CLINICAL VIGNETTE

Takayasu's Arteritis with Coronary Ectasia, Sclerosing Cholangitis and Liver Cirrhosis

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Introduction

Takayasu's arteritis (TA) is a relatively rare chronic idiopathic inflammatory granulomatous arteritis that primarily affects large arteries such as the aorta, its main branches, and the pulmonary arteries.[1] The disease process results in stenosis, thrombosis, and aneurysm formation of the arteries. Stenotic vascular lesions are reportedly more common than aneurysmal lesions.[2] The inflammatory process appears to begin at the vasa vasorum at the border of the media and adventitia and then extends to the adventitia, media, and intima of blood vessels. In chronic phase, there is adventitial and intimal thickening, disruption of elastic fibers, fibrosis, and scarring in the media.[3] Coronary artery involvement has been reported in 10% of TA patients.[4] Inflammatory involvement of coronary arteries may lead to arterial wall thickening and stenosis and, in rare cases, weakening of the arterial wall and formation of coronary aneurysm.[5]

We present the case of a young female with TA and asymptomatic coronary arteries ectasia. Interestingly, the patient also was found to have sclerosing cholangitis (SC) and resulting liver cirrhosis, an association with TA that has not been reported in medical literatures, which highlights the complexity in the clinical management of the patient in regards to starting anti-platelet therapy for prevention of ischemic cardiovascular events.

Case Presentation

A 23-year-old Latino female with history of TA, sclerosing cholangitis, and liver cirrhosis was referred to cardiology for evaluation. Her story dates back to the age of 9 when she was found to be hypertensive (blood pressure 240/120) during an inguinal hernia repair surgery. Her workup included a computed tomography angiography (CTA) at age 10, which revealed active severe arteritis of large vessels of type V Takayasu's distribution including ascending aorta, aortic arch and its branches, thoracic descending aorta, abdominal aorta, and renal arteries. She was managed with low-dose steroids, cyclophosphamide, and methotrexate, as well as antihypertensive medications. Her initial laboratory tests were within normal limits. Eight years after her initial diagnosis, she was tapered off of her cytotoxic medications with satisfactory blood pressure controlled on only one antihypertensive medication and normal renal function. During subsequent follow-up visits, she was found to have some elevated blood pressures and started to complain of both lower extremities claudication symptoms after walking two blocks, as well as abdominal pain especially with larger meals. Magnetic resonance angiography (MRA) of the chest and abdomen was obtained and revealed a normal-caliber ascending aorta, aortic arch, and descending thoracic aorta, as well as narrowing of the infrarenel aorta and prominent thoracic and lumbar collateral arteries, suggestive of significant infrarenal aortic occlusive disease (Figure 1). The left renal artery showed some irregular areas, suggestive of possible underlying stenosis. Multiple areas of parenchymal abnormalities with cortical loss and scarring were also found in the left kidney, suggesting the possibility of underlying renal infarctions.

The patient eventually underwent an angiography for further evaluation of renal artery stenosis and possible endovascular intervention. Angiography revealed only an approximately 10% stenotic left renal artery with areas of post-stenotic dilatation and a patent right renal artery without evidence of stenosis. It also confirmed significant disease of the infrarenal aorta with diameter of less than 10 mm. Additionally the lateral aortogram demonstrated approximately 40% stenosis of celiac artery with a patent superior mesenteric artery but significant occlusive branch disease beyond the first large branch artery. Given that there was no critical stenosis of left renal artery and considering technical difficulty, it was decided that the risk was prohibitive for interventional procedure on left renal artery. CTA of the abdomen and pelvis further revealed irregular areas of focal narrowing in the common iliac arteries. The external iliac arteries were small and irregular in caliber. However both internal iliac arteries were relatively well-preserved and appeared to provide collaterals to the common femoral arteries via femoral circumflex arteries.

As the workup was being completed, the patient developed elevated serum aminotransferase levels (alanine aminotransferase (ALT) of 111, aspartate aminotransferase (AST) of 117), alkaline phosphatase (ALP of 800), and was referred to a hepatologist for further evaluations. MRI and MRCP of the abdomen revealed a macrolobulated liver with ill-defined areas of T2 hyperintensity in the liver, compatible with fibrosis as well as tortuous vessels in porta hepatic, suggesting portal venous occlusion with developed collaterals. It also showed mild dilatation of the central intrahepatic bile ducts as well as multiple short-segment stenosis, the characteristic beaded appearance suggestive of sclerosing cholangitis. A subsequent liver needle biopsy showed grade 2 inflammation and stage 4 fibrosis, compatible with cirrhosis. An esophagogastroduodenoscopy demonstrated mild to moderate esophageal varices in the distal esophagus. Immunoglobulin G4 (IgG4), perinuclear antineutrophil cytoplasmic antibodies (p-ANCA), cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA), anticardiolipin (aCL) antibodies, antinuclear antibodies (ANA), anti-mitochondrial antibodies (AMA), smooth-muscle antibodies (SMAs), and liver-kidney microsomal type 1 (LKM-1) were all negative. Only double-stranded DNA (dsDNA) antibodies showed a moderate increase.

She also developed palpitations with exercise and was referred to the cardiology clinic. Twelve-lead electrocardiogram and Holter monitoring were normal. A transthoracic echocardiogram (TTE) showed normal left and right ventricular size with quantitated left ventricular ejection fraction of 53%. Additionally TTE showed trileaflet aortic valve with mild aortic insufficiency, mild tricuspid regurgitation, mild mitral regurgitation, normal pulmonary artery pressure, and mild pulmonary regurgitation. Dilated right and left coronary arteries were noted (at least 7mm and 9 mm, respectively) (Figure 2 A-C).

The patient underwent CTA of the coronary arteries, which revealed ectatic proximal right coronary artery (Figure 3) and left main stem coronary artery, suggestive of changes related to prior inflammation. Similarly, there was mild irregularity and ectasia of the proximal brachiocephalic artery and irregularity of the proximal portion of the left common carotid and left subclavian artery. The thoracic aorta showed scattered calcification compatible with sequelae related to prior inflammation.

Discussion

The presence of coronary aneurysm, even in the absence of obstructive disease, is believed to change blood flow dynamics, which can promote thrombus formation and predispose to myocardial ischemia and infarction.[6] However, coronary aneurysms rarely progress to vascular rupture.[7] Corticosteroids remain the standard of care for the treatment of TA, although the effect of corticosteroids on coronary artery aneurysms is not well defined.[8] Surgical management has been recommended for patients with coronary ostial stenosis to prevent myocardial ischemia. The management of coronary artery aneurysm in TA, however, is more controversial. Anti-platelet therapy alone or in addition to anticoagulation has been used for medical management of patients, although, there are some reports of surgical management of coronary artery aneurysms in TA.[8]

Our patient presented with liver cirrhosis, coagulopathy, and significant esophageal varices, which further complicated the management of coronary artery aneurysm with anti-platelet therapy; therefore, the decision was eventually made not to start anti-platelet therapy due to the greater risk of bleeding.

Another challenging issue is her lower extremities claudication, which in turn has led to ambulatory dysfunction and a sedentary lifestyle. Our patient is not a good candidate for general anesthesia given her liver cirrhosis. Furthermore, she has significant aortoiliac disease, which further complicates an aortic bifemoral bypass. The extra-anatomical bypass may be considered as an alternative to the anatomical aortic intervention for her in future.

Another interesting finding in our patient was the association of sclerosing cholangitis with TA. The clinical manifestations of TA preceded SC and the development of liver cirrhosis. Both SC and TA are relatively uncommon disorders. Although the precise mechanism of SC is not well understood, autoimmune process is believed to be involved. The association of SC with autoimmune vasculitides like polyarteritis nodosa and giant cell arteritis suggest that the immune-mediated vascular injury may play an important role in the pathogenesis of SC.[9] Another commonly postulated theory is that sclerosing cholangitis is caused by ischemia as similar cholangiographic and histologic changes have been reported after iatrogenic biliary vascular injury.[9] Confirming whether our patient had autoimmune liver disease or her liver cirrhosis was the consequence of chronic ischemia is challenging since primary immune mediated liver disease frequently occurs in the presence of circulating autoantibodies that were absent in our patient. On the contrary, she was found to have some celiac and hepatic artery disease, although a significant arterial stenosis was not found and ischemia did not seem to be a major contributor to her underlying biliary and liver disease.

The association of TA and SC raises a number of yet unanswered questions regarding the nature of association and how they might possibly influence each other. Further research and clinical studies are warranted to determine the impact of this association.

Figures

Figure 1. MRA of the abdomen, showing stenoses of the infrarenal aorta and the common iliac arteries.

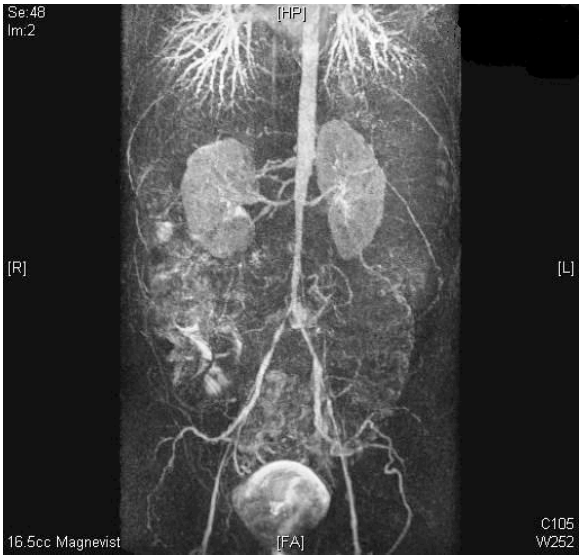
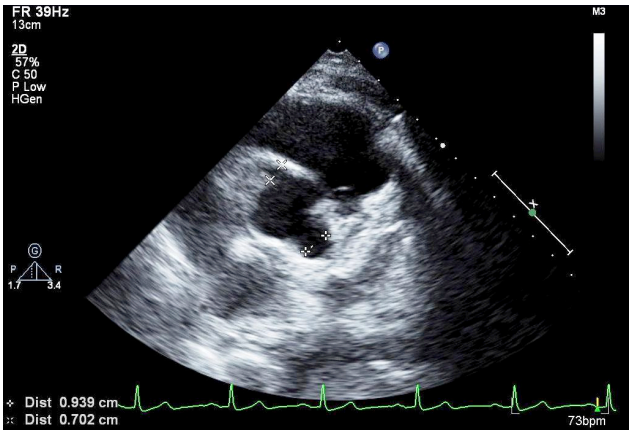
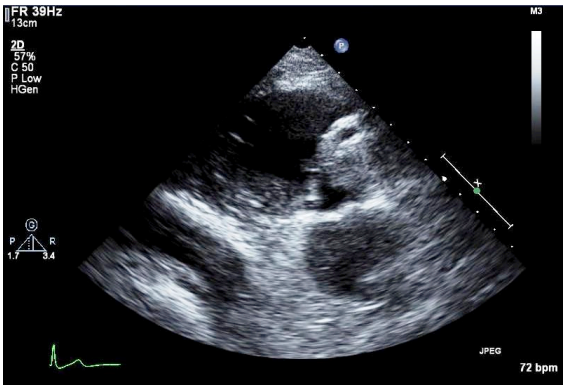


Figure 2. (a) Transthoracic echocardiography, short axis view, demonstrating ectatic right and left coronary arteries (maximum diameter of the ectatic segments 7 mm and 9.4 mm, respectively).



(b) Transthoracic echocardiography, long axis view, showing ectatic right coronary artery.



(c) Transthoracic echocardiography with color doppler, long axis view, showing flow through the proximal right coronary artery.

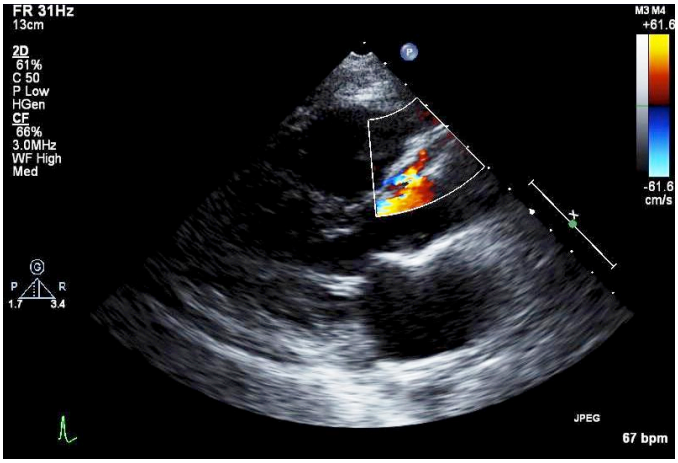
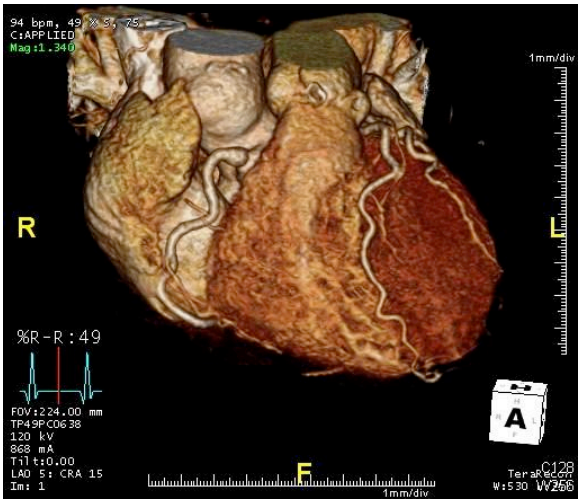


Figure 3. Three-dimensional (3D) reconstruction CTA image, showing proximal ectasia of the right coronary artery.



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