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REVIEW ARTICLE

Review on Retroperitoneal Fibrosis: Ormond's Disease

V. Sai Chitra Prathyusha*, Ramesh Dhani

Ratnam Institute of Pharmacy, Pidathapolur, Muthukur, SPSR Nellore, Andhra Pradesh, India.

ABSTRACT

Ormond's disease is also known as retroperitoneal fibrosis & it is a rare disease of unknown etiology, characterized by inflammation and fibrosis of the retro peritoneum resulting in compression and encasement of the ureter, and/ or the retro peritoneal blood vessels. RPF may be Primary /idiopathic (most common) or secondary (eg., drug-reduced, inflammatory iatrogenic) patients often present with not-specific symptoms (eg., fever, malaise, weight loss, flank pain, etc) Bilateral apteral obstruction, with subsequent hydro nephritis and obstructive nephropathy, is common. Diagnosis is often suspected in patents who present with bilateral hydro nephrosis of unknown etiology. Contrast CT is the diagnostic test of choice and reveals a retriperitoneal mass encasing and obtstructing the ureters and/or the aorta and IVC diagnosis is confirmed on CT guided biopsy of the mass High dose glucocorticoids are the mainstay of treatment of primary RPF secondary RPF is managed by treating the underlying cause (stopping the offending drug, treating the infection, etc) Symptomatic/severe obstruction of the retroperitoneal structures require treatment cureteric stenting, uteceric stenting, ureterolysis, arterial stenting etc) prognosis of non-malignancy – induced RPF is good, but recurrence rates are high (70%).

Keywords: Retroperitoneal fibrosis, bilateral hydro nephrosis, glucocorticoids, IVC diagnosis, flank pain.

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CORRESPONDING AUTHOR
V. Sai Chitra Prathyusha
Ratnam Institute of Pharmacy,
Pidathapolur, Muthukur,
SPSR Nellore, Andhra Pradesh, India.
MS-ID: WJPBT3639

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CONTENTS

1. Introduction

Ormond's disease is a disease featuring the proliferation of fibrous tissue in the retroperitoneum, the compartment of the body containing the kidney's aorta, renal tract, and various other structures. It may present with lower back pain, kidney failure, hypertension, deep vein thrombosis and other obstructive symptoms. It is named after John kelso Ormand, who rediscovered the condition in 1948.

Retroperitoneal fibrosis (RPF)

It is a condition that has previously been described as chronic periaortitis. It is an uncommon fibrotic reaction in the retroperitoneum that typically presents with ureteric obstruction. The disease is part of a spectrum of entities that have a common pathogenic process consisting of an inflammatory response to advanced atherosclerosis of the abdominal aorta, combined with autoimmunologic factors:

- Idiopathic retroperitoneal fibrosis (IRF)
- Perianeurysmal retroperitoneal fibrosis
- Isolated periaortitis: corresponds to a non-aneurysmal form of chronic periaortitis
- Inflammatory abdominal aortic aneurysm (IAAA)

Idiopathic retroperitoneal fibrosis

Idiopathic retroperitoneal fibrosis (IRF) is a subtype of retroperitoneal fibrosis where no obvious cause is found. It includes a spectrum of diseases which are characterized by fibro inflammatory tissue encasing the abdominal aorta and the iliac arteries. This process may extend into the retroperitoneum often enveloping the adjacent structures e.g. ureters.

Inflammatory abdominal aortic aneurysm (IAAA)

Inflammatory abdominal aortic aneurysm (IAAA) is a variant of abdominal aortic aneurysm (AAA) characterized by inflammatory thickening of the aneurysm wall, perianeurysmal fibrosis and adherence to surrounding structures.

Perianeurysmal retroperitoneal fibrosis

Retroperitoneal fibrosis causing ureteral obstruction in association with an abdominal aortic aneurysm has been reported infrequently. The diagnosis of an abdominal aortic aneurysm with perianeurysmal fibrosis was made only at the time of surgery to repair bilateral ureteral obstruction It is important to consider the presence of an occult abdominal aortic aneurysm in patients suspected of having retroperitoneal fibrosis because of the serious prognostic and therapeutic implications..

Isolated periaortitis

Periaortitis may be a local immune response to antigens like oxidized low density lipoproteins and ceroid found in the atherosclerotic plaques of the abdominal aorta. The disease tends primarily to involve the vascular structures causing stenosis of the major branches of the abdominal aorta (e.g. coeliac trunk, superior mesenteric artery, renal arteries).

2. Epidemology

Prevalence: Rare (1 per 2, 00,000-5,00,000 of the general Population) Primary /Idiopathic RPF: most common (70% of the cases)

Peak age of Incidence: 40-60 Years.

Sex:- …..>…..(2:1)

- Primary / Idiopathic retroperitoneal fibrosis
- Immune reaction to antigens within aortic atherosderotic plaques.
- Systemic autoimmune disease of large arteries > periaortic inflammation
- Inflammation and fibrosis in the Periaortic.
- IGg4-related disease (immunoglobulin) G4 related disease) characterized by an infiltration of various organs by.
- IgG4- bearing Plasma cells which cause inflammation and fibrosis
- Secondary retroperitoneal fibrosis:
- Drugs: Ergot alkaloids (methysergide, ergotamine)
- Dopamine agonists : pergolide, methyldopa
- B-blokers, analgesics (Phenacetin), Hydralazine etc.
- **Biological agents:** Infliximab, etanercept etc.
- **Malignancies:** Primary retroperitoneal malignancies, retroperitoneal metastates, carcinoid fumours.
- **Infections:** Mycobacterium tuberculosis, actinomycosis histoplasmosis.
- **Latrogenic:** Surgery or radiation therapy to the retroperitoneal hemorrhage > Tobacco use.
- Enposure to asbestos.
- Malignancies and exposure to methysergide are the most commoncauses of secondary RPF 1

Pathophysiology:

The etiological factors incite an immune response in the retroperitoneum – Inflammation of the retroperitoneal tissue – healing by fibrosis. Fibrosis can entrap & obstruct retroperitoneal structures.

3. Causes and clinical features

Causes: Its association with various immune- related conditions and response to immune suppression have led speculation regarding an autoimmune cause of Idiopathic RPF. One third of the causes are secondary to malignancy, medication (methysergide, hydralazine) (beta blockers), aortic aneurysm, or certain infections.

Clinical features:

- Pain in the lower back/flanks (most common Symptom)
- Constitution Symptoms: Fever, anorexia, weight loss, nausea etc.
- Specific Symptoms.
- Ureters > Upper urinary tract obstruction.
- **Hydronephrosis:** and features of chronic renal failure (obstructive nephropathy uremia, hypertension, etc)
- Infrarenal aortaliliac arteries > chronic mesenteric ischaemia, lower limb and gluteal claudication pain,etc.
- Inferior venacaval iliac veins > deep vein thrombosis, renal vein thrombosis.
- Gonadal vessels > hydrocaele, varicocoele testicular pain.

- Cymphatic channels > cymphedema.

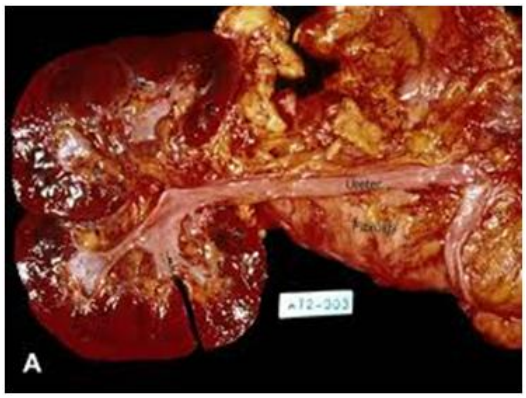

Figure 1: Retroperitoneal Fibrosis

- Ormond's disease is a diffuse or localized fibroblastic proliferation associated with chronic inflammation.
- Although benign, this lesion can be locally aggressive, with compression or obstruction of the ureters and vascular structures, including the aorta.
- Cause is unknown, but frequent association with immune disease and response to steroids suggests being immune-related (hyper-immunoglobulin G4 syndrome: elevated serum IgG4 and plasma cells are IgG4+).
- Gastrointestinal involvement is unusual, but may occur.

Clinical:

- Usually occurs in adults; rarely in children.
- Patients present with a history of pain in the lower abdomen, flank, or lower back.
- One third of cases associated with drugs (esp. methysergide, adrenergic blocking agents and methyldopa).
- May occur with malignancies (lymphoma, sarcoma or carcinoma), trauma or immune-mediated connective tissue disease.
- May be a part of multiple fibro sclerosis (systemic idiopathic fibrosis).

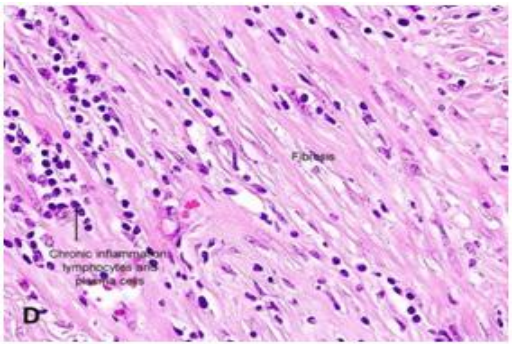

Figure-2: Idiopathic Retroperitoneal Fibrosis

Gross: ill-defined fibrous mass usually centered at the 4th and 5thlumbar vertebrae and often encasing one or both ureters (hydronephrosis) and/or vasculature as well (image A).

Histology:

- Fibroblastic proliferation with densely hyalinized collagen.
- Variable (but generally obvious) chronic inflammatory infiltrate composed of lymphocytes and plasma cells (image B), (image C), & (image D).
- IgG4 positive plasma cells are present.
- Germinal center formation may occur with marked inflammation.

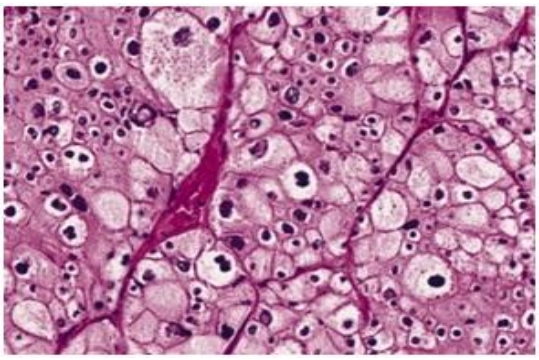

Figure -3: Retroperitoneal Fibrosis

4. Retroperitoneal cavity

- Retroperitoneal fibrosis can be drug-induced, malignancy-related or idiopathic.
- A proportion of cases of idiopathic retroperitoneal fibrosis (Ormond's disease) are considered to represent IgG4 –RD.
- Main affected sides are regions around thoracic and lumbar spine, abdominal aorta and branching arteries, and ureters.

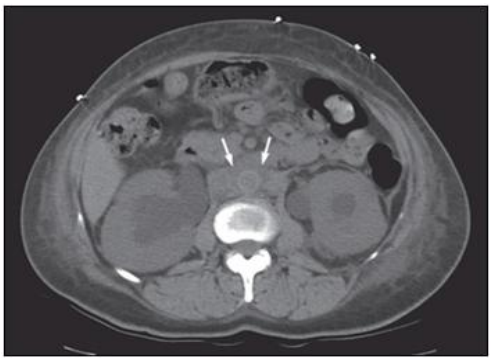

Figure-4: Perianeurysmal Retroperitoneal Fibrosis

A slowly progressive condition of unknown etiology, characterized by deposition of fibrous tissue in the retroperitoneal space compressing the ureters, great vessels, bileduct, and other structures. When associated with abdominal aortic aneurysm, it may be called chronic periaortitis or inflammatory perianeurysmal fibrosis.

Objective:

Perianeurysmal fibrosis (PAF) with involvement of neighboring viscera can render open repair of inflammatory aneurysms technically difficult and therefore hazardous. For this reason, endovascular repair (EVAR) has been advocated

as the preferred approach for this condition. EVAR is known to induce a systemic inflammatory response in patients but the nature of the local response remains unknown. If significant, such a response could exacerbate rather than ameliorate PAF. The aim of the study was to examine the incidence, course and consequences of perianeurysmal fibrosis detected by computerized tomography (CT) before and after EVAR. Material and Methods: the clinical records of patients treated by EVAR and followed for at least 6 months were reviewed. Pre and post-operative CT images were independently graded for PAF by three radiologists according to a standard protocol. Results: PAF was documented preoperatively in six out of a total of 61 patients. In two of these PAF worsened after EVAR resulting in ureteric obstruction and hydronephrosis requiring ureteric stents. In the remaining 4 patients PAF did not reduce postoperatively. PAF of low grade developed postoperatively in 10 out of 55 patients (18%) in whom there was no evidence of PAF on preoperative imaging. Median follow-up was 18 months (range 6–36 months). The development of periaortic fibrosis de novo postoperatively was statistically significant (McNemar's test p=0.002). Conclusion: EVAR does not seem to reverse PAF if this is present preoperatively and it induces this condition in approximately one sixth of patients without evidence of preoperative PAF. The potential for this adverse inflammatory local response should be taken into account when considering EVAR for treatment of aneurysms with perianeurysmal fibrosis and must be weighed against the perceived benefits of this approach.

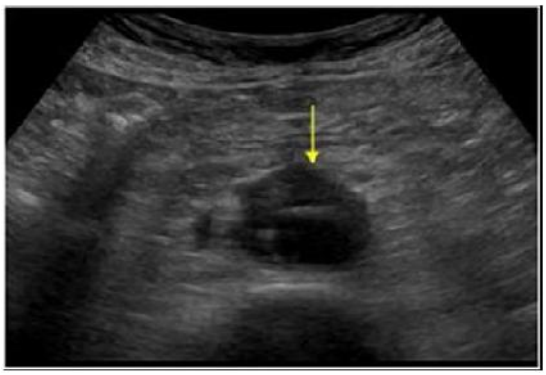

Figure-5 Retroperitoneal Fibrosis –Abdominal Aortic Aneurysm (AAA)

Atherosclerotic aneurysms occur most frequently in the abdominal aorta (abdominal aortic aneurysm, often abbreviated the common iliac arteries, the arch, and descending parts of the thoracic aorta can also be involved Pathogenesis AAA occurs more frequently in men and rarely develops before age 50. Atherosclerosis is a major cause of AAA other contributors include: hereditary defects in structural components of the aorta (e.g., defective fibrillin production in Marfan disease affects elastic tissue synthesis) an altered balance of collagen degradation and synthesis mediated by local inflammatory infiltrates and the destructive proteolytic enzymes.

Abdominal aortic aneurysm (AAA or triple A) is a localized enlargement of the abdominal aorta such that the diameter is greater than 3 cm or more than 50% larger than normal diameter. They usually cause no symptoms except when ruptured. Occasionally, abdominal, back, or leg pain may occur. Large aneurysms can sometimes be felt by pushing on the abdomen. Rupture may result in pain in the abdomen or back, low blood pressure, or loss of consciousness, and often results in death. AAAs occurs most commonly in those over 50 years old, in men, and among those with a family history. Additional risk factors include smoking, high blood pressure, and other heart or blood vessel diseases. Genetic conditions with an increased risk include Marfan syndrome and Ehlers-Danlos syndrome.

5. Diagnosis

The Diagnosis of retroperitoneal fibrosis cannot be made on the basis of results of laboratory studies. CT is the best diagnostic modality. A confluent mass surrounding the aorta can be seen on a CT scan. Although biopsy is not usually recommended, it is appropriate when malignancy or infection is suspected. Biopsy should also be done if the location of fibrosis is atypical or if there is an inadequate response to initial treatment.

- Diagnostics
- Laboratory tests:
- Raised inflammatory markers elevated CRP and ESR.
- Renal Parameters blood urea nitrogen, serum creatinine and serum electrolyte levels.
- Auto antibodies: eg: Ana cantinentrophilic antibody) ANCA (antineutrophilic Cytoplasmic antibody).

Imaging:

- Contrast – enhanced CT Scan
- Investigation of choice to diagnose RPF

Finding:

- Para – aortic mass: extending from the renal arteries to the common iliac arteries.
- Encasement and /or compression of the areters, IVC, and/or aorta.
- May identify malignancies.
- MRI and MRA: Useful in patients in whom contrast administration is contraindicated.
- Intravenous urography and retro grade pyclography
- Reneal Ultrasonography: Useful in assessing response to therapy

Biopsy (Confirmatory test):

- CT – guided/Laparoscopic biopsy of the retroperitoneal mass.
- Early stage: Hyper vascular tissue with perivascular Lymphocytic infiltrate and lipid laden macrophages.
- Late Stage: Avascular fibrous tissue which is devoid of cells.

6. Treatment

- In the absence of severe urinary tract obstructions (which generally requires surgery with omental wrapping), treatment is generally with glucocorticoids initially followed by DMARDS

either as steroid as steroid –sparing agents or if refractory on steroids. The SERM tamoxifen has shown to improve the condition in various small trails, although the exact mechanism of its action remain unclear.

- Associations include:
- Riedel's thyroiditis
- Previous radiotherapy
- Sarcoidosis.
- Inflammatory abdominal aortic aneurysm
- Drugs.

Medical Therapy:

Primary RPF:

- Oral high dose glucocorticoids : First line therapy with high dose prednisone (Img/kg/day for the first month)
- Tamoxifen: Indicated as monotherapy in patients with contraindications to glucucorticoid therapy.
- Immuno suppressants: Indicated in glucocorticid resistant disease.

Secondary RPF:

- Treatment of the underlying etiology: - e.g., discontinue the causative drug, treat.
- Chronic infections, treatment of Lymphoma, etc.
- Oral High dose glucorticoids : Indicated in Symptomatic /sever drug – induced cases of secondary RPF.

Decompression of obstructed retroperitoneal structures:

- Kidneys and ureters (treatment of upper tract obstruction)
- Conservative therapy:
- Patients with mild hydronephrosis and normal renal parameters respond well to medical therapy alone.
- Mild hydroneprhosis with abnormal renal parameters: Cystoscopy guided ureteric stenting.
- Obstructive nephropathy: urgent decompression with percutaneous nephrostomy followed by surgery.
- Surgical decompression : Open/laproscopic ureterolysis (release of the ureter from fibrotic tissue)
- Aorta (or) iliac arteries; See "Revascularization" in peripheral arterial disease.
- IVC (or)iliac veins : see "Treatment" in deep vein thrombosis.

Prognosis:

- Prognosis of non-malignancy induced RPF is good, with symptomatic and clinical improvement obvious within a few weeks of initiating therapy.
- High recurrence rates of idiopathic RPF.
- Poor prognosis of malignancy – Induced RPF.

Associations include:

- Riedel's thyroiditis.
- Previous radiotherapy
- Sarcoidosis
- Inflammatory abdominal aortic aneurysm
- Drugs.

Primary RPF:

Oral high –dose glucorticoids: First line therapy with high dose prednisolone (Lmgl/kg/day for the first month)

Tamoxifen: Indicated in glucocorticid-resistant disea.

7. Conclusion

John Ormond is credited with the first description of idiopathic RF in the English literature. Seventeen years later, he speculated correctly that the disease was systemic and was in the same group of diseases as lupus, scleroderma and periarteritis. Presently, idiopathic RF is considered part of a recently defined group of diseases known as IgG4-related diseases. The disease is generally treated with medical therapy but surgery is needed if there is a ureteric obstruction.

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