

Death due to Severe Occlusion of the Subclavian Artery; a Case Report

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Abstract

Takayasu arteritis is a rare, large vessel disease. It commonly affects aorta and its main branches. The characteristic features are absent or diminished pulse, vascular bruits, hypertension, chest pain, retinopathy, and dyspnoea. Some studies have shown that there is an association between hypothyroidism and Takayasu arteritis. We report a death of a 56-year-old female with suggestive symptoms of Takayasu Arteritis. She was diagnosed to have diabetes mellitus and ischaemic heart disease for 10 years. Lately, she was suffering from upper and lower limb pain. Three days before she died she developed severe limb pain and swelling of the body including upper and lower limbs. She was admitted to the tertiary care hospital and died on the following day. The electrocardiography showed subtle ischemic changes. Laboratory investigations were performed due to body swelling which confirmed hypothyroidism. At autopsy, there were severe occlusions of the left subclavian artery and severe stenosis of all coronary arteries. Histological examinations were performed since these findings are commonly seen in Takayasu arteritis. However, microscopy of Haematoxylin and Eosin stains revealed the occlusions in the left subclavian artery as atherosclerotic. Cause of death was given as atherosclerotic heart disease.

Keywords: Atherosclerosis, large vessel vasculitis, Takayasu's arteritis

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Introduction

Takayasu's arteritis (TA) is an aortoarteritis of unknown aetiology, resulting in segmental stenosis, occlusion, dilatation and aneurysm, which primarily affect the aorta and its branches and occasionally the pulmonary and the coronary arteries. The manifestations can range from asymptomatic to catastrophic, with dizziness, hypertension, claudication, cerebral infarction, chest pain and dyspnea. The incidence of TA is about 2/10,000 person-years, with a ten-fold predominance in women, especially in those under 40 years of age. The female gender along with the reproductive age group and an Asian origin are the known factors which are associated with higher disease prevalence. [1] The diagnosis of Takayasu's arteritis is always challenging, as the clinical presentation may vary considerably. TA may also mimic diseases such as Behçet's syndrome, giant cell arteritis (Temporal arteritis), Wegener

Granulomatosis, Kawasaki disease, rheumatoid arthritis, Systemic Lupus Erythematosus (SLE), atherosclerosis, sarcoidosis, neurofibromatosis, Buerger's disease and developmental abnormalities (aortic coarctation) or infections (e.g. tuberculosis, syphilis). Most of these conditions have specific features that enable diagnosis. Therefore, occlusive diseases of blood vessels require histological confirmation for the purpose of diagnosis or exclusion.

Case Report

A 56-year-old female was diagnosed to have diabetes mellitus and ischaemic heart disease for 10 years. There was no past medical history of dyslipidemia. She was advised to get a bypass surgery done which was defaulted by her. There was no family history of TA. Lately, she was suffering from upper and lower limb pain.

Three days before she died she developed severe limb pain and swelling of the body including upper and lower limbs. She was admitted to the tertiary care hospital and died on the following day. The electrocardiography showed subtle ischemic changes. Thyroid function test was performed due to body swelling and Thyroid stimulating hormone (TSH) level was >150 mIU/L and free thyroxin (free T4) level was <0.1 ng/dL which confirmed hypothyroidism.

At autopsy, her stature was normal with apparent normal body weight. There was no significant ankle oedema. There were severe occlusions of the left subclavian artery (Fig.1) and severe stenosis of all coronary arteries. The heart was normal size, chambers were unremarkable, wall thicknesses were normal in range. There were no focal lesions in the myocardium. Few atheromas were seen in the abdominal portion of the aorta. Rest of the organs were unremarkable.

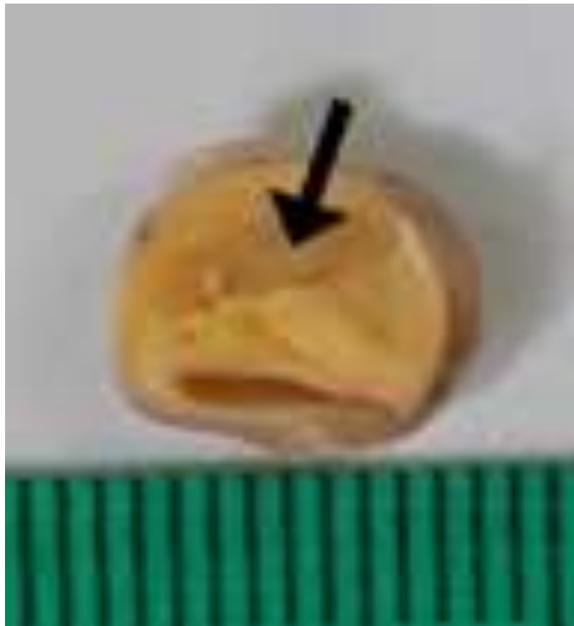


Figure 1: Macroscopic appearance of subclavian artery showing eccentric narrowing with atherosclerosis

Histological examinations were performed since these findings are commonly seen in TA. However, microscopy on Haematoxylin and Eosin (H&E) stains revealed the occlusions in the left subclavian artery as atherosclerotic (Fig. 2, 3 and 4). Cause of death was given as atherosclerotic heart disease.

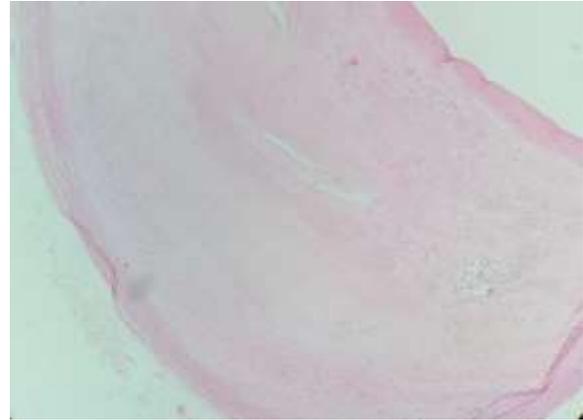


Figure 2: Microphotograph of subclavian artery showing atheroma (H&E stain, 10x10, Light microscope)

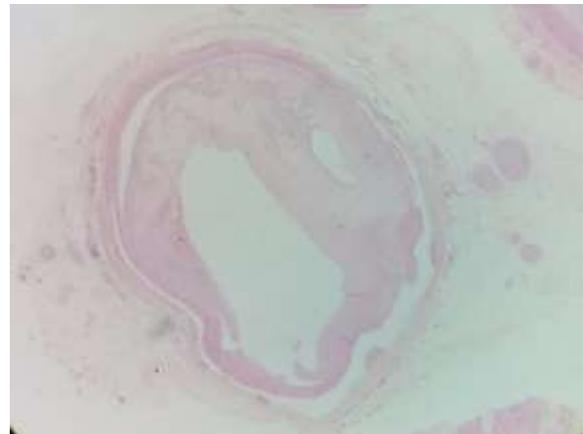


Figure 3: Microphotograph of a coronary artery showing atheroma (H&E stain, 10x10, Light microscope)

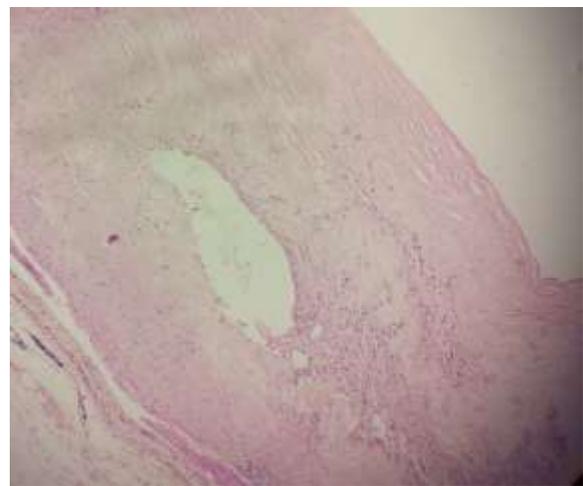


Figure 4: Microphotograph of a coronary artery showing atheroma (H&E stain, 10x20, Light microscope)

Discussion

Takayasu's arteritis is also known as 'pulseless disease', occlusive thromboarteropathy and Martorell's syndrome.^[2]

TA is a disease of young, oriental females with probable genetic and infectious strands to the aetiology. It is thought that TA may also run in families and occurs with greater frequency in certain races. Studies have shown an increased frequency of TA in Asians who have a particular antigen on chromosome 6 (HLA-Bw52).^[3] In our case, this was excluded from history. In 1990, the American College of Rheumatology suggested a set of criteria for the diagnosis of TA. The criteria include (a) age less than 40 years, (b) claudication of an extremity, (c) decreased brachial artery pulse, (d) systolic blood pressure difference of more than 10 mmHg between the left and right arm, (e) a bruit over the subclavian arteries or the aorta and (f) angiographic evidence of the narrowing or occlusion of the aorta or its primary or proximal branches. The presence of three of these six criteria is required for the diagnosis of TA.^[4] TA is rare but it is most commonly seen in Japan, South East Asia, India and Mexico and till date, 5000 patients have been registered. The four most important complications are Takayasu's retinopathy, secondary hypertension, aortic regurgitation and aneurysm formation.^[5, 6] The overall five-year survival rate after diagnosis was 83.1%.^[6] 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.^[7] Non-specific features of TA include fever, night sweats, malaise, weight loss, arthralgia, myalgia, and mild anaemia. As the inflammation progresses and stenosis develops, the more characteristic features become apparent, influenced by the development of collateral circulation. Diagnosing TA relies on clinical presentation, characteristic structural arterial abnormalities, and evidence of inflammatory vasculopathy on imaging or histology.^[8] Our patient presented with non-specific symptoms of upper and lower limb pain and swelling of the body. Stenotic lesions predominate and tend to be bilateral. Nearly all patients with aneurysms also have stenosis and most have extensive vascular lesions.

Because of considerable morbidity and mortality, accurate and early diagnosis plays a crucial role in improving the outcomes for patients with TA.^[9] Unfortunately, the non-specific clinical presentations and laboratory test results frequently contribute to late diagnosis and delayed treatment. Since large-artery biopsies cannot easily be done, imaging examination is essential for providing the diagnosis and differential diagnoses in patients with suspected TA. Conventional angiography has been traditionally considered the gold standard for the diagnosis of TA.^[10] However, multidetector CT angiography (CTA) is emerging as a reliable tool in non-invasively depicting both luminal and mural lesions in the aorta and its main branches, which may facilitate the detection of vasculitis during the early phase of TA. Imaging studies were not carried out in our patient.

In TA, biopsy specimens are seldom available and hence morbid anatomic features are based on autopsy findings^[11]

or segments excised during bypass surgery.^[12] On histology, the lesions can be active, chronic, or healed.^[13] TA is a panarteritis, the initial site of inflammation is around the vasa vasorum and at the medio-adventitial junction.^[12] There is oedema and mononuclear cell infiltration (CD4 and CD8 lymphocytes, plasma cells, and macrophages) in the outer thirds of the media and adventitia. Giant cell granulomatous reaction and laminar necrosis can also be present.^[13] Fragmentation of elastic fibres with "elasticophagia" is prominent. Rapid or more severe inflammation leads to loss of smooth muscle cells, medial weakening, vascular dilatation, and even aneurysm formation.^[13] In the chronic phase, there is patchy mononuclear inflammatory infiltrate with medial scarring and vascularization, while the healed phase shows only fibrosis in all layers; these two phases are often seen.^[13] In our case, the histology examination revealed atheroma.

The differential diagnoses should include common diseases such as atherosclerosis, giant cell arteritis and Polyarteritis nodosa. Atherosclerosis is the most common cause of subclavian artery stenosis. Atherosclerosis is a chronic inflammatory disease.^[14] Atherosclerosis begins with fatty streak which is an accumulation of lipid-laden foam cells in the intimal layer of the artery.^[15] Lipid retention is the first step in the pathogenesis of atherosclerosis which is followed by chronic inflammation at susceptible sites in the walls of the major arteries lead to fatty streaks, which then progress to fibroatheromas which are fibrous in nature.^[16,17] Giant cell arteritis is an unlikely diagnosis, given our patient's lack of ocular symptoms and chronic granulomatous inflammation. She had no upper respiratory tract symptoms to suggest granulomatosis with Polyangiitis. It is not an easy task to differentiate aortic calcification in TA from that in atherosclerosis. Atherosclerotic plaques are more common in patients aged 45 years and above and not usually associated with long segment luminal stenosis.^[9, 18] Calcification in ascending aorta can be observed in some TA patients, but it is rare in atherosclerosis. According to the literature, some studies have revealed that patients with Takayasu's arteritis have a high rate of atherosclerotic plaques. Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis that typically affects medium-sized muscular arteries, with occasional involvement of small muscular arteries.^[19] Fibromuscular dysplasia is a non-inflammatory disease, which mainly affects renal, carotid and vertebral arteries that causes focal, multifocal or adventitial fibroplasia. This requires special staining (eg: Masson's Trichrome) which exclude rare conditions such as fibromuscular dysplasia. Syphilis tends to affect an older age group, with calcification, sparing the descending thoracic aorta, and stenosis are not a feature.^[20]

Our case was a death of a woman who presented like Takayasu but with microscopic investigations, the diagnosis was excluded.

One of the studies done by Sevuk et al. has shown that hypothyroidism could be a risk factor for carotid artery plaque ulceration. [21] Therefore, thyroid functions may be useful for risk stratification of patients with internal carotid artery stenosis.

Conclusions

Clinicians are supposed to follow basic principles in medicine such as history taking, general examination and systemic examination rather than performing sophisticated investigations to arrive at a diagnosis. As the findings of the above case are common in TA, one should exclude TA and other differential diagnoses before arriving at the cause of death. Histopathology examination is important in excluding these conditions. The pathological features of TA vary with the stage of the disease and include granulomatous inflammation, elastophagia, adventitial and medial fibrosis, vessel dilatation, and stenosis or occlusions of the involved arteries.[22] There are challenges for detecting TA in autopsy cases because the American College of Rheumatology criteria for diagnosis is based on clinical signs.

Since the patient was also diagnosed with hypothyroidism, it is worth studying the association between the hypothyroidism and occlusion of arteries further.

Disclosure statement

Conflicts of interests: The authors declare that they have no conflicts of interests.

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