Retroperitoneal Fibrosis

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KEYWORDS

• Retroperitoneal fibrosis • Chronic periaortitis • Review • Management

KEY POINTS

- Retroperitoneal fibrosis (RPF) is a fibroinflammatory disorder of unknown etiology that surrounds the infrarenal aorta and may progress to surrounding structures.
- A lack of standardized definition of disease, small numbers of patients, and differing end points in research publications has limited our efficiency in understanding the optimum treatment.
- There are currently 5 different diseases that lead to infrarenal periaortitis: inflammatory abdominal aortic aneurysm, perianeurysmal retroperitoneal fibrosis, RPF, Erdheim-Chester disease, and immunoglobulin G4–related disease.
- Management includes alleviation of urinary obstruction and Immunosuppressive therapy.

INTRODUCTION

Retroperitoneal fibrosis (RPF) is a condition characterized by the presence of inflammation and fibrosis in the retroperitoneal space. Unfortunately, no standard definition exists that clearly defines the criteria that must be present for the diagnosis of RPF. It is this ambiguity that has made formal investigation into this disease challenging and comparison of multiple different reports vulnerable to misinterpretation. As a starting point, most agree that a pathologic specimen obtained anywhere in the retroperitoneum indicating fibrosis is not sufficient for the diagnosis of RPF. Rather, the salient feature that must be present is the radiographic finding of periaortitis. There are currently 5 different diseases that lead to infrarenal periaortitis: inflammatory abdominal aortic aneurysm (IAAA), perianeurysmal retroperitoneal fibrosis, RPF, Erdheim-Chester disease (ECD), and immunoglobulin G4 (IgG4)-related disease. In most reports IAAA, perianeurysmal retroperitoneal fibrosis, and RPF have been lumped together for the purposes of analysis. ECD, while sharing some similar radiographic features, has a distinct histologic and clinical presentation. IgG4-related disease was not recognized as a possible isolated condition until 2003. It is unclear how many, if any, of these patients were included in analyses of patients with RPF.

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Because no standard definition exists, it is important to establish the definition to be used when reviewing the literature on RPF. The following must be present:

1. A soft-tissue density surrounding the infrarenal aorta or iliac vessels by contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI).
2. Absence of a biopsy in the retroperitoneum that is positive for malignancy.
3. Absence of a systemic, multicentric, fibrosis processing such as IgG4-related disease.

RPF begins with clinical symptoms of flank pain and unexplained weight loss. Radiographically, fibrosis starts to surround the infrarenal aorta, and progresses inferiorly toward the iliac bifurcation and laterally toward the renal hilum and surrounding structures, ultimately leading to ureteral obstruction and acute renal failure. Historically, treatment has focused on relieving the obstruction with percutaneous or cystoscopic assisted placement of ureteral stents followed by more definitive resolution of ureteric obstruction with open or laparoscopic ureterolysis, with or without omental wrapping.

Over the past several years, case reports and small series have documented successful, nonsurgical management with the use of various immunosuppressive agents including prednisone, cyclosporine, methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil (MMF), infliximab, rituximab, colchicine, and the selective estrogen receptor antagonist tamoxifen.[1–10] Management therefore has shifted from primarily a surgical approach to a therapy aimed at modulation of the immune system.

This review focuses on the recent advances in the classification, epidemiology, pathophysiology, pathology, imaging, and treatment of these disease states.

DEMOGRAPHICS

Patients with RPF present to medical attention in the fifth, sixth, and seventh decades of life with a mean age of 54 years.[11] There is a slight male to female predominance with ratios ranging from 1:1 to 3:1, depending on the report.[11–14] All races appear to be affected equally. Few epidemiologic studies exist that accurately characterize the incidence and prevalence of the disease. One report from the Netherlands suggests an incidence of 0.10 per 100,000 individuals.[15]

RISK FACTORS

The proposed risk factors for RPF are listed in **Box 1**. Multiple agents have been suggested as possible etiologic factors in RPF. Of the suggested pharmacologic agents, methysergide and ergotamine are the best studied and documented. A frequently used medication to treat migraine headaches, methysergide is a serotonin antagonist. Increased circulating levels of endogenous serotonin have been suggested to lead to endocardial, pulmonary, and retroperitoneal fibrosis. RPF has been ascribed to methysergide in up to 12% of cases in older series; however, the present-day incidence is much lower, secondary to infrequent use of this medication.[16] Ergotamine-derived agents stimulate serotonergic receptors, causing proliferation of myofibroblasts and increased fibrotic deposition.[17] Although alternative agents have been found to treat migraine headaches, ergot derivatives are still used to treat Parkinsonism (pergolide, cabergoline, and bromocriptine) and the use of these agents should be specifically noted in the history.

Other medications that have been associated with RPF include β-blockers, methyldopa, phenacetin, and hydralazine.[18–23] These associations have been presented in