A rare case report of Familial Takayasu arteritis

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ABSTRACT

Takayasu arteritis (TA) is a chronic, idiopathic, inflammatory and stenotic disease of medium and large-sized arteries. The disease is more common in middle aged women. We report a 40 year female (mother) who presented with complaints of claudicating pain in both her lower limbs and upper limbs on her daily activities. On examination pulses were absent in both upper limbs and on further inquiring about her family history similar symptoms were experienced by her daughter. On further clinical examination and Radiodiagnostic technique, both females were fitting into the American College of Rheumatology criteria (ACR) for Takayasu arteritis. The etiology of TA is still unknown, but this case and review of literature indicates that there are genetic factors that play a major role in development of TA. Hence we should maintain a high index of suspicion for the possibility of TA in the siblings or other family members of affected patients.

Key words: Familial Takayasu arteritis, claudication

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INTRODUCTION

Takayasu arteritis (TA) is an inflammatory and stenotic disease of medium and large sized arteries characterized by a strong predilection for the aortic arch and its branches.[1] For this reason, it is often referred to as the "Aortic arch syndrome". TA is a chronic, idiopathic large vessel vasculitis.[2,3] The disease is more common in females. It is predominant in Asian countries, although it has a worldwide distribution.[4] The exact etiopathogenesis of TA still remains unknown. Infections such as tuberculosis, autoimmunity and genetic factors may play a role in its pathogenesis.[5] Usually patients present with dizziness, malaise, fever, night sweats, arthralgias, syncope, feeble or absent pulse and hypertension. In 1951, Shimizu and Sano proposed the term 'Pulseless disease' to describe the triad of: (a) absent radial pulsation, (b) signs and symptoms referable to hyperactive carotid sinus reflex, (c) hypotensive ophthalmoangiopathy.[6] In Southeast Asia and Africa, middle aortic syndrome, narrowing of descending thoracic and abdominal aorta with renovascular lesions, is more common. There are associations between HLA alleles and TA as described in few review articles but the results are heterogeneous and they vary among different groups of population.[7, 8, 9] A review of the literature suggests that familial TA may not be as rare as once thought and this finding may have both etiological and clinical implications for family screening.[4] Here, we report a case of familial TA in a 40-year-old mother and 22-year-old daughter.

CASE: 1

This is a case of 40 year female (mother) who presented with complaints of claudicating pain in both lower limbs and upper limbs while doing her routine work (for 1 year and worsening since 2 months). On examination pulses were absent in both upper limbs, blood pressure was not recordable in both the upper limbs. It was recorded 160/100 mm

Hg in right lower limb and 150/90 mm Hg in the left lower limb. Carotid bruit was heard on the left side and abdominal bruit present on the right side. On cardiac auscultation, findings correlated with aortic regurgitation. On investigation, her ESR was 105 mm/1st one hour and CRP was 2.6 mg/dL.

Blood urea was 57 mg/dL, serum creatinine was 1.8 mg/dL and her creatinine clearance was 34.7 ml/minutes. Complete urine examination showed mild proteinuria. Ultrasonography of abdomen suggested findings of shrunken left kidney and uterine fibroid. Echocardiogram showed moderate aortic regurgitation, good left ventricular function, no regional wall motion abnormality, no mitral regurgitation and no clots. CT and MRI Angiogram of the aorta showed diffused mild stenosis of descending thoracic aorta and severe stenosis of left renal artery. Mild stenosis was noted in the left common carotid artery.

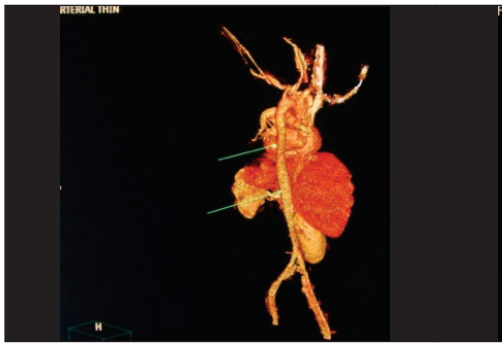

Figure 1a

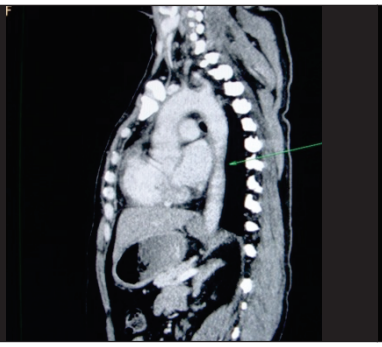

Figure 1b

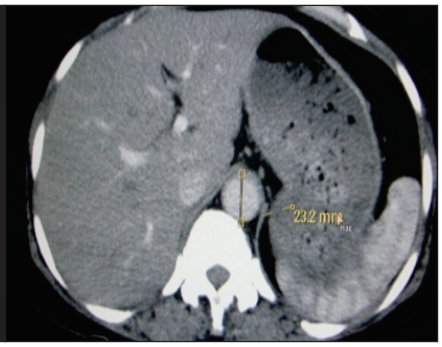

Figure 1c

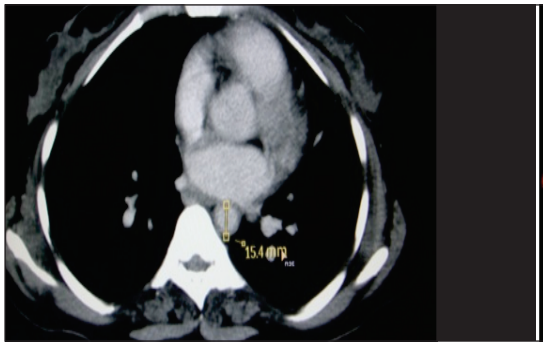

Figure 1d

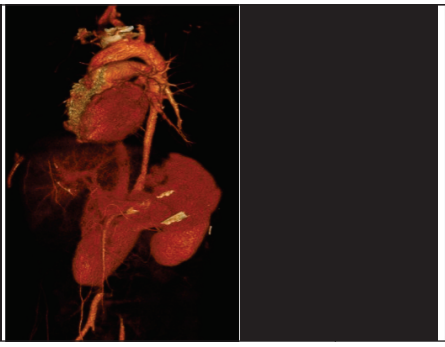

Figure 2a

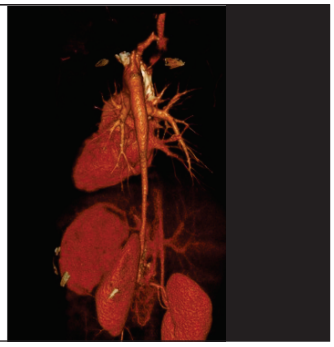

Figure 2b

Figure 1a-1d: CT angiogram showing diffuse mild stenosis of the descending thoracic aorta. Mild stenosis noted in left common carotid artery, in Case 1.

Figure 2a-2b: CT angiogram of abdominal aorta showed diffuse stenosis in abdominal aorta, extending from diaphragmatic hiatus to the level of bifurcation of aorta. Moderate stenosis of origin of coeliac trunk. Mild stenosis at the origin of both renal arteries, in Case 2.

CASE: 2

Her daughter, aged 20 years, upon inquiry had similar complaints of claudicating pain in both upper and lower limbs while doing her daily household work. On examination peripheral pulses could not be appreciated, blood pressure was not recordable in upper limbs and it was 140/80 mm Hg in right lower limb and 110/70 mm Hg in left lower limb. Bilateral carotid bruit was heard, but more on the right side. Abdominal bruit present on both sides. On investigation, ESR was 40 mm/1st one hour and CRP was positive (1.2mg/dL). Blood urea was 26 mg/dL and serum creatinine was 0.9 mg/dL. Complete urine examination reveals no proteinuria. Carotid Doppler showed bilateral intimal hyperplasia. Near total occlusion of left common carotid and internal carotid arteries was noted. Echocardiography reveals trivial aortic regurgitation, good left ventricular systolic function, normal sized chambers, no clot and no pericardial effusion. CT angiogram of abdominal aorta showed severe stenosis in abdominal aorta, extending from diaphragmatic hiatus to the level of bifurcation of aorta. A moderate to severe stenosis was present at the origin of coeliac trunk and mild stenosis was present at the origin of both renal arteries. In view of carotid artery stenosis, MRI

cerebral angiogram was done, which showed proximal and distal stenosis of left subclavian artery, right distal part of common carotid artery stenosis noted. Diffuse stenosis in left common carotid artery and internal carotid artery were noted. Near total occlusion of left common carotid artery was also noted.

DISCUSSION

The individual case reports of TA in a family consistently refer to the rarity of this condition. A lot of research has been focused on HLA association. Although some consistent HLA associations have been identified with HLA- A10, B5, Bw52, DR2, DR4, B21 and B22, many of these remain unconfirmed and variable across different ethnic groups.[10,11,12] Among this HLA A10, B5, Bw52, DR2 and DR4 is associated with TA in Japanese and Koreans, whereas TA is associated with HLA B22 in the Americans[13]and with HLA B5 and B21 in Indian patients.[14] Kasuya et al, showed that association of TA with HLA Bw52 results in higher incidence of coronary artery and myocardial involvement and a worse prognosis.[15] There were reports of a multiple families with TA which raise the question of whether there could be an autosomal recessive form of the disease.[16] The exact pathogenesis of the arteritis is still unknown, but more emphasis has been given on an immunopathological cause.[17]

The Takayasu Conference (1994) proposed a classification based on angiographic abnormalities: type I: Aortic arch involvement, type II: Thoracoabdominal involvement, type III: Diffuse involvement, type IV: Pulmonary involvement, type V: Aneurysmal type. The clinical signs and symptoms depend on the site of lesion in the aorta.[18,19,20]

The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis is as follows: 1. Age of onset of symptoms or signs <40 years, 2. Claudication of extremities, in muscles of one or more extremities while in use, especially the upper limb claudication, 3. Decrease brachial arterial pulse (one or both), 4. Blood pressure difference in arms (difference of >10 mm Hg of SBP in arms), 5. Bruit audible on auscultation in one or both subclavian arteries or abdominal aorta and 6. Arteriogram – arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities, not due to arteriosclerosis, fibro-muscular dysplasia, or similar causes: changes usually focal or segmental. The presence of 3 or more of these 6 criteria showed a sensitivity of 90.5% and a specificity of 97.8%.[21,22]

In our case, Mother presented at 40 years age with severe claudicating pain, absent pulses in upper limbs, a bruit heard over the abdomen. Her CT angiogram showed severe stenosis of left renal artery. Mild stenosis noted in the left common carotid artery. As the above findings were fitting the criterion (5 out of 6), mother was diagnosed with TA.

Daughter was diagnosed at the age of 22 with complaints of claudicating pain in both upper limbs, absent brachial artery pulsations, blood pressure was not recordable in both the upper limbs and carotid bruit was heard**.** CT angiogram and MRI cerebral angiogram showed stenosis at different levels of aorta and branches.

Daughter was diagnosed Takayasu arteritis, since she was fitting 5 out of 6 ACR criteria. After we diagnosed the mother as TA, and with a high index of suspicion for familial TA, we inquired daughter, who gave similar complaints with lesser severity. Examination findings were also similar. Then, we advised non-invasive imaging modalities such as ultrasound, CT, MRI, and confirmed the diagnosis. In our review of familial TA cases, patients were diagnosed late only after they presented with severe signs and symptoms of disease, without proper prior evaluation. In few case reports such as, a familial TA between two brothers aged 17 and 14 reported by Makino et al, the younger brother was diagnosed 4 years after older brother when he presented with neck pain and general malaise.[23]

The cases of two teenage sisters were reported by Tsai et al, revealed that there was a significant delay in diagnosis of the second sister in part due to failure to palpate pulses and obtain 4 limb blood pressures at the time of initial evaluation.[24]

In a case report of TA between two sisters by Morishita et al where the older sister was diagnosed at the age of 10 years and died at 15 years due to same disease, the younger sister had been diagnosed as TA at the age of 4 years after presenting with hypertension and persistently raised inflammatory markers and catheter arteriography at the time of diagnosis revealed stenotic abnormalities of the superior mesenteric, renal and internal carotid arteries.[4]

CONCLUSION

TA in a family is an important entity and the incidence is not as rare as once thought to be. The etiology of TA is still unknown, but this case and review of literature indicates that there are genetic factors that play a major role in development of TA. Hence we should maintain a high index of suspicion for the possibility of TA in the siblings or other family members of affected patients. Pulse and blood pressure should be checked in all four limbs and advising proper investigations in siblings and children of affected individuals is necessary to rule out Takayasu Disease in family.

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