Case Report

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An Interesting Case of Takayasu's Arteritis with an Atypical Presentation in an Adolescent Asian Girl

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ABSTRACT

Introduction: Takayasu arteritis (TA) is a chronic non-specific inflammatory disease mainly affecting the medium and large arteries and is a common cause of renovascular hypertension among young Asian females. The initial symptoms and signs vary due to the heterogeneity of affected vessels.

Case Presentation: Here we reporting a case of a rare disease in a 15 years old female presenting with abdominal distension, swelling over feet, facial puffiness lasting 1 month after which she was transferred to our hospital for further treatment. Blood Pressure showed significant discrepancy in upper limb and lower limb. Her laboratory results showed an elevated C-reactive protein and D-dimer. Also Color Doppler ultrasound and Computed Tomography Aortography (CTA) leading to diagnosis of TA, after which we started the patient on medical treatment and cardiological intervention. Vasculitis-induced renovascular secondary hypertension resulted in myocardial dysfunction, which recovered with treatment of hypertension and TA. Delayed diagnosis and lack of specific treatment could explain the extent and the clinical severity of the disease at time of hospital admission.

Conclusion: Takayasu arteritis is a relatively rare disease with various clinical manifestations, such as ascities, anasarca as in our case. Currently, there are multiple diagnostic tools and treatment options available, and more under investigation. Early, appropriate diagnosis and initiation of proper therapy could avoid further progression and reduce complications of the disease. Hence early diagnosis and treatment is warranted.

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Received: June 11, 2021; **Accepted:** June 18, 2021; **Published:** June 25, 2021

Keywords: Takayasu arteritis, Renovascular Hypertension, Vasculitis, CT Aortography

Abbreviations

HFrEF- Heart failure with reduced ejection fraction

TA – Takayasu's Arteritis

PET - positron emission tomography

DSA – Digital Subtraction Angiography

Introduction

Takayasu arteritis (TA) or nonspecific aortoarteritis, is a type of primary systemic vasculitis affecting medium and large arteries, including the aorta and its branches, pulmonary and coronary arteries [1].

Histologically, it presents as 'panarteritis', with intimal fibrous thickening, cellular infiltration and collagenous fibrosis in the media and thickened adventitia with cellular infiltration around vasa vasorum. Some researchers have proposed that cellular immunity against vascular endothelial cells causes inflammatory damage to large vessels [2, 3].

Inflammation of the vessel wall leads to wall thickening, stenosis, occlusion, dilatation, and aneurysmal formation in the affected vessels. The signs and symptoms exist due to systemic inflammation or ischemia of an organ or limb, and encompass claudication, peripheral pulselessness, murmurs, ischemic stroke, myocardial infarction, severe systemic arterial hypertension, etc [1]. The symptoms are secondary to the involved artery. The prevalence of Takayasu Arteritis in Indian patients has been reported in numerous studies. Sen et al. and Chhertri et al. have reported a female to male ratio of 1.58:1 in Indian patients [4, 5]. However, the female-to-male ratio varies, from 9:1 in Japan and 6.9:1 in Mexico to 1.2:1 in Israel [6]. TA is the most common cause of renovascular hypertension in India, China, Korea, Japan and other countries of South East Asia [7].

Furthermore, TA is associated with significant morbidity and can be life threatening. Around 20% of patients experience monophasic and self-limited disease, whereas others can have a progressive or remitting disease. Moreover, the overall 10-year survival rate for this disease is approximately 90% which can be reduced in the presence of major complications [8]. Here we present a case of TA in a 15-year-old female.

Case Presentation

A 15-year-old Asian female presented to our institution with complaints of abdominal distension, swelling over feet, facial puffiness of one month duration. There was no history of chest pain, syncope, palpitations, altered bowel habits or menstrual irregularities, abdominal pain, fever, night sweats, hemoptysis, joint pains, visual changes, eye pain or redness, headaches. The patient had no other significant past medical, surgical and family history. On general physical examination patient had mild pallor, jugular venous distension, bilateral lower extremity edema. She was afebrile, Systemic blood pressure was 146/84 mmHg in the right arm, 132/78 mmHg in the left arm but 110/78 in right leg and 112/76 in left leg in supine; oxygen saturation of 100% without supplemental oxygen, pulse was 90 beats/min and respiratory rate was 28 breaths/minute. Her cardiovascular examination showed muffled heart sounds, heart rate was regular, systolic murmur over pulmonary area, loud P2 and apex palpable in sixth intercostal space, lateral to midclavicular line. Abdominal examination revealed hepatomegaly 5 cm below costal margin, ascites and no abdominal bruits. Her central nervous system and respiratory examinations were unremarkable.

Based on the history and examination, we ordered pertinent laboratory tests along with other specific tests which revealed white blood cells (WBCs) of $10.1 \times 10^3/\mu\text{L}$, hemoglobin (Hb) of 7.4 g/dL and platelets (PLTs) of $139 \times 10^3/\mu\text{L}$, peripheral smear shows microcytic hypochromic anaemia with neutrophilic leukocytosis, elevated erythrocyte sedimentation rate (10 mm/1st hr) and C-reactive protein level (166.68 mg/L), Sr Bilirubin of 3.97 mg/dl and SGPT of 421 IU/L. The lipid panel showed sr cholesterol of 71 mg/dl (<200 mg/dl), triglyceride of 63 mg/dl (10-170 mg/dl). Her coagulation test was only significant for elevated D-dimer of 2.21 mg/L with partial thromboplastin time (PT) and activated partial thromboplastin time (APTT) both within normal limits. Mantoux test was negative. Hormonal studies, ASO and ANA titre were normal. Further CPK-MB was 35 IU/L, Sr Homocysteine level was 15.68 $\mu\text{mol/L}$, Antiphospholipid antibodies (IgM and IgG) levels were 0.32 and 0.30 COI which are negative. Blood cultures, venereal disease research laboratory test and autoimmune serological findings were negative.

Chest Xray revealed cardiomegaly with bilateral pulmonary congestion. USG abdomen s/o ascites, bilateral pleural effusion and hepatomegaly. CT Aortography shows minimal wall thickening of arch of aorta, thrombus at descending thoracic aorta which extends till D12 level, severe long segment narrowing of abdominal aorta from L1-L3 levels with thrombosis, severe narrowing of superior mesenteric and both renal arteries, severe cardiomegaly with IVC dilatation, mild pleural effusion and severe ascites. 2D Echo shows DTCMP, All cardiac chambers dilated, Severe global hypokinesia, LVEF – 22%, RV dysfunction, Type III diastolic dysfunction, moderate MR, moderate PH. Hepatic Venous Doppler s/o Venous congestion, ascites and hepatomegaly. USG aortic artery color doppler s/o circumferential thickening of intima at lower aorta, bilateral iliac arteries and femoral arteries and no thrombosis s/o aortoarteritis.

On the basis of clinical manifestations and angiographic findings, the diagnosis of Takayasu arteritis with renovascular hypertension and congestive heart failure was made. We started the patient on oral prednisone (60 mg) once daily on a tapered basis and consulted the department of vascular surgery for a possible surgical intervention. For treatment of hypertension and initiation of guideline-directed therapy for HFrEF, an angiotensin-converting enzyme inhibitor and betablocker therapy was initiated. Eventually she underwent a

Digital subtraction angiography and balloon dilation of abdominal aorta with a favorable final outcome. Inflammatory parameters normalized within 3-weeks. She was discharged from hospital.

Follow-Up

Methylprednisone was gradually reduced at a maintenance dosage of 12 mg/day. She remained free of symptoms. Repeat 2D-Echo after one month shows LVEF improved to 28%. After initial improvement patient lost to follow up further and after 8 months demised due to discontinuation of treatment.

Discussion

Takayasu's arteritis (TA), also known as 'Aortoarteritis', is a rare and chronic idiopathic inflammatory condition which is most frequently observed in young women. The prevalence of Takayasu Arteritis in Indian patients has been reported in numerous studies. Sen et al. and Chhertri et al. have reported a female to male ratio of 1.58:1 in Indian patients [4, 5]. Although the female-to-male ratio varied from 9:1 in reports from Japan, 6.9:1 in Mexico to 1.2:1 in Israel [8, 9]. Though TA is predominantly a disease of young adults in the second and third decades of life, but not uncommon in childhood and in adults older than 40 years [10, 11]. The youngest patient described was 1.5–4 months and the oldest one was 75 years [12-14]. Our patient was a 15-year-old female.

The etiology of the disease remains unknown. Tuberculosis was proposed as a predisposing factor. Various other mechanisms such as autoimmunity and genetic predisposition have been proposed [15].

The nature of the disease is autoimmune, involving arterial walls resulting in panarteritis [1, 9].

TA damages vasculature through transmural infiltration of arterial walls by inflammatory cells, causing granuloma formation [16]. Classically, TA affects large vessels, specifically the aortic arch and its major branches [6].

Pediatric TA is a common form of childhood chronic vasculitis that has various clinical manifestations. Even today, the rate of under diagnosis and misdiagnosis is high due to atypical symptoms. The clinical course of the disease is divided into an early active inflammatory phase and late chronic phase. The active phase lasts for weeks to months and may have a remitting and relapsing course. It should be highlighted that the correct diagnosis of TA is seldom made in the early phase [15]. The late chronic phase is the result of arterial stenosis and/or occlusion and ischemia of organs.

This case represents an atypical presentation of TA in a young Asian woman with ascites, anasarca, HFrEF and severe hypertension. TA is the most common cause of renovascular hypertension in India, China, Korea, Japan and other countries of South East Asia [5-8].

The majority of Indian patients had hypertension at the time of presentation and only 16% of patients had constitutional symptoms of fever weight loss and arthralgia. Hypertension has been a predominant feature in most of the studies from India [16, 17]. It commonly results from the involvement of renal arteries (involved in 90% cases in different series). Kumar A et al. reported that for young patients with renovascular hypertension, the predominant cause was TA (69.4%) [18].

The mechanism of hypertension in TA is not well defined but likely involves mechanical vascular obstruction, neural activation

of baroreceptors from aortic arch involvement, and hormonal factors. TA involves the renal arteries, resulting in stenosis in 23% to 31% of cases, leading to activation of the renin-angiotensin-aldosterone-system (RAAS), contributing to severe hypertension. Heart failure has been described as a comorbidity in 13.2% of TA patients. Kumar A et al. reported the presence of congestive cardiac failure in patients of TA. It was related to hypertension and the possible involvement of myocardium has also been described by Talwar et al. The incidence of aortic regurgitation has been low (7- 115%) in many series from India but Subramaniyan et al. have reported a higher incidence (24%) [17-20].

A detailed careful physical examination, and appropriate laboratory tests are needed in all cases to determine the type of onset, course of illness, organ systems affected, and extent of involvement. The main finding is absent pulse(s) or a pulse discrepancy of greater than 10 mm Hg between the right and left arms. Other significant signs include vascular bruits, focal neurologic deficits, hypertension, retinal ischemia and microaneurysms, eclampsia, subarachnoid hemorrhage, leg edema, heart failure, and rarely, anginal symptoms.

In our patient, initial physical examination demonstrated reduced pulse and discrepancy of BP in UL and LL, which raised suspicion of Takayasu arteritis. According to a recent study, individual physical examination findings had poor sensitivity and good to excellent specificity [19].

Diagnosis can be made using Modified Ishikawa's criteria or American College of Rheumatology criteria or Sharma criteria [21].

Table I: Ishikawa's Criteria for the Diagnosis of Takayasu's Arteritis [21]

The Vessels involved	Clinical features
1. Aortic branches	Malaise, decreased or absent pulse of upper extremities, dysfunction of upper extremities, headaches, dizziness, vision and orientation disturbances, syncope.
2. Aortic arch	Congestive heart failure, aortic valve insufficiency, arterial hypertension.
3. Coronary arteries	Ischemic heart disease, myocardial infarction.
4. Pulmonary arteries	Chest pain, dyspnea, coughing, hemoptysis, congestive heart failure.
5. Abdominal aorta or celiac trunk	Ischemia of the stomach and intestines, abdominal pain, nausea, vomiting
6. Renal arteries	Arterial hypertension, chronic renal failure

A diagnosis of TA is primarily based on clinical and radiological findings, as the results of biopsy are nonspecific as the histopathology may imitate other types of vasculitis [18].

Overall, CTA and Doppler both have great sensitivity and specificity in terms of the diagnosis of Takayasu arteritis, and they are able to show early changes in the vessel wall that DSA fails to illustrate.

In our setting, we conducted 2D Echo, DSA and the findings were sufficient to achieve a diagnosis of TA.

The method we did not use on this patient is positron emission tomography (PET) due to unavailability and unaffordability of patient.

As seen in our patient, Takayasu arteritis can cause severe damage to the overall health condition and quality of life, or even be life-threatening sometimes. So it would be beneficial to diagnose the disease at an early stage. Several biomarkers have been suggested by recent studies which include IL-6, matrix metalloproteinase (MMP)-2, MMP-3, MMP-9 and pentraxin 3 (PTX3). But all of these biomarkers are still under investigation [22].

Management includes combination of medical therapy with oral steroids and corrective vascular intervention in suitable cases [14-18].

Immunosuppressants such as prednisone and/or methotrexate can lead to significant improvement [9].

Anti-inflammatory therapy can lead to a dramatic improvement in TA. Therapy is continued until patients achieve remission. Hypertension is treated with antihypertensive agents, and aggressive therapy is necessary to prevent complications.

As most of Indian patients present in the chronic phase, steroid therapy has not been used very commonly, though it is being employed more frequently than in the past [20].

In the presence of symptomatic stenotic or occlusive lesions, endovascular revascularization procedures like bypass grafts, patch angioplasty, endarterectomy, percutaneous transluminal angioplasty, or stent placement should be taken into consideration in addition to medical therapy [18].

Khalilullah et al., Sharma et al. and Kumar et al. have reported a high success rate with percutaneous transluminal angioplasty of renal, subclavian and iliac artery lesions [23-25]. In our patient by DSA we conducted ballon dilatation at the affected aortic site.

A high degree of clinical suspicion along with appropriate imaging techniques is required for an accurate diagnosis.

Conclusion

Takayasu arteritis is a relatively rare disease with various and sometimes devastating clinical manifestations that is both diagnostically and therapeutically challenging to physicians, such as HFrEF as the initial presentation in our case. Early appropriate diagnosis and initiation of proper therapy could avoid further progression and reduce complications of the disease.

In this case, complete myocardial recovery was achieved with guideline-directed medical therapy, adequate blood pressure control, immunosuppression and surgical intervention for TA.

Data Availability

All data underlying the results are available as part of the article and no additional source data are required.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A

copy of the written consent is available for review by the Editor-in-Chief of this journal.

Declaration

Authors declare no conflicts of interest. Authors declare that no financial assistance was taken from any source. Authors declare that they have no commercial or proprietary interest in any drug, device, or equipment mentioned in the submitted article.

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