

CLINICAL VIGNETTE

Deep Vein Thrombosis /Pulmonary Embolism in a patient with Retroperitoneal fibrosis: A case Report

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Case Report

A 62-year-old obese Caucasian male with hypertension on chronic beta-blocker therapy for two years presented with sub-acute left sided non-radiating lower back pain for 5 days. He had no history of trauma, fever, abdominal surgeries or other recent illness. He was afebrile and normotensive. Physical examination was non-revealing except for mild bilateral pedal edema. Initial labs included a mild WBC elevation with normal Hgb and platelets. Comprehensive metabolic panel, amylase and lipase were normal. Sedimentation rate (ESR) was 20. C-reactive protein (CRP) was normal. The edema was described by the patient as long standing, symmetric and was thought to be due to venous stasis. Blood and urine cultures were negative. Echocardiography revealed moderate LV dysfunction, with ejection fraction of 45%. Computerized Tomography (CT) scan with contrast of the abdomen and pelvis revealed large segments of inflammatory stranding involving the periaortic retroperitoneum extending from the kidneys to the pelvis, encasing the left Iliac veins. Differential diagnosis included mesenteric infarction, lymphoma, and metastatic mass. Magnetic Resonance Imaging (MRI) showed an abnormal soft tissue mass in left para-aortic region without signal characteristics to differentiate the pathology. CT guided retroperitoneal core biopsy showed fibrofatty tissue admixed with lymphoplasmacytic infiltrate with scattered lymphoid aggregates accompanied by infiltration of eosinophils and numerous foamy macrophages. Immunohistochemistry demonstrated normal distribution of CD20 -positive B-cells and CD3-positive B-cells without coexpression of CD5. A diagnosis of RPF was made given the clinical, imaging and pathological presentation and the patient was started on prednisone 40 mg daily. His beta-blocker therapy was stopped.

Two months later, patient presented with acute shortness of breath and increasing left lower extremity

edema. There was no history of trauma, long travel, infection or any other precipitating events. Electrocardiogram showed new atrial fibrillation, raising concern for possible pulmonary embolism. Lower extremities Doppler revealed occlusive left sided popliteal DVT. CT Angiography demonstrated segmental and sub-segmental pulmonary emboli of the right lower lobe. The patient was anticoagulated with heparin and bridged to warfarin before discharge after 5 days. Repeat CT scan three months later showed stable retroperitoneal mass with no further progression.

Introduction

Retroperitoneal fibrosis (RPF) is a clinicopathological condition characterized by inflammatory fibrotic reaction around infrarenal aorta, iliac vessels and surrounding retroperitoneum with myriad presentations¹.

RPF has estimated incidence of 1-2 per 100,000². Given the rarity of the condition the diagnosis may be missed if not included in the initial differential diagnosis. Early diagnosis and treatment may help avoid complications including Deep Venous Thrombosis (DVT), Pulmonary Embolism (PE), renovascular hypertension, ureteral obstruction, and Chronic Kidney Disease³. Although the disease process is better understood, lack of diagnostic criteria and treatment protocols still remain a challenge.

Discussion

RPF most commonly presents with dull, aching low back or flank pain. Systemic features of inflammation like weight loss, anorexia, fever, easy fatigability are common presenting symptoms. Patients can also present with local complications including renovascular hypertension, lower extremity edema, hydrocoele, and DVT⁴. Idiopathic cases account for

nearly two third of the presentations.

Beta-blockers, including metoprolol and eye drops containing timolol have been reported to associated with RPF⁵. Other reported medications include Ergot derivatives⁶, hydralazine⁷, bromocriptine⁸, methyldopa⁹ and pergolide¹⁰. Lymphomas, gastric and pancreatic cancers are also associated with RPF¹¹. In addition, radiation therapy³ has been found to be a significant risk factor associated with RPF. Prior surgery¹² and infections like tuberculosis¹³ actinomycosis¹⁴ and schistosomiasis¹⁵ have been reported to cause RPF.

Although the pathogenesis is poorly understood, recent suggest autoimmune mechanisms. Proposed hypothesis include excessive immune reaction in response to steroid and oxidized LDL molecules in localized aortic atherosclerosis¹⁶. RPF has been described in association with certain autoimmune diseases like thyroiditis and in association with the HLA-DRB1*03 allele¹. IgG4 bearing plasma cells may also play a role¹⁷.

Investigators have proposed a staging system based on imaging. Stage I RPF has fibrosis limited to infra-renal aorta or iliac vessels; stage II involves progression of fibrosis to inferior vena cava. Stage III further lateral extension of fibrosis occurs causing compression of the ureters and in stage IV the renal vessels are also involved. The same investigators also proposed diagnostic criteria for idiopathic RPF in the absence of aneurysmal dilatation of the aorta or any mass in pelvic and abdominal cavity³.

Imaging remains the mainstay in diagnosing RPF. CT and MRI are preferred to identify and stage the disease process¹⁸. On MRI, RPF appears hypointense on T1 weighted images and hyperintense on T2 weighted images¹.

Fluorodeoxyglucose positron emission technology (PET) has potential to identify other involved sites, associated autoimmune or neoplastic disorders and for surveillance of disease activity¹⁹. Biopsy can identify disease histopathology²⁰. It may be required when infection or malignancy is strongly suspected, if the location of lesion is atypical raising doubt about the diagnosis, or if surgical intervention is being planned.

Treatment of RPF can include both medical and surgical measures depending on the presentation. Stopping possible inciting medications is the first step. Our patient had been on chronic beta-blocker therapy for two years. It was stopped and steroids were started and the patient remained stable for three

months. Steroids are first line therapy in the absence of mass effect such as compression of surrounding structures, vascular extension into the surrounding veins and arteries, compression of ureters or organ function compromise. Steroid resistant disease can be treated with other immunosuppressive agents including cyclophosphamide, methotrexate, mycophenolate mofetil²¹ colchicine²² and tamoxifen²³.

Disease activity can be followed with serial imaging including contrast enhanced CT, MRI and PET. Measuring Serum Ig4 level²⁴ ESR/CRP²⁵ and renal function may also be helpful, though this remains to be validated in larger studies. If the disease does not respond to these measures, the diagnosis should be reconsidered and other causes ruled out. Ureteral entrapment and consequent renal dysfunction is one of the most recognized complications of RPF³. Studies have shown that incidence of DVT and PE is also increased in patients with RPF and prophylactic anticoagulation should be considered on a case by case basis if patients have evidence of inferior vena cava and/or iliac vessel involvement causing venous stasis and lower extremity edema³. To our knowledge there have been no randomized trials evaluating the duration of treatment and prophylactic use of anticoagulation in this patient population. A strong argument can be made for more frequent imaging surveillance i.e every 3 to 6 months, to assess the progression of disease in lieu of anticoagulation.

Conclusion

Our patient presented with lower extremity edema and imaging revealed extension of RPF to involve common iliac vessels. With beta-blockers as a possible inciting event, RPF causing iliac vein compression and venous stasis followed by DVT/PE. A-fib may be a very important symptom of PE especially in patients who had their beta blockers discontinued recently.

REFERENCES

1. **Vaglio A, Palmisano A, Corradi D, Salvarani C, Buzio C.** Retroperitoneal fibrosis: evolving concepts. *Rheum Dis Clin North Am.* 2007 Nov;33(4):803-17, vi-vii. Review. PubMed PMID: 18037118.
2. **Uibu T, Oksa P, Auvinen A, Honkanen E, Metsärinne K, Saha H, Uitti J, Roto P.** Asbestos exposure as a risk factor for retroperitoneal fibrosis. *Lancet.* 2004 May 1;363(9419):1422-6. PubMed PMID: 15121404.
3. **Scheel PJ Jr, Feeley N.** Retroperitoneal fibrosis: the clinical, laboratory, and radiographic presentation. *Medicine (Baltimore).* 2009 Jul;88(4):202-7. PubMed PMID: 19593224.

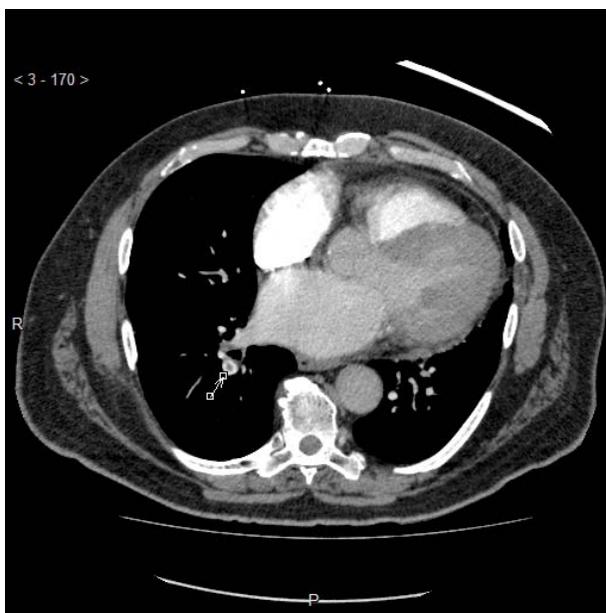
4. **Vaglio A.** Retroperitoneal fibrosis: new insights into clinical presentation and diagnosis. *Medicine* (Baltimore). 2009 Jul;88(4):208-10. PubMed PMID:19593225.
5. **Bullimore DW.** Retroperitoneal fibrosis associated with metoprolol. *Br Med J* (Clin Res Ed). 1982 Feb 27;284(6316):664. PubMed PMID: 6802283; PubMed Central PMCID: PMC1496203.
6. Fibrosis due to ergot derivatives: exposure to risk should be weighed up. *Prescrire Int.* 2002 Dec;11(62):186-9. PubMed PMID: 12472101.
7. **Waters VV.** Hydralazine, hydrochlorothiazide and ampicillin associated with retroperitoneal fibrosis: case report. *J Urol.* 1989 Apr;141(4):936-7. PubMed PMID: 2926894.
8. **Herzog A, Minne H, Ziegler R.** Retroperitoneal fibrosis in a patient with macroprolactinoma treated with bromocriptine. *BMJ.* 1989 May 13;298(6683):1315. PubMed PMID: 2500220; PubMed Central PMCID: PMC1836500.
9. **Ahmad S.** Methyl dopa and retroperitoneal fibrosis. *Am Heart J.* 1983 Jun;105(6):1037-8. PubMed PMID: 6858825.
10. **Apostolakis EE, Baikoussis NG, Tselikos D, Koniari I, Prokakis C, Fokaeas E, Karanikolas M.** Cardiac surgery in a patient with retroperitoneal fibrosis and heart valvulopathy, both due to pergolide medication for Parkinson's disease. *J Cardiothorac Surg.* 2009 Nov 13;4:65. PubMed PMID: 19912629; PubMed Central PMCID:PMC2780395.
11. **Vaglio A, Salvarani C, Buzio C.** Retroperitoneal fibrosis. *Lancet.* 2006 Jan 21;367(9506):241-51. Review. PubMed PMID: 16427494.
12. **Katz R, Golijanin D, Pode D, Shapiro A.** Primary and postoperative retroperitoneal fibrosis-experience with 18 cases. *Urology.* 2002 Nov;60(5):780-3. PubMed PMID: 12429295.
13. **Greco P, Vaglio A, Corradi D, Cobelli R, Zompatori M, Buzio C.** Tuberculosis as a trigger of retroperitoneal fibrosis. *Clin Infect Dis.* 2005 Oct 1;41(7):e72-5. Epub 2005 Aug 31. PubMed PMID: 16142654.
14. **Milam MR, Schultenover SJ, Crispens M, Parker L.** Retroperitoneal fibrosis secondary to actinomycosis with no intrauterine device. *Obstet Gynecol.* 2004 Nov;104(5 Pt 2):1134-6. PubMed PMID: 15516426.
15. **Rollino C, Guzman H, Beltrame G, Ferro M, Quattrocchio G, Bellis D, Quarello F.** Retroperitoneal fibrosis and schistosomiasis: a causal relationship? *Eur J Intern Med.* 2008 Jun;19(4):297-9. Epub 2008 Feb 20. PubMed PMID: 18471683.
16. **Parums DV.** The spectrum of chronic periaortitis. *Histopathology.* 1990 May;16(5):423-31. Review. PubMed PMID: 2193863.
17. **Oguchi T, Okada M, Endo F, Hattori K, Fujisaki A, Ikeda M, Shiga Y, Yashi M, Muraishi O.** [IgG4-related idiopathic retroperitoneal fibrosis: a case report]. *Hinyokika Kyo.* 2009 Dec;55(12):745-8. Japanese. PubMed PMID: 20048557.
18. **Vivas I, Nicolás AI, Velázquez P, Elduayen B, Fernández-Villa T, Martínez-Cuesta A.** Retroperitoneal fibrosis: typical and atypical manifestations. *Br J Radiol.* 2000 Feb;73(866):214-22. PubMed PMID: 10884739.
19. **Piccoli GB, Consiglio V, Arena V, Pelosi E, Anastasios D, Ragni F, Fiori C, Cortese G, Deagostini MC, Porpiglia F, Scarpa RM.** Positron emission tomography as a tool for the 'tailored' management of retroperitoneal fibrosis: a nephro-urological experience. *Nephrol Dial Transplant.* 2010 Aug;25(8):2603-10. Epub 2010 Feb 15. PubMed PMID: 20157170.
20. **Cavalleri A, Brunner P, Monticelli I, Mourou MY, Bruneton JN.** CT-guided biopsy in two cases of retroperitoneal fibrosis. *Clin Imaging.* 2008 May-Jun;32(3):230-2. PubMed PMID: 18502353.
21. **Swartz RD.** Idiopathic retroperitoneal fibrosis: a review of the pathogenesis and approaches to treatment. *Am J Kidney Dis.* 2009 Sep;54(3):546-53. Epub 2009 Jun 10. Review. PubMed PMID: 19515472.
22. **Vega J, Goecke H, Tapia H, Labarca E, Santamarina M, Martínez G.** Treatment of idiopathic retroperitoneal fibrosis with colchicine and steroids: a case series. *Am J Kidney Dis.* 2009 Apr;53(4):628-37. Epub 2008 Dec 31. PubMed PMID: 19117656.
23. **Frankart L, Lorge F, Donckier J.** Tamoxifen for retroperitoneal fibrosis. *Postgrad Med J.* 1997 Oct;73(864):653-4. PubMed PMID: 9497980; PubMed Central PMCID: PMC2431468.
24. **Marumo K, Tatsuno S, Noto K.** Elevated serum IgG4 may predict sensitivity to steroid therapy in retroperitoneal fibrosis. *Int J Urol.* 2009 Apr;16(4):427. PubMed PMID: 19416408.
25. **Magrey MN, Husni ME, Kushner I, Calabrese LH.** Do acute-phase reactants predict response to glucocorticoid therapy in retroperitoneal fibrosis? *Arthritis Rheum.* 2009 May 15;61(5):674-9. PubMed PMID: 19404998.

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Figure Legend



Computerized Tomographic scan showing the iliac veins incased by fibrosis (Red Arrow)



Computerized Angiography Revealing Sub-Segmental Pulmonary Arterial Emboli (Black Arrow)