td>
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<td>Inflammation</td>
<td>Chronic retroperitoneal inflammation, mainly due to aortitis (a result of severe atherosclerosis and plaque necrosis)</td>
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<tr>
<td>Medication</td>
<td>Beta-blockers, methysergide and methyldopa</td>
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**TABLE I**

**ACQUIRED ETIOLOGIES OF RETROPERITONEAL FIBROSIS**

![Figure 1. Abdomen and pelvis CT scan. (a) Patient scan upon presentation, with diffuse infiltration of the retroperitoneal fat surrounding the aorta and inferior vena cava. (b) CT scan six months later, following steroid therapy.](image-url)
and immune-electrophoresis followed, showing absence of monoclonality. Further workup with urinary 5-hydroxy-indoleacetic acid was also negative. Upper endoscopy followed, showing mild active gastritis, and biopsy revealing the presence of Helicobacter pylori. Colonoscopy revealed no abnormalities.

Following improvement in clinical and laboratory findings, a laparoscopic bilateral release of retroperitoneal adhesions was performed, with biopsy of the retroperitoneal adipose tissue, which was sent to pathology. A Mycobacterium tuberculosis polymerase chain reaction (PCR) was done, with negative results.

Histology revealed focal adipose tissue invasion by dense hyaline fibrosis, with inflammatory exudates composed of plasma cells and few neutrophils (Fig. 2). The conclusion was compatible with idiopathic retroperitoneal fibrosis.

The patient was treated with steroids (1 mg/kg) for six months.

A repeat abdomen-pelvis CT scan done six months later showed significant improvements, with decreased retroperitoneal fat infiltration, and decreased peritoneal thickening (Fig. 1b). Three months later, the double JJ stents were successfully removed, with creatinine remaining persistently normal for up to four months post removal. A repeat CT scan was normal as well. The scrotal edema progressively resolved over a period of two months after initiation of steroid therapy. He was kept on low dose steroids for two years with a maintained response.

PATHOLOGY

Examination reveals dense retroperitoneal plaques, on the anterior aspect, beginning at the aortic bifurcation, extending caudally to envelop the aorta and inferior vena cava, as well as the ureters, bilaterally in 2/3 of cases [10].

The aortic branches may also be involved, namely the gonadal, renal, celiac and superior mesenteric arteries.

Association with other vasculitic and connective tissue disease has been described, such as ankylosing spondylitis, polyarteritis nodosa, systemic lupus erythematosus and others [9-11].

In the early disease stages, the plaque consists of a highly vascularized tissue, with collagen deposition and leukocyte infiltrates (macrophages, polyclonal B cells, CD4 + T cells). Rarely, vasculitic lesions may be found in that inflammatory magma [9, 12].

Gradually, the tissue is replaced by fibrosis. The periaortic infiltrate in Ormond’s disease is comparable to that of inflammatory abdominal aortic aneurysm.

Severe aortic atherosclerosis and damage to the aortic media is usually, however not uniformly, present.

The breaching of the media has raised the suggestion that retroperitoneal fibrosis develops as an autoimmune response to antigens within the severely atherosclerotic aorta [13]. In some cases, the immune reaction is triggered by an external agent, and some drugs are implicated, namely methylsergide, methyldopa and β-blockers [3]. These agents act as haptons, triggering a hypersensitivity or autoimmune reaction. Methylsergide is a strong serotonin antagonist, causing a rebound serotonin release following prolonged intake. In patients with carcinoid tumors, again, serotonin or its metabolites has been found to trigger the immune response.

The association of the disease with familial, as well as connective tissue diseases suggests a role for genetic factors [14]. As an example, the human leukocyte antigen (HLA) B27, present in ankylosing spondilitis, has also been demonstrated in several patients with retroperitoneal fibrosis [15].

Further investigation also showed an association with the abundant presence of plasma cells. These cells are rich in immunoglobulins, specifically the IgG class 4 (IgG4). The findings led investigators to implement the term “hyperimmunoglobulin G4 syndrome” [16].

PATHOGENESIS

Sixty to 70% of retroperitoneal fibrosis cases are idiopathic [4, 17-18]. Associated etiologic factors comprise the rest of the conditions leading to secondary disease, Table I.
Some connective tissue diseases have been associated with retroperitoneal fibrosis [9, 11, 13, 19] (Table II).

### CLINICAL FEATURES

Symptoms are vague and nonspecific, leading to a late diagnosis (6-12 months following the onset of physical complaints) [9-10].

The peak incidence in adults is around 40-60 years of age [6]. Presentation in childhood is extremely rare, with around 33 cases in patients younger than 18 years of age being reported [19-20].

In around 90% of the cases, the most common symptoms are colicky poorly localized pains in the lower abdomen, flanks, back or scrotum [21]. Fever, thrombophlebitis and lower limb edema are also reported. Uncommon nonspecific symptoms include anorexia, nausea, vomiting and weight loss.

Review of the literature reveals reports of Raynaud’s phenomenon, limb claudication and urinary symptoms, such ureteral colics, hematuria and frequency. Another rare and confusing manifestation of idiopathic retroperitoneal fibrosis is scrotal involvement and edema, resulting from the extrinsic compression of the gonadal venous and lymphatic systems [22-23], making the presentation of our patient unique.

Patients with autoimmune conditions such as inflammatory bowel disease and sclerosing cholangitis may have associated retroperitoneal fibrosis.

As such, diagnosis requires a high degree of suspicion.

The disease progresses through two clinical stages: an early stage, related to the onset of the inflammatory process, and a late stage, due to compression and entrapment of the retroperitoneal organs [21]. Symptoms can be grouped as early and late, as in table III.

### DIAGNOSIS

As previously stated, diagnosis of retroperitoneal fibrosis requires a high index of suspicion.

Confirmatory laboratory results include: elevated inflammatory markers (such as ESR, CRP and alkaline phosphatase), normocytic normochromic anemia (compatible with chronic inflammatory disease), raised urea and creatinine levels (in 50 to 75% of cases due to ureteral entrapment), and polyclonal hypergammaglobulinemia (and hyper IgG4 [16]).

Imaging may include intravenous pyelography (IVP), showing medially deviated and narrowed ureters, with proximal dilatation and various degrees of hydronephrosis. The middle third portion is the most involved. These findings, however, are not specific for retroperitoneal fibrosis [10]. Ultrasound is used as well, revealing clearly marginated and markedly hypoechogenic retroperitoneal infiltrative masses. As for the CT scan, it shows a sharply marginated homogeneous soft tissue mass encasing the ureters and abdominal aorta, enhancing with contrast. The inferior vena cava may be encased between the renal hila and the sacral promontory [10]: Magnetic resonance imaging (MRI) is the diagnostic method of choice, revealing the chronic retroperitoneal mass with intermediate T1 signal intensity, and low T2 intensity.

Despite the advances in imaging techniques, a biopsy is required for histological confirmation, and differentiation of idiopathic retroperitoneal fibrosis from secondary retroperitoneal fibrosis due to other causes.

### MANAGEMENT

Goals of management are to preserve renal function, prevent organ involvement and relieve symptoms, which require integration of both surgical and nonsurgical therapies.

Empirical treatment regimen includes corticosteroids and immunosuppressive therapies.

Corticosteroids offer beneficial effects through anti-inflammatory actions, and inhibition of fibrotic tissue maturation. In 2002, Van Bommel [24] reported a satisfactory outcome with corticosteroids, however, despite their successes, the use of these agents as first-line therapy is still controversial. A standard protocol is prednisolone 40-60 mg/day, tapered to 10 mg/day within two to three months, and discontinued within one to two years.

Combining corticosteroids with azathioprine or peni-
Retroperitoneal fibrosis is a rare disease, occurring as primary Ormond’s disease, or secondary to many etiological factors. Diagnosis is based on a high index of suspicion, as symptoms are vague, and the disease is insidious. Treatment is a combination of medical and surgical therapy, and future immune modulators and disease-modifying agents are promising. Because of asymptomatic recurrences of retroperitoneal fibrosis, patients require close follow-up.

REFERENCES