Takayasu’s arteritis - a comprehensive review


Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, India

ABSTRACT

Takayasu’s arteritis (TA) is a chronic inflammatory disease of unknown aetiology. The mechanism of this disease is not exactly defined. The inflammatory process is generally (but not exclusively) initiated in the second or third decade of life through the actions of non-specific inflammatory cells. As the disease progresses, fibrotic stenosis occurs in aorta and its main branches. The consequence of this inflammatory process can be stenosis, thrombosis, dilatation or aneurysm formation in aorta and/or its branches. Majority of cases have been observed in Asia, Africa, and Latin America. In Asia, its incidence (2.69 in a million per year) has been reported to be 100 times higher than in Europe and North America. Because of the delay in diagnosing the disease, patients often experience claudication, absence of pulses, hypertension, myocardial infarction (MI), and cerebrovascular accidents (CVAs). Accurate and early diagnosis of TA can reduce the economic, social, and psychological burdens. Considering the fact that classical TA has mainly been described in Asia.

Background

Takayasu arteritis (TA) is a large vessel vasculitis (LVV) characterized by granulomatous inflammation of the vessel wall with an unknown etiopathogenesis. TA predominantly affects young females during the second or third decades of life and mainly involves the aortic arch and its primary branches, ascending aorta, thoracic descending aorta and abdominal aorta (Figure A and B). Early in the disease course, inflammation of the involved arteries progresses, resulting in segmental stenosis, occlusion, dilatation and/or aneurysm. This may cause extremity pain, claudication, bruits, absent or diminished pulses and loss of blood pressure. TA generally follows an insidious course, however, presentation with acute visual loss or stroke may also occur[1-2]. TA may show different patterns of arterial involvement, disease expression and prognosis in different regions of the world[3-4]. Multiple genetic factors were recently shown by a whole-genome approach in TA and an association between the extent of vascular involvement and the major genetic risk factor HLA-B*52 was reported in Turkish TA patients, suggesting that genetic factors might influence disease severity[5-6]. Yamamoto described the case of a 45 year old man with persistent fever who developed impalpable upper limb and carotid pulses associated with weight loss and dyspnoea. Takayasu, professor of ophthalmology at Kanazawa University Japan, presented the case of a 21-year-old woman with characteristic fundal arteriovenous anastamoses. Onishi and Kagosha each described similar cases...
A diagnosis of Takayasu arteritis requires that at least 3 of the 6 criteria are met.

**Criteria**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at disease onset &lt;40 years</td>
<td>Development of symptoms or findings related to Takayasu arteritis at age &lt;40 years</td>
</tr>
<tr>
<td>Claudication of extremities</td>
<td>Development and worsening of fatique and discomfort in muscles of 1 or more extremity while in use, especially the upper extremities</td>
</tr>
<tr>
<td>Decreased brachial artery pulse</td>
<td>Decreased pulsation of 1 or both brachial arteries</td>
</tr>
<tr>
<td>Blood pressure difference &gt;10 mm Hg</td>
<td>Difference of &gt;10 mm Hg in systolic blood pressure between arms</td>
</tr>
<tr>
<td>Bruit over subclavian arteries or aorta</td>
<td>Bruit audible on auscultation over 1 or both subclavian arteries or abdominal aorta</td>
</tr>
<tr>
<td>Arteriogram abnormality</td>
<td>Arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities, not caused by arteriosclerosis, fibromuscular dysplasia, or similar causes; changes usually focal or segmental</td>
</tr>
</tbody>
</table>

A diagnosis of Takayasu arteritis requires that at least 3 of the 6 criteria are met.

**Table 1:** 1990 ACR criteria for the classification of Takayasu arteritis.
Aortic root involvement may lead to dilatation and aortic vessel wall with intimal wrinkling is seen16. When aortic the cases, irregular thickening of the aortic and its branch narrowing of coronary ostia even obliterated. The coronary and renal arteries may be equally affected (Figure E). Histological findings may range from an adventitial mononuclear infiltrate with perivascular cuffing of the vasa vasorum (channels supplying blood vessels) to marked mononuclear inflammation the media17. Aortic root involvement may lead to dilatation and aortic valve insufficiency15. Myocardial infarction may result in narrowing of coronary ostia19.

Clinical features

- Diminished or absent pulses in 84–96% of patients associated with limb claudication and blood pressure discrepancies.
- Vascular bruits in 80–94% of patients, often multiple, and particularly affecting the carotids, subclavian, and abdominal vessels20.
- Hypertension in 33–83% of patients21, generally reflecting renal artery stenosis, which is seen in 28–75% of patients22.
- Takayasu retinopathy in up to 37% of patients23.
- Congestive cardiac failure associated with hypertension, aortic regurgitation, and dilated cardiomyopathy24.
- Neurological features secondary to hypertension and/or ischaemia, including postural dizziness, seizures, and amaurosis.
- Pulmonary artery involvement in 14–100% of patients, depending on the method used to assess pulmonary vasculature. Oligaemic 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 involvement25, but can be useful in the differential diagnosis by helping to confirm Takayasu arteritis.

Serological markers

No reliable serological marker of disease course has been identified. In the past, ESR normalisation was used as a remission criterion, but recently it has been shown that it has a low specificity and sensitivity, because ESR is raised in nearly half of the patients in clinical remission, while it is normal in 28% of the patients with active disease26. Serum concentrations of interleukin-6 and regulated on activation normal T cell expressed and secreted (RANTES) are elevated in patients with active disease and concentrations parallel to the activity of the disease27. Similarly, matrix metalloproteinase-3 and metalloproteinase-9 levels can be used as activity markers, whereas high serum concentrations of metalloproteinase-2 can suggest the presence of Takayasu’s arteritis without any relation with the activity of the disease28.

Radiological findings

The American College of Rheumatology included arteriogram abnormalities in the diagnostic criteria of the disease. Angiography is the gold standard for evaluation of vascular lesions; in particular panangiography allows a correct assessment of the extension of the disease, which correlates with its severity. Some authors underline the high incidence of coronary involvement in Takayasu’s arteritis (15%) and recommend to perform a coronarographic exam29. Assessment of pulmonary vasculature by angiography is not universally recommended being reserved for patients with symptoms of pulmonary hypertension30. However, non-invasive techniques (i.e. lung scan) have demonstrated lung perfusion abnormalities in about two thirds of asymptomatic patients31. Angiography allows a topographic classification which correlates anatomic involvement, clinical manifestations and prognosis. Angiography, however, is an invasive method, it is not able to differentiate active from burned-out lesions and exposes the patients to risks connected with radiation and the contrast medium. In the early phase of Takayasu’s arteritis, the thickening of vascular wall of the aorta or pulmonary artery can be detected by computed tomography (CT) or nuclear magnetic resonance (NMR). CT combined with injection of contrast medium (the so-called angio-CT), allows to study wall inflammation but it has a low spatial resolution and cannot evaluate medium-size arteries32.
NMR is a good alternative method to CT, especially angiographic NMR, which is equally or more sensitive than angiography in detecting lesions of large vessels. However, it is less sensitive in detecting smaller branch involvement and may overestimate the degree of stenosis in renal and subclavian arteries. More recently, fluorodeoxyglucose positron emission tomography (FDG-PET) has been proposed as a promising technique in the early diagnosis and assessment of response to treatment in Takayasu arteritis as well as in other large vessel vasculitis, because it seems to be a more sensitive method than conventional clinical methods in measuring continuing vascular inflammation. Finally, color Doppler ultrasonography plays an important role for screening, detection and follow-up of carotid (Figure F and G) and subclavian arteries where it is easy to discriminate between atherosclerotic and inflammatory lesions.

Classification

Classification of Takayasu's arteritis has been made to classify the disease on the basis of angiographic findings (Table 2). Ishikawa clinical classification and diagnostic criteria of Takayasu arteritis shown in Table 3 and Table 4.

Medical treatment

Medical treatment is to control active inflammation and minimize arterial injury. To prevent the development of vascular complications and induce remission, early initiation of immunosuppressive treatment is crucial. Prednisolone is the first line agent, and the EULAR (European League Against Rheumatism) guidelines recommend an initial dose of 1mg/kg/day (total maximum dose 60mg/day), with gradual tapering. Adjunctive steroid-sparing immunosuppression is required in the majority of patients to minimise steroid-related complications and control disease progression, particularly as there is considerable risk of relapse when steroid treatment is stopped. There are studies suggesting methotrexate and azathioprine are effective at inducing remission and halting progress of arterial lesions. A recent review published of 84 patients with TA treated with tumour necrosis factor-α antagonists including infliximab and etanercept revealed complete remission in 37%, partial remission in 53.5%, and 9.5% nonresponders. Of note, side effects (mainly infections and hypersensitivity reactions) were observed in 20% of cases. Likewise, anti-IL-6 receptor monoclonal antibody tocilizumab may help control refractory disease and the published cases have recently been reviewed in the literature.

Surgical treatment

With symptomatic stenotic or occlusive lesions, it appears appropriate and often necessary to revascularize. The indications for considering intervention include uncontrolled hypertension as a consequence of renal artery stenosis, severe symptomatic coronary artery or cerebrovascular disease, severe aortic regurgitation or coarctation, stenotic or occlusive lesions resulting in critical limb ischemia, and aneurysms at risk of rupture. In these cases the risk benefit ratio for surgery is good.
Conclusion

- Takayasu’s arteritis is a nonspecific inflammatory disease of the arteries which is more commonly seen in Asian countries and predominantly affects women. Manifestations in our study range from asymptomatic disease, impalpable pulses or arterial bruises, to catastrophic neurological impairment.

- Disease presentation varies between different populations.

- Angiography remains the gold standard and was helpful in confirming the diagnosis and planning the treatment. Comprehensive angiographic evaluation followed by percutaneous angioplasty and stenting is useful in properly selected cases.

- The four most important complications for classification are Takayasu retinopathy, secondary hypertension, aortic regurgitation, and aneurysm formation, each being graded as mild/moderate or severe at the time of diagnosis.

- Treatment should aim to control disease activity and preserve vascular competence, with minimal long term side effects; those with disease that carries a good prognosis should not be put at risk by treatment that is more harmful than the disease itself.

References


