Early View Article: Online published version of an accepted article before publication in the final form.

Journal Name: International Journal of Case Reports and Images (IJCRI)

doi: To be assigned

Early view version published: October 12, 2017

**How to cite the article:** Sharma H, Bansiwal SK, Manocha R, Prabal R, Paras K. Takayasu arteritis: A rare presentation as pulseless disease of lower limb with middle aortic syndrome. Forthcoming 2017.

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TYPE OF ARTICLE: Case Report

TITLE: Takayasu arteritis: A rare presentation as pulseless disease of lower limb with middle aortic syndrome

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Short Running Title: Takayasu Arteritis
Guarantor of Submission: The corresponding author is the guarantor of submission.
ABSTRACT

Takayasu arteritis (TA) also known as pulseless disease is an inflammatory and stenotic disease of medium and large sized arteries characterized by a strong predilection for the aortic arch and its branches. However, it is rarely reported as a cause of middle aortic syndrome (MAS). MAS are characterized by localized or extended narrowing of the descending thoracic or abdominal aorta. Hypertension proximal to the aortic stenosis and relative hypotension distal to it, are characteristic findings in MAS. We present a case of 24 year old hypertensive male, who presented with abdominal pain, decreased urine output and lower limb claudication, found to have involvement of abdominal aorta, visceral, renal and lower limb arteries on imaging. Though it is a rare cause of hypertension, a high index of suspicion is necessary for diagnosis and early treatment.

Keywords: Middle aortic syndrome, Takayasu arteritis, Hypertension
INTRODUCTION

TA is a rare chronic inflammatory vasculitis that primarily affects young females in 2nd and 3rd decade. It occurs worldwide with wide geographical variation, mainly seen in Japan, South East Asia, India and Mexico [1]. TA has an annual incidence of 0.8 per million and prevalence of 4.7 per million. It is characterized by panarteritis with inflammatory cells in vessel wall, leading to stenosis of lumen with or without thrombosis. It usually affects subclavian artery (93%), common carotid (58%), abdominal aorta (47%), renal artery (38%) and other visceral arteries. Carotid intimal thickness, C-reactive protein, & elevated ESR are important markers for disease activity, which are followed up in TA [2].

MAS also known as coarctation of abdominal aorta, is rarely reported with TA. It may be congenital, with incomplete fusion or overfusion of the paired embryonic aortas, or acquired, such as with Takayasu or giant cell arteritis, neurofibromatosis, or retroperitoneal fibrosis [3]. This condition can also involve renal and other visceral arteries leading to hypertension and other features. American College of Rheumatology criteria (ACR), imaging and other investigations aid the diagnosis. Medical therapy is given to control hypertension and halt the progress of disease. Surgery is required to revert the hypertension and its complications, if not controlled by medical therapy.

CASE REPORT

A 24 year old male presented to us with a history of abdominal pain in right lumbar and iliac area, decreased urine output and lower limb claudication for one and a half month. Patient denied any history of fever, vomiting, shortness of breath, chest pain, hematuria or visual disturbances. Inquiry about joint pain, photosensitivity, oral ulcers and recurrent infections were not contributory. The past history was unremarkable.

On examination, the patient was conscious and oriented. His blood pressure was not recordable in both lower limbs while bilateral upper limb showed reading of 200/100 mm of Hg. Pulses of upper limb were regular and did not show any radio radial delay while in lower limbs pulses were not palpable. A head to toe examination was unrewarding. On systemic examination, a bruit was heard over the infraumbilical
region while the examination of other systems was unrewarding. Fundus examination revealed grade two hypertensive changes. Laboratory data showed hemoglobin of 11.8 g/dL (13-16g/dL) and total leukocyte count of 6,680 cells (4000-11000 cells/ul) with 68% neutrophils. Other baseline biochemical investigations were within normal limits including kidney function test, total cholesterol, serum triglycerides, serum HDL levels, 24 hour urinary protein and urine routine microscopy. Anti-nuclear antibody (ANA) test was positive with high titers (1:160) while anti ds DNA, anti-phospholipid antibody (APLA), protein C, protein S, factor V leiden, anti-thrombin, homocystiene levels were normal. HIV was non-reactive. hsCRP (C - reactive protein) with value >3mg/L (low risk < 1mg/L) and erythrocyte sedimentation rate (ESR) with value 98 mm/ hr (0-20mm/hr) were significantly raised while mantoux test was insignificant.

On chest radiography, no significant abnormality was detected while ECG and echocardiography showed left ventricular hypertrophy (LVH).

Ultrasonography of abdomen with renal doppler was done, which revealed shrunken left kidney (size 5x4 cm) and normal sized right kidney. Right renal artery and interlobar arteries demonstrated normal spectral wave forms but left intrarenal flow was decreased. There was large atheroma filled in abdominal aorta distal to superior mesenteric artery (SMA), flow in both renal arteries was showing turbulence at the site of origin of arteries which may be due to atheroma filled in aorta.

CT Angiography of thoracic aorta revealed normal aortic root, ascending aorta, arch of aorta with its branches and descending thoracic aorta (Figure 1) while CT Angiography of abdominal aorta corroborated the findings on ultrasonography and showed thrombosis, stenosis, calcification of juxtarenal, infrarenal aorta upto aortic bifurcation; complete occlusion of celiac, superior mesenteric, inferior mesenteric, left renal arteries with severe stenosis of right renal artery at origin; reformation of distal visceral arteries (collaterals) and both common iliac arteries through intercostal, lumbar, superior, inferior, epigastric and circumflex arteries (Figure 2a,2b) . For further evaluation, CT Angiography of bilateral lower limb was done which demonstrated stenosis of right anterior and posterior tibial arteries in distal third of leg with stenosis of peroneal artery in distal half, delayed opacification of
distal anterior and posterior tibial arteries on left side, suggestive of sluggish distal flow. (Figure 3a, 3b)

Using American College of Rheumatology criteria 1990, patient was diagnosed with type IV Takayasu Arteritis (4 out of 6 criteria were met) with lower limb involvement. The patient was put on anti-hypertensive: prazocin (5mg PO 12hr), amlodipine (5mg PO 24 hr), clonidine (0.25mg PO 8hr) and methyl prednisolone 250 mg / day for 5 days, tapered to maintenance dose of 7.5 mg / day. He received atorvastatin (20 mg PO 24hr) and anti-coagulation with LMW heparin (6mg SC q 12hr) and warfarin (5 mg PO 24 hr) and INR was monitored subsequently. Patient responded well to the treatment and has been on irregular follow-up. Patient was referred to vascular surgery department for further management.

DISCUSSION

TA is a rare, systemic auto inflammatory disease of young females which usually involves aortic arch and its branches. It affects the vessel walls leading to stenosis or thrombosis of vessels and thus hampers the blood supply of the concerned organs. It can result in weak pulses or loss of pulse in arms, legs and organs. For this reason it is referred as "pulseless disease". TA can have a spectrum of presentation ranging from being asymptomatic to a catastrophic disease presenting as malignant hypertension. As symptoms are non-specific and the disease is so rare that there is often a delay in detecting it.

Tuberculosis has remained an important differential diagnosis which has been ruled out in our case. American College of Rheumatology 1990 criteria (Table 1) is the most widely accepted criteria for diagnosis of TA which included arteriographic abnormality, best seen on angiography (Table 2) [4].

Type III and type IV are also known as middle aortic syndrome (MAS) (Table 2). MAS, either of congenital or acquired etiology, are a rare and important cause of hypertension in young. Hypertension is the cardinal clinical feature in MAS and is present in more than 90% of cases, weak or absent femoral pulses may be appreciated and an audible bruit are typically heard over aorta [6]. The most common anatomic form in MAS of either etiology is interrenal (19-52%), followed by suprarenal (11-40%), infrarenal (19-25%) and diffuse (12%) [3]. Stenosis of the renal
arteries is common (60-90%), with less involvement of the celiac and superior mesenteric arteries (20-40%), and infrequent involvement of the inferior mesenteric arteries [3,7,8].

High titre of ANA was attributable to autoimmune mechanism affecting large vessels, which responded to immunosuppressive agents. After excluding other connective tissue disorders affecting large vessels and hypercoagulable states, clinical and radiological assessment aided the diagnosis. Hence, a diagnosis of MAS of TA origin causing malignant hypertension in a young male patient was made. The rarity of disease has led to paucity of data in the literature.

The mainstay of treatment is to decrease inflammation with immunosuppressive drugs and to control hypertension with anti hypertensive drugs. Surgery is required if there is uncontrolled hypertension due to renal artery stenosis, extremity claudication limiting activities of daily life, cerebrovascular ischemia, moderate aortic regurgitation and ischemia due to coronary artery involvement. Our patient responded well to high dose steroids along with anti hypertensive drugs. If left untreated such patients die by age of 35 years [3,7].

Rare presentation of pulseless lower limbs in a young hypertensive male attributing to Middle Aortic Syndrome of Takayasu Arteritis origin are being highlighted in our case.

CONCLUSION

Takayasu Arteritis is a chronic systemic auto inflammatory disease of young females which usually involves large vessels, most commonly the aorta. Middle aortic syndrome of TA origin, which is characterized by coarctation of distal descending thoracic and abdominal aorta, is rarely reported as a cause of hypertension in young. Clinical examination and radiology play an important role in its diagnosis. There is a need to have a thorough workup of a young hypertensive patient, especially to differentiate congenital and acquired causes, as the course of treatment varies accordingly. A high index of suspicion is necessary for diagnosis and early treatment as the mortality is high, if left untreated.
CONFLICT OF INTEREST
None

AUTHOR’S CONTRIBUTIONS
Harshita Sharma
Group 1 - Conception and design, Acquisition of data, Analysis and interpretation of data
Group 2 - Drafting the article, Critical revision of the article
Group 3 - Final approval of the version to be published

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Paras Kathuria
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Group 2 - Critical revision of the article
Group 3 - Final approval of the version to be published
ACKNOWLEDGEMENTS

None

REFERENCES


Table 1: ACR criteria for classification of Takayasu’s arteritis[^4] (A diagnosis of Takayasu’s arteritis requires that at least 3 of the 6 criteria are met)

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Age at disease onset ≤ 40 years.</td>
</tr>
<tr>
<td>2.</td>
<td>Claudication of extremities.</td>
</tr>
<tr>
<td>3.</td>
<td>Decreased brachial artery pulse.</td>
</tr>
<tr>
<td>4.</td>
<td>Blood pressure difference &gt; 10 mm Hg.</td>
</tr>
<tr>
<td>5.</td>
<td>Bruit over subclavian arteries or aorta.</td>
</tr>
<tr>
<td>6.</td>
<td>Arteriogram abnormality.</td>
</tr>
</tbody>
</table>

[^4]: Additional details or references related to ACR criteria for Takayasu's arteritis.
Table 2: Angiographic classification of Takayasu’s arteritis (Takayasu conference, 1994)[5] (Involvement of the coronary or pulmonary arteries should be designated as C (+) or P (+) respectively.)

<table>
<thead>
<tr>
<th>Type</th>
<th>Vessel involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>Branches from the aortic arch</td>
</tr>
<tr>
<td>Type IIa</td>
<td>Ascending aorta, aortic arch, and its branches</td>
</tr>
<tr>
<td>Type IIb</td>
<td>Ascending aorta, aortic arch, and its branches, thoracic descending aorta.</td>
</tr>
<tr>
<td>Type III</td>
<td>Thoracic descending aorta, abdominal aorta, and/or renal arteries.</td>
</tr>
<tr>
<td>Type IV</td>
<td>Abdominal aorta and/or renal arteries.</td>
</tr>
<tr>
<td>Type V</td>
<td>Combined features of Type IIb and IV.</td>
</tr>
</tbody>
</table>
FIGURE LEGENDS

Figure 1: CT Angiography showing normal ascending aorta, aortic arch, descending aorta, stenosis of abdominal aorta with collateral formation

Figure 2: (A, B): CT Angiography abdominal aorta showing non visualization of left kidney and multiple collateral vessels.

Figure 3: (A, B): CT Angiography abdominal aorta and lower limbs showing non visualization of left kidney, collaterals between abdominal aorta and common iliac artery with sluggish flow in right and left anterior and posterior tibial arteries.

FIGURES

Figure 1: CT Angiography showing normal ascending aorta, aortic arch, descending aorta, stenosis of abdominal aorta with collateral formation
Figure 2 (A & B): CT Angiography abdominal aorta showing non visualization of left kidney and multiple collateral vessels.
Figure 3 (A & B) : CT Angiography abdominal aorta and lower limbs showing non visualization of left kidney, collaterals between abdominal aorta and common iliac artery with sluggish flow in right and left anterior and posterior tibial arteries.