Case Report

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Tocilizumab and Renal Artery Stent- Therapeutic Strategy for Takayasu Arteritis

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Abstract

Takayasu vasculitis (TAK) is a form of large vessel vasculitis clinically manifesting as pulseless disease or hypertension. It is more common in South East Asia and Japan, India, and Mexico[1]. It is increasingly being recognized due to increased awareness among the medical fraternity and better imaging modalities. Undetected hypertension, pulselessness, and syncope are more common symptoms, and presentation during pregnancy is unusual but, unfortunately, might lead to bad pregnancy outcomes with eclampsia. Once diagnosed in pregnancy, it would be difficult to control BP and prevent the inevitable miscarriage. Recent evidence supports the use of tocilizumab for inducing remission in Takayasu arteritis. We report this rare case of vasculitis presenting in pregnancy as malignant hypertension. A 20-year-old pregnant woman (45 days) presented with a headache and found BP 180/110. She had a history of intermittent claudication of her legs for the past three years but was not evaluated. She had two missed abortions. During the examination, apart from high BP, pulses were felt normally, no murmurs in cardiac auscultation, but she had abdominal bruit (renal vessels), and other systems were normal. Her pregnancy test was positive in urine, and serum HCG (human chorionic gonadotrophin) levels were 5643 m IU /ml. Blood investigations showed anemia (Hb 9.8mg/dl) elevated CRP (12mg/L), ESR (60mm/hr). White blood cell count (6200/cu mm), ECG showed left ventricular hypertrophy. ECHO showed dilated ascending aorta, mild Aortic regurgitation, and left ventricular hypertrophy. Ultrasound abdomen showed no ascites or organomegaly. Doppler of renal vessels showed features of narrowing of renal arteries. (severe stenosis on the right and left side showed normal caliber). Unfortunately, she had to undergo termination of pregnancy (high BP).She then had a CT angiogram showing features of Takayasu arteritis with type 5 pattern - She had methylprednisolone induction followed by Tocilizumab 400 mg monthly three doses. Once remission was achieved, she had recanalization by percutaneous transluminal angioplasty with stenting of infrarenal abdominal aorta & right renal artery. Her BP was 130/70 and 110/80 in the right and left upper limbs following the angioplasty. She is currently maintained on aspirin and telmisartan. Awareness of causes of high BP, inputs by radiologists, cardiologists, rheumatologists, and understanding by the patient and family helped achieve a good outcome, albeit the miscarriage. The appropriate intervention helped to control the BP and thereby to achieve remission of vasculitis early.

Background

Takayasu arteritis (TAK) is a rare, chronic large vessel vasculitis affecting the aorta and its branches up to the pelvis. Clinical manifestations are varied and relate to the vessel affected by stenotic lesions, such as the aortic arch (pulseless disease), descending thoracic or abdominal aorta (atypical coarctation), renal arteries, coronary arteries, and pulmonary arteries and reflect end-organ ischemia. It is a condition which most commonly affects young women in the second or third decade of life, originating mainly from

Asia and Eastern Europe. This may lead to the development of severe vascular complications, such as stenosis, aneurysms, and aortic dissection. Poor prognostic features lead to major complications or pregnancy loss. Type IV and V angiographic classification (i.e., involvement of entire aorta and its branches) is an independent predictive factor for high disease activity in TAK. Predicting the outcome of the disease is challenging because of the wide variation in the course of TAK.

Takayasu Arteritis classification criteria: (ACR Classification Criteria 1990)

- Age of onset < 40
- Claudication of extremities
- Decreased brachial artery pulse
- Greater than 10mm Hg difference in systolic blood pressure between the arms.
- A bruit over the subclavian artery or the aorta or renal bruit
- Arteriographic evidence of narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities.

(3 or more criteria must be met for a diagnosis of the TA, having a sensitivity of 90.5% and specificity of 97.8%)[2]

Takayasu is a disease that commonly affects the women in reproductive age group; there are chances that women may want to get pregnant or is already pregnant before the diagnosis. Corticosteroids are being used mostly at diagnosis, while tocilizumab is useful as steroid-sparing treatment during the remission and maintenance phase of the treatment.

Case Report

A 20-year-old woman presented with complaints of headache and was found to have BP 170/100 on the 45th day of gestation. She had a history of intermittent claudication for the past three years and a history of two miscarriages but was not evaluated. She did not report any symptoms of giddiness, blurring of vision, chest pain, dyspnea, and palpitation. The two miscarriages were within 70 days of gestation and told BP was slightly high. She was not taking any medications.

On examination, pulse was 92/min, Blood pressure was 190/130 mm Hg in right upper limb and 186/124 mm Hg in left upper limb and abdominal bruit (likely due to the renal artery) heard, because of which renal artery narrowing was suspected. Doppler study of renal vessels was done that suggested right renal artery stenosis. Her bloods showed elevated CRP (12mg/L) & ESR (60mm/hr). She was given Labetalol and Methyldopa, despite which her BP was high (190/110 mm Hg).

Since her BP was not reduced, there was a concern about her pregnancy, so induced miscarriage was advised, and she agreed to have it done. After a miscarriage, her BP was 150/110 mm Hg.

Then she went on to have CT Aortogram,

Arch of Aorta	30% narrowing in the proximal left subclavian artery. Normal right subclavian artery.
Descending thoracic aorta	Diffusely diseased starting at the lower end of descending thoracic aorta and has smaller caliber.
Celiac artery	Ostial 60% stenosis.
Abdominal Aorta	60-70% stenosis starting just below the Right Renal artery below the superior mesenteric artery origin.
Right renal artery	80% stenosis
Left renal artery	Normal

Based upon the angiographic findings, the diagnosis was suggestive of Takayasu Arteritis Type 5.

She had active vasculitis, and as per the Rheumatologist's opinion, she was treated with methylprednisolone induction followed by Tocilizumab 400 mg monthly three doses for remission. No steroids or any second-line drugs were given. Successful remission was achieved, and then she underwent Recanalization Percutaneous transluminal angioplasty with stenting of Infrarenal abdominal aorta & right renal artery. (Figure 1, 2, 3)

PTA Stenting of Infrarenal Aorta

From left radial access, 6F pigtail catheter was taken over 035 guide wires till a level of occlusion. Then, the right common femoral artery 6F JR catheter was taken over 035 glide wire until the occlusion. A peripheral angiogram was done simultaneously from above and below.

Attempts to cross the occlusion from the left radial approach using 5F MP diagonal catheter and the Terumo glider's soft end were unsuccessful and resulted in a fast track. Hence the catheter and the wire was pulled back into the CTO segment. Retrograde probing using a 6F, JR diagnostic catheter and an 0.018/0.013 Astato 30 guidewire with both the catheter aligned resulted in guidewire passing through the CTO segment into the MP catheter kept from above. The catheter from the RFA approach was tracked up to the DTA, and the guidewire was replaced with an ASS guidewire. The lower right renal artery was marked using a diagnostic catheter and a 0.018" RR guidewire from the left radial approach.

Figure 1: Percutaneous transluminal renal angioplasty

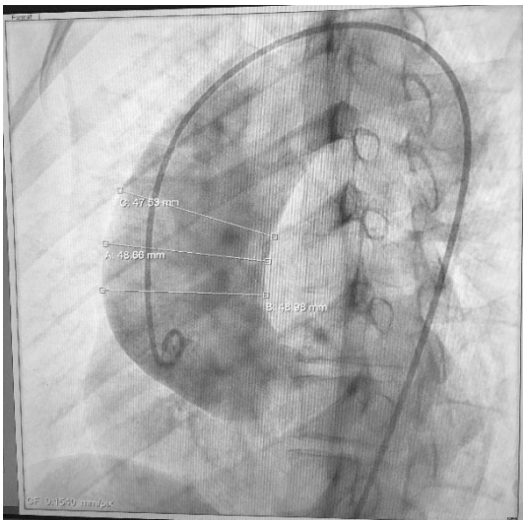

Figure 2: Aortic arch angioplasty

Figure 3: After renal stent

Covered stenting of the Infrarenal abdominal aorta:

A lifestream 10*58 mm stent was deployed at 10 atm. There was no gradient across the stented segment. The proximal end of the stent was placed below the right renal artery, and the lower end was just across the IMA. At discharge, the patient's blood pressure was 130/70 and 110/80 in the right and left upper limbs, respectively. The patient was discharged in good condition. Regular BP monitoring was advised to maintain at BP< 130/80 mm Hg. She was given Aspirin and Telmisartan on discharge. On regular follow-up, it has been observed that the patient has not developed any symptoms post-treatment with Tocilizumab, and remission has been achieved.

Discussion

Takayasu vasculitis has two phases –the active inflammatory stenosing phase and the fibrotic stenotic phase. The diagnosis of TAK should preferably be made before critical stenosis or occlusion occurs in the involved arteries. Clinical presentation often occurs during the thirties and pregnancy; patients need special attention. Malignant hypertension is a life-threatening complication that causes high mortality among TAK patients. Adequate control of BP improves the outcome. The aggressive intervention helped the BP control and paved the way for achieving remission of Vasculitis in our patient. Early diagnosis with appropriate medical or surgical management is essential for a long-term healthy life.

Assessing disease activity is essential for tailoring treatment in Takayasu arteritis.

Imaging is considered the cornerstone for the diagnosis of Takayasu arteritis. Angiography has been the criterion-standard imaging tool for the diagnosis and evaluation of TAK.

CT Angiography (CTA) is a reliable tool in non-invasively showing both luminal and mural lesions in the aorta and its main branches, which may facilitate the detection of vasculitis during the early phase of TAK. Even with effective treatment, relapse can occur in individuals with TAK. Biologics should be tried in treatment-resistant Takayasu arteritis patients. Evidence has shown that Tocilizumab is a valid treatment in critically ill patients to achieve rapid remission.[3] TCZ has been proven again to be effective in Takayasu arteritis in this case.

Apart from diagnosis, CT Angiography helps in monitoring the role of disease activity. Post Immunosuppressive therapy, studies have shown aortic wall enhancement resolves and wall thickening decreases.[4]

Treatment of TAK consists of two strategies: immunosuppressive therapy for inflammation control and management of vascular diseases, including control of blood pressure and surgical or interventional procedures. The indications for considering intervention include uncontrolled hypertension due to renal artery stenosis, severe symptomatic coronary artery or cerebrovascular disease, severe aortic regurgitation or coarctation, stenotic or occlusive lesions resulting in critical limb ischemia, and aneurysms at risk of rupture.[5]

Revascularization procedures may be performed during the inactive phase of Takayasu arteritis.

Following steroids, most patients require additional drugs- Methotrexate or Azathioprine and limited evidence are available for cyclophosphamide, mycophenolate, and cyclosporine.

Tocilizumab is a recombinant, humanized, anti-IL-6 receptor antibody that has been reported to be successful in treating patients with TAK.[6] Recently tocilizumab is an effective option in inducing and maintaining remission in both treatment-naïve as well as

refractory cases of giant cell arteritis and TA.[7] Hence long-term remission can be achieved.

Key Message

Tocilizumab can be considered for selected patients before surgical revascularization or those with contraindications for standard treatment, including steroids in Takayasu Vasculitis.

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