



A Rare Case of Pulmonary Hypertension Due to Takayasu's Arteritis

KEYWORDS

Takayasu's arteritis, Aortoarteritis, pulmonary hypertension

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ABSTRACT *Takayasu's arteritis also known as aortoarteritis is an inflammatory disease of the large elastic arteries occurring in the young resulting in occlusive or ectatic changes mainly in the aorta and its immediate branches as well as the pulmonary artery and its branches. Vessel inflammation leads to wall thickening, fibrosis, stenosis, and thrombus formation. Symptoms reflect end organ ischemia. More acute inflammation can destroy the arterial media and lead to aneurysm formation. The exact cause is not known, though it is suggested to be due to an autoimmune response to an unknown antigen. We report a case of 47 years old female presenting with severe pulmonary hypertension, congestive cardiac failure that turned out to be a case of Takayasu's Arteritis.*

Introduction-

In 1908, Mikito Takayasu, a Japanese ophthalmologist described a peculiar wreath-like appearance of retinal blood vessels with absence of radial pulse which thereafter was also called as Pulse less disease, Occlusive thromboarthropathy, Mortell syndrome(1)

Clinical diagnosis of aortoarteritis is often delayed due to non specific initial presentation. It was originally based on proposed diagnostic criteria by Ishikawa in 1988(2). These consist of one obligatory criterion (age <40 years at diagnosis or onset of disease), two major criteria (left and right mid subclavian artery lesions) and nine minor criteria (high ESR, common carotid artery tenderness, hypertension, aortic regurgitation or annulo-aortic ectasis, lesions of pulmonary artery, left common carotid artery, distal branchio-cephalic trunk, thoracic aorta and abdominal aorta). In addition to the obligatory criterion, the presence of two major criteria, or one major plus two or more minor criteria; or four or more minor criteria suggests a high probability of the presence of aortoarteritis. These criteria have greater sensitivity for patients with active disease than for those with inactive disease.

Later on, American College of Rheumatology (1990) has selected '6' criteria for diagnosis of aortoarteritis. These include age of onset of disease <40 years; claudication of extremities, decreased brachial artery pulse; BP difference >10 mmHg between arms; bruit over subclavian arteries or aorta and arteriogram abnormality. Presence of at least 'three' of these 'six' criteria suggests the diagnosis of aortoarteritis, which have a sensitivity of 90.5% and a specificity of 97.8 %.(3)

Case report-

A 47 years old female admitted with exertional dyspnea, fatigue and pedal edema since one month. She also had occasional episodes of giddiness. No other known co morbidities were present. On examination she had heart rate 120/min, Blood pressure 94/60 mm Hg right arm supine position. She had engorged neck veins, bilateral pitting pedal edema. Her right carotid artery pulse was weak with minimal tenderness. Other peripheral pulses were well felt. On cardiovascular examination she had Pan systolic murmur of grade IV/VI in tricuspid area, loud pulmonary component of second heart sound. Per abdominal examination revealed congestive he-

patomegaly. Rest physical examination was normal.

Investigations- Hemogram – normal, ESR- 32mm at end of one hour

Sr. bilirubin- indirect – 2.2 mg/dl, direct was normal

ECG- right axis deviation, right ventricular hypertrophy

Chest X ray showed bilateral moderate pleural effusion

2D Echo- Dilated right atrium and right ventricle, Moderate tricuspid regurgitation. Pulmonary artery systolic pressure was 60mm Hg. There was no regional wall motion abnormality, clot vegetation or effusion.

HRCT Thorax showed dilated pulmonary trunk and main pulmonary arteries (image1). No evidence fresh pulmonary thromboembolism. Lung parenchyma was normal.

Arch aortogram revealed normal thoracic and abdominal aorta.

In view of repeated episodes of giddiness carotid Doppler was done which showed severe narrowing of both common carotid arteries. Right carotid artery had only 1.5mm lumen patent. The patient underwent MRI brain and MR Angiography (Refer to images 2). It showed bilateral diffuse narrowing of common carotid, both internal carotid arteries and mild narrowing of both external carotid arteries. Right middle cerebral artery was significantly narrowed in cavernous, supraclinoid and carotid canal portion with significantly compromised flow. There was significantly reduced flow in A1 segment of right interior cerebral artery.

In view of diffuse narrowing of major branches of aorta with involvement of pulmonary artery causing pulmonary hypertension with raised ESR and carotid artery tenderness in a female without other plausible explanation led to the diagnosis of Takayasu's Arteritis. She was treated with oral prednisolone 40 mg dose, diuretics for congestive cardiac failure and oral sildenafil 25 mg for pulmonary hypertension. Patient responded well to treatment and was advised regular follow up.

Discussion

Takayasu's Arteritis is believed to occur in a genetically predisposed individual due to autoimmune responses to a yet unknown stimulus. Several workers from India and Japan have suggested hypersensitivity to *Mycobacterium tuberculosis* as a possible factor in the pathogenesis. Immunohistochemical studies of aortic tissue samples from patients with TA have shown that the infiltrating cells mainly consisted of gamma delta T lymphocytes, natural killer cells, macrophages, cytotoxic T lymphocytes and T helper cells thereby suggesting a cell-mediated immune response. A 65 kDa heat shock protein (HSP) is a major immunogenic component of *M. tuberculosis* and expression of HSP has been shown to be strongly induced in the aortic tissue. This may enhance the cytotoxicity of the infiltrating lymphocytes. It is possible that TA is caused by a humoral/cell-mediated immune response after the human host is exposed to bacterial HSP (HSP kDa). Manifestations range from asymptomatic disease found as a result of impalpable pulses or bruits, to catastrophic neurological impairment.

Based on vessel involvement, classification of Takayasu's Arteritis. (Ref to image 3)

Type 1 : Braches from aortic arch.

Type 2 a: Ascending aorta, aortic arch, and its branches.

Type 2 b: Ascending aorta, aortic arch, and its branches, thoracic descending aorta.

Type 3: Thoracic descending aorta, abdominal aorta and / or renal arteries.

Type 4: Abdominal aorta and / or renal arteries

Type 5: Combined features of type 2 b and 4.

According to this classification system, involvement of Coronary and Pulmonary artery should be designated as C (+) or P (+) respectively. Pulmonary artery involvement occurs in 14–100% of patients, depending on the method used to assess pulmonary vasculature. Oligoemic lung fields on plain chest x ray correlate with pulmonary vasculopathy in approximately a third of cases. Pulmonary artery disease shows little correlation with the systemic pattern of arterial involvement but can be useful in the differential diagnosis by helping to confirm Takayasu arteritis. The natural history has two distinct phases; an active or pre-pulse less phase and a chronic or pulse less phase. Active phase may remit spontaneously in three months or may progress insidiously into the chronic phase. There can be exacerbations of activity during the chronic illness. In 50% of patients, the onset of disease is heralded by constitutional symptoms such as fever, anorexia and arthralgia. The National Institutes of Health (NIH) have arbitrarily defined active disease as new onset or worsening of at least two of the following four features: (i) signs and symptoms of vascular inflammation or ischemia (claudication, decreased or absent pulses or blood pressure in the extremities, bruits or carotidodynia); (ii) elevated ESR; (iii) angiographic abnormalities; and (iv) systemic symptoms not attributable to another disease, e.g. fever, polyarthralgia, polymyalgias.

Other manifestations of Takayasu's Arteritis include vascular bruits in 80–94% of patients, often multiple, and particularly affecting the carotids, subclavian, and abdominal vessels. Hypertension is seen in 33–83% of patients, generally reflecting renal artery stenosis, which is seen in 28–75% of patients. Patients can present with pulmonary hypertension, congestive cardiac failure or neurovascular deficit. Takayasu retinopathy occurs in up to 37% of patients. Aortic regurgitation resulting from dilatation of the ascending aorta and valve thickening in 20–24%

Differential diagnosis includes Inflammations of large arter-

ies such as the aorta and its major branches like Kawasaki's syndrome, Behçet's syndrome, rheumatoid arthritis, syphilis, and tuberculosis.

Management of active TA: Ideally, the disease needs to be picked up in the active phase so that immunosuppressive therapy can be started. Glucocorticoids are the mainstay of therapy for active TA and success rates of 20%–100% have been reported. Oral prednisolone is recommended at a daily dose of 30 mg, followed by tapering upon normalization of activity. Cytotoxic agents like azathioprine and cyclophosphamide re recommended if active disease persisted or steroid withdrawal was difficult. Obstructive lesions need to be tackled by revascularization techniques such as angioplasty and surgery, while active disease needs to be treated with immunosuppressive agents.

Summary-

Takayasu arteritis is a well known yet rare form of large vessel vasculitis. Its pathogenesis probably starts with a genetically predisposed individual followed by exposure to an unidentified antigen (which may or may not be tuberculosis) leading to an immune response that targets the large vessels. Suppression of inflammation and preservation of vascular competence are the aims of treatment.

Image 1 – Dilated pulmonary trunk due to pulmonary hypertension



Image 2- Narrowing of internal carotid and cerebral vessels

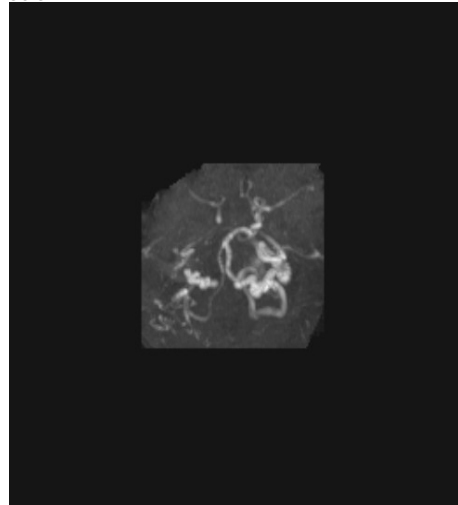
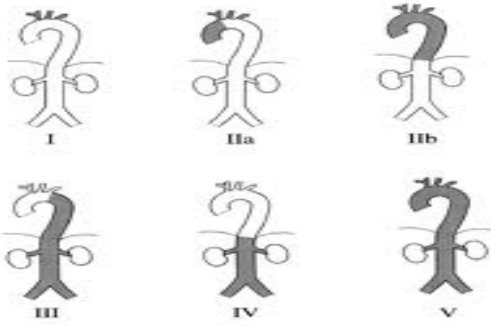


Image 3 – Classification of Takayasu's arteritis

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