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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 presentations[1].

RPF has estimated incidence of 1-2 per 100,000[2]. 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 Disease[3]. 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 DVT[4]. 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 RPF[5]. Other reported medications include Ergot derivatives[6], hydralazine[7], bromocriptine[8], methyldopa[9] and pergolide[10]. Lymphomas, gastric and pancreatic cancers are also associated with RPF[11]. In addition, radiation therapy[3] has been found to be a significant risk factor associated with RPF. Prior surgery[12] and infections like tuberculosis[13] actinomycosis[14] and schistosomiasis[15] 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 atherosclerosis[16]. RPF has been described in association with certain autoimmune diseases like thyroiditis and in association with the HLA-DRB1*03 allele[1]. IgG4 bearing plasma cells may also play a role[17].

Investigators have proposed a staging system based on imaging. Stage I RPF has fibrosis limited to infrarenal 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 cavity[3].

Imaging remains the mainstay in diagnosing RPF. CT and MRI are preferred to identify and stage the disease process[18]. On MRI, RPF appears hypointense on T1 weighted images and hyperintense on T2 weighted images[1].

Fluorodeoxyglucose positron emission technology (PET) has potential to identify other involved sites, associated autoimmune or neoplastic disorders and for surveillance of disease activity[19]. Biopsy can identify disease histopathology[20]. 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, mycophemolate mofetil[21] colchicine[22] and tamoxifen[23].

Disease activity can be followed with serial imaging including contrast enhanced CT, MRI and PET. Measuring Serum Ig4 level[24] ESR/CRP[25] 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 RPF[3]. 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 edema[3]. 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.

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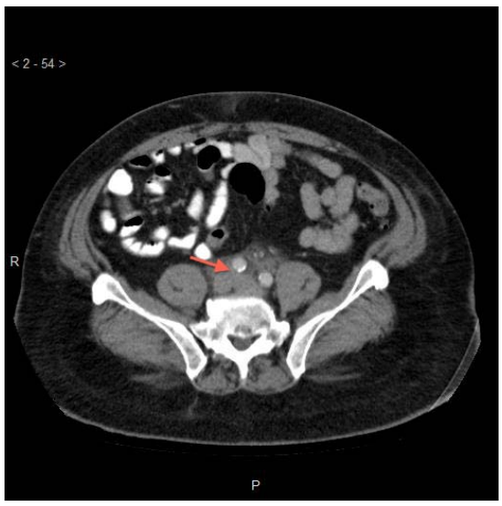
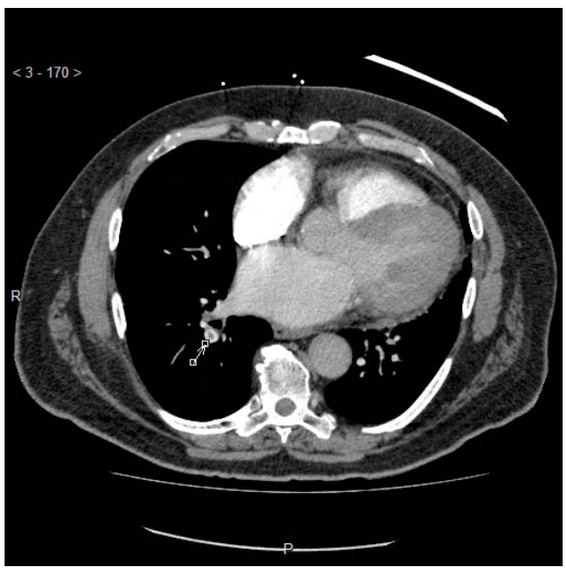
Figure Legend



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



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