

## Review Article

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# Takayasu's disease: a review

Oliver R. Tann,<sup>1</sup> Robert M.R. Tulloh,<sup>2</sup> Mark C.K. Hamilton<sup>1</sup>

<sup>1</sup>Department of Clinical Radiology, Bristol Royal Infirmary, Marlborough St. Bristol; <sup>2</sup>Department of Paediatric Cardiology, Bristol Royal Hospital for Children, Bristol, United Kingdom

**Abstract** Takayasu's disease is a rare chronic vasculitis of unknown aetiology. Initial symptoms and signs are non-specific, and a high index of suspicion is needed to make the correct diagnosis. The disease is associated with a high incidence of morbidity, and a significant risk of premature death. Serological tests have proved unreliable in distinguishing active from quiescent disease, with non-invasive imaging currently offering the best option for early diagnosis, and monitoring the response to treatment. In this review, we detail the epidemiology, pathophysiology, clinical features, imaging characteristics, and currently available treatments.

Keywords: Arteritis; pathophysiology; imaging; treatment

**T**AKAYASU'S DISEASE IS A RARE CHRONIC VASCULITIS of unknown aetiology, predominantly affecting the aorta and its main branches, and the pulmonary arteries. It produces a variety of ischaemic symptoms due to stenosis and thrombosis of major arteries (Fig. 1). Acute progression of the disease can lead to destruction of the arterial media, formation of aneurysms, or arterial rupture.

The first description of Takayasu's disease was given in 1830 by Rokushu Yamamoto. He described a 45-year old man with fever, pulselessness, loss of weight, and breathlessness, who died in his 11th year of follow-up. In 1905, Mikito Takayasu, professor of ophthalmology, described a 21 year old woman with peculiar arteriovenous malformations of her optic funduses. Although Takayasu did not indicate that any other arteries were involved, in the discussion that followed, two other ophthalmologists, Onishi and Kagoshima, described similar ocular findings, along with absence of the radial pulse. In 1951, the clinical features of Takayasu's disease were summarised

in an English journal under the name of the pulseless disease.<sup>1</sup>

## Epidemiology

Takayasu's disease is the third commonest vasculitis in childhood worldwide, but is relatively uncommon in Europe and North America.<sup>2</sup> In 1990, the Japanese government added Takayasu's disease to the list of intractable diseases, with 5000 cases added to the list over the subsequent decade.<sup>1</sup> A North American study of patients in Minnesota found the incidence to be 2.6 cases per million population in each year.<sup>3</sup> The true extent of the disease in the west is not known. In 2006, a pilot paediatric registry, in North America and Canada, was set up for chronic vasculitis, including Takayasu's disease, to answer some basic questions about epidemiology, presenting and diagnostic features, and initial therapeutic approaches at the onset of disease.<sup>4</sup>

The disease commonly presents between the ages of 10 and 20 years, with three-quarters of patients presenting in this period, with a ratio of males to females of 1 to 8.5.<sup>5</sup> There is, nonetheless, a wide range of presenting age, with some presenting as early as 24 months.<sup>6</sup> A delay between symptoms and diagnosis of 2 to 11 years is seen in the west,<sup>5</sup>

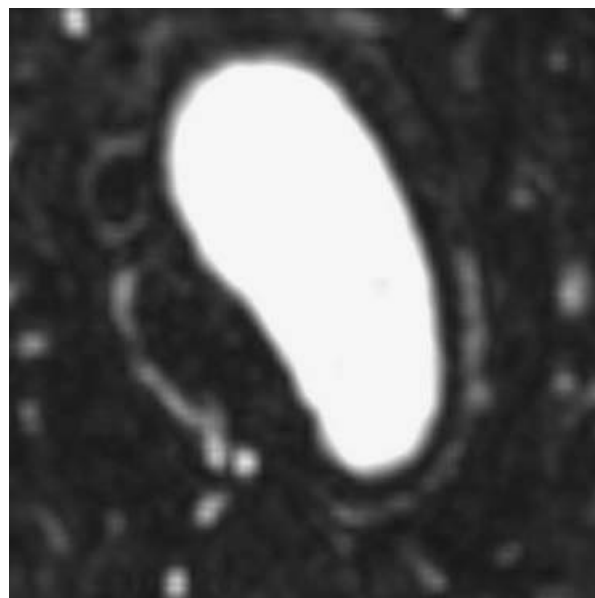
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Correspondence to: Oliver Tann, Department of Clinical Radiology, Bristol Royal Infirmary, Marlborough St., Bristol BS2 8HW, United Kingdom. Tel: (0)117 928 2672; Fax: (0)117 928 3267; E-mail: olivertann501@btinternet.com

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**Figure 1.** Maximum intensity projection magnetic resonance angiogram subsequent to administration of gadolinium, demonstrating a severe long segment stenosis of the left common carotid artery involving its origin.



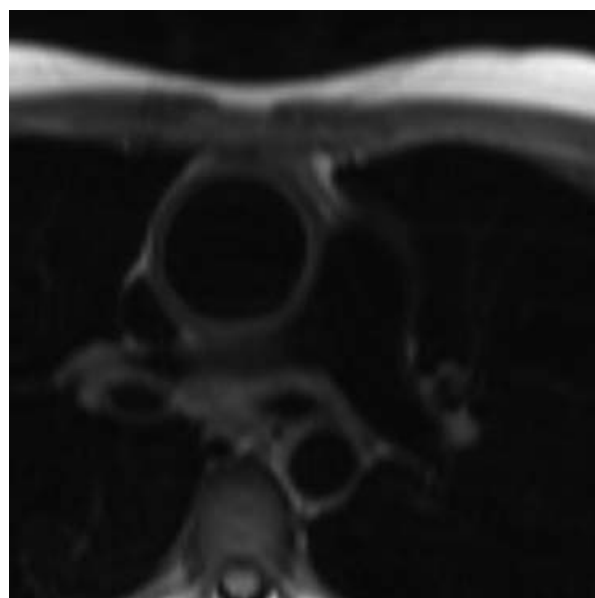
**Figure 2.** Magnetic resonance angiogram after administration of gadolinium. Axial image at the level of the aortic arch. A thin rim of high signal can be seen posteriorly (neovascularisation within the outer layer of the aortic wall) separated from the aortic lumen by a thick area of low signal (the thickened aortic media).

with greater delay observed in juveniles as opposed to adult populations.<sup>7</sup> A study in India<sup>8</sup> of patients with Takayasu's disease under 18 years of age reported a delay of only 2.5 to 5.5 months. This presumably reflects the higher incidence in the Indian sub-continent, and thus increased clinical awareness.

### Pathophysiology

Takayasu's disease can be divided into two stages, with an acute period of large vessel vasculitis, followed by fibrosis and scarring. In the acute stage, the adventitial vessels of the arterial walls become inflamed. The media is infiltrated by lymphocytes and occasional giant cells. Neovascularisation originates at the junction of the media and adventitia, and subsequently fans out to incorporate the entire media (Fig. 2). The intima becomes thickened, with depositions of mucopolysaccharides, smooth muscle cells, and fibroblasts.

In the chronic stage, the elastic tissue is replaced by fibrosis, with thickening of all three layers. There is patchy luminal narrowing, often affecting multiple sites. Macroscopically, the intima may be rigid, with a "tree bark" appearance, a feature common to many arteritides.<sup>9</sup> Aneurysmal formation also occurs, as an abnormal response to mural stress because of inflammation, and may be exacerbated by increased volume, as with aortic regurgitation (Fig. 3).



**Figure 3.** Axial T1-weighted magnetic resonance image at the level of the bifurcation of the pulmonary trunk. The ascending aorta is dilated, and surrounded by an intermediate signal thickened wall.

Infection, in particular tuberculosis, has been implicated in the pathogenesis of Takayasu's disease. One study reported caseating granulomatous lymphadenitis in over two-thirds, compared with less than one-tenth of the control population.<sup>5</sup> A South

American study reviewed the clinical features in 26 children, and found a high frequency of positive purified protein derivative, in almost three-quarters, and lymphadenopathy in over one-third, with a histological picture of caseating granulomas, suggesting a link with atypical mycobacterial infection.<sup>10</sup> A retrospective study in India, found that one-fifth of patients had strongly positive skin tests for tuberculosis, and had been started on anti-tubercular therapy. Less than one-twentieth, however, had active tuberculosis, with all cases involving pulmonary infection.<sup>11</sup> Given the endemic nature of tuberculosis in Asia, and South America, it is unclear as to whether this represents a causal immunopathogenic relationship, or whether this is coincidence.

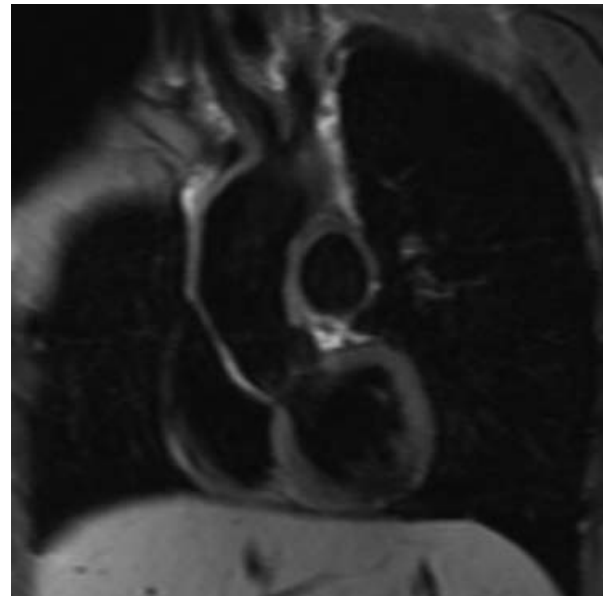
Further support to infection as a trigger for Takayasu's disease is lent by immunopathologic analyses. Expression of 65 kDa heat shock protein, as well as human leucocyte antigens of the first and second classes, are enhanced in Takayasu's arteritis lesions, supporting the pathogenic role of CD4 and CD8 T-cells.<sup>12</sup>

### Clinical features

The clinical manifestations of Takayasu's disease are commonly divided into early, pre-pulseless, and late pulseless phases. During the early phase, non-specific systemic symptoms and signs predominate, albeit often unrecognised. The late phase is characterised by ischaemia, and symptoms secondary to arterial occlusion. Recurrent disease often occurs in new arterial territories, with the coexistence of active and quiescent disease.

Symptoms and signs include

- Fever, breathlessness, haemoptysis, headache, dizziness, vertigo, angina, chest wall pain and claudicant pain.
- Reduced or absent pulses, resulting in discrepancies of blood pressure between limbs in over half the patients.<sup>5,5,11</sup>
- Hypertension in from one-third to three-quarters.<sup>3,5,7</sup> This is secondary to a number of overlapping factors. Marked narrowing of the aorta is associated with renovascular disease in up to two-thirds,<sup>3,5,7,13</sup> with reduced aortic elasticity, and aortic regurgitation in around one-quarter.<sup>7,10</sup>
- Vascular bruits are heard in over four-fifths,<sup>3,5,7</sup> mostly involving the carotid arteries, and rarely the femoral and renal arteries. Multiple bruits are heard in one-third.<sup>7</sup>
- The aortic regurgitation found in up to one-quarter of patients results from aortic dilation, separation of the attachments of the valvar leaflets at the sinotubular junction, and thickening of the leaflets.<sup>7,11</sup>



**Figure 4.** Coronal oblique T1-weighted magnetic resonance image, demonstrating intermediate signal thickening of the aorta, arch vessels, and left pulmonary artery.

- Congestive cardiac failure is seen in up to half the patients.<sup>5,14</sup> This may be related to hypertension, aortic regurgitation, and occasionally dilated cardiomyopathy.<sup>11</sup>
- Pulmonary arterial involvement is encountered in up to five-sixths of patients (Fig. 4).<sup>13,15–17</sup> The lowest frequency was seen in an Indian population,<sup>13</sup> whereas the highest frequencies were observed in Japanese populations.<sup>16–17</sup>
- Coronary arterial disease is found in one-tenth.<sup>18</sup> This is usually observed at autopsy, since involvement is not apparent until the onset of angina, myocardial infarction, or congestive cardiac failure. Three types of disease are identified: stenosis or occlusion of the coronary arterial orifices and proximal segments of the coronary arteries; diffuse or focal coronary arteritis, which may extend diffusely to all epicardial branches, or may involve focal segments, so-called skip lesions; and coronary arterial aneurysms.
- Major neurological events occur in one-half. These can be transient ischaemic attacks, cerebral infarction, hypertensive encephalopathy, seizures,<sup>7</sup> and even moyamoya phenomenon.<sup>19</sup> These events are related to a combination of carotid and vertebral arterial disease, and hypertension.
- Hypertensive retinopathy is seen in almost one-third, and Takayasu's retinopathy in one-sixth.<sup>20</sup> Classical ophthalmic features of the disease are due to reduced ocular perfusion, which manifests as hypoxic retinal changes.

Occlusion of branches of the retinal artery has also been described.<sup>21</sup>

- Raynaud's syndrome, also seen in one-sixth, is directly related to involvement of large arteries. Other dermal lesions, seen in one-eighth, include erythematous nodules on the legs, ulceration, malar flush, urticaria, and livedo reticularis.<sup>22</sup>

### Diagnostic criteria

A diagnosis of Takayasu's disease requires that at least 3 of 6 criteria be met as outlined by The American College of Rheumatology (Table 1). The presence of 3 or more of these 6 criteria demonstrates a sensitivity of 90.5%, and a specificity of 97.8%.<sup>23</sup>

### Prognosis

The prognosis of the disease is affected by the clinical classification (Table 2). The five-year survival rate from diagnosis is 100% for those in groups 1 and 2a, and from 70 to 80% for those in groups 2b and 3.<sup>11,24</sup> Survival is worse by one-sixth in those with hypertension,<sup>25</sup> since this may cause cardiac failure, stroke, and renal failure.<sup>11</sup> The main cause of death is cardiac failure, as a result of hypertension or aortic regurgitation.<sup>11,26</sup>

### Serological investigations

The erythrocytic sedimentation rate is elevated in active disease in up to three-quarters of those in all age groups,<sup>7,24</sup> but it is a poor predictor of death and acute events. In one small study, albeit of only four patients, who had bypass surgery, and histologically proven active disease from arterial biopsy at the time of surgery, only one patient had an elevated erythrocytic sedimentation rate.<sup>7</sup> A further study found that, despite multiple serological investigations, no test was reliably able to distinguish between healthy volunteers and patients with active Takayasu's arteritis.<sup>27</sup> Recently, work has focused on the role of inflammatory cytokines. Interleukin-6 and interleukin-18 are elevated in Takayasu's disease. Interleukin-18 correlates well with disease activity and may prove a useful marker for monitoring treatment response.<sup>28</sup>

### Radiological investigations

#### *Chest radiograph*

Changes in the appearance of the aorta manifest as abnormal calibre, along with aortic calcification in some. Undulation of the aortic margin can be seen, with alternating areas of stenosis and dilation, and also with skip areas of involvement. If segmental calcification is seen to outline an area of aortic

Table 1. The American College of Rheumatology 1990 criteria for the diagnosis of Takayasu arteritis.<sup>23</sup>

Criterion	Definition
Age at disease onset less than 40 years	Development of symptoms or findings related to Takayasu's arteritis at age $\leq 40$ years
Claudication of limbs	Development and worsening of fatigue and discomfort in muscles of 1 or more limb while in use, especially the arms
Decreased brachial arterial pulse	Decreased pulsation of one or both brachial arteries
Blood pressure difference of greater than 10 mmHg	Difference of more than 10 mmHg in systolic blood pressure between arms
Bruit over subclavian arteries or aorta	Bruit audible on auscultation over 1 or both subclavian arteries or abdominal aorta
Arteriographic abnormality	Arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal limbs, not caused by arteriosclerosis, fibromuscular dysplasia, or similar causes; changes usually focal or segmental

Table 2. Clinical classification of Takayasu's disease as described by Ishikawa.<sup>24</sup>

Group	Clinical Features
Group 1	Uncomplicated disease with or without involvement of the pulmonary arteries
Group 2a	Mild to moderate disease with one of the following complications: retinopathy; secondary hypertension; aortic regurgitation; aortic or arterial aneurysm
Group 2b	Severe disease with one of the following complications: retinopathy; secondary hypertension; aortic regurgitation; aortic or arterial aneurysm
Group 3	Two or more complications present

narrowing, this is characteristic of Takayasu's disease.<sup>29</sup>

Prominent pulmonary arteries signify pulmonary hypertension. Involvement of the intrapulmonary arterial branches may result in areas of oligoemia. Oligoemic lungs on plain chest radiography correlate with pulmonary arterial disease in one-third.<sup>30</sup>

Rib notching occurs in the presence of collateral arterial flow secondary to aortic or subclavian artery stenosis, but is unusual since it takes many years to develop.

Hilar lymphadenopathy has been described.<sup>29</sup> There are, however, a few reports of the coexistence of sarcoidosis and large vessel vasculitis,<sup>7,31</sup> both of which may be steroid responsive, and therefore if seen, a coexistent disease should be considered.

### Ultrasound

Ultrasound demonstrates homogenous, intermediate echoic circumferential thickening of the involved vessels, which is quite different from that seen in ordinary atherosclerosis.<sup>32</sup> This finding, particularly in young women, is highly specific for Takayasu's disease. In transverse section, the circumferentially thickened intima-media complex is termed the "macaroni sign".<sup>33</sup> Other findings include vascular dilation, occlusion, and acceleration of flow through regions of stenosis. A reduction in diameter of one-half is required to modify the triphasic Doppler signal in the peripheral arterial tree.<sup>34</sup> Visualisation of the abdominal vasculature is difficult, but can be partially overcome with transoesophageal imaging of the thoracic aorta, or by intravascular ultrasound.<sup>35</sup> Transcranial Doppler may be used to assess the intracranial arteries. In one study, sensitivity and specificity for transcranial Doppler and magnetic resonance angiography were both greater than 95%.<sup>36</sup> The main advantage of colour Doppler flow imaging over magnetic resonance angiography is its ability to visualise residual blood flow. Overestimation of stenosis by magnetic resonance angiography is a well-known phenomenon related to intravoxel dephasing resulting from turbulence of flow at the narrowed segment.

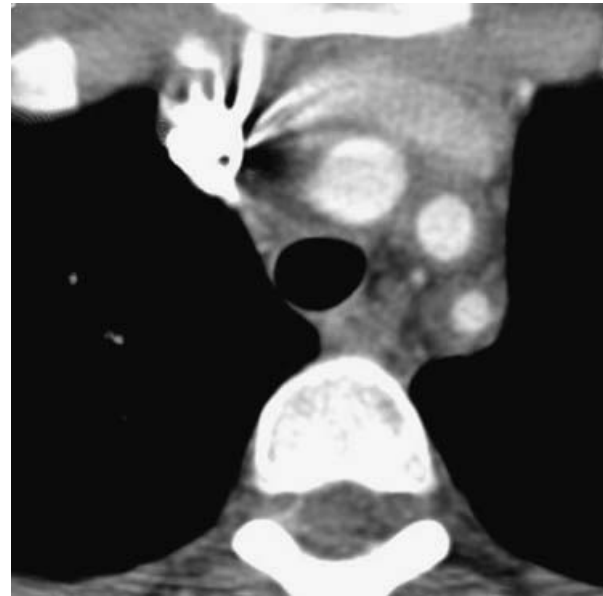
### Angiography

Digital subtraction angiography, of the aorta and its branches, has traditionally been the method for definitive diagnostic assessment.<sup>37</sup> Luminal changes range from smooth tapering stenoses to frank occlusion, and collateral vessels may be seen.<sup>38</sup> The coronary arteries can be evaluated at the same time as the aorta, and if a systemic vein is cannulated, then the pulmonary circulation can be visualised.<sup>39</sup> Angiography is essential if percutaneous intervention is to be considered, for definitive sizing of balloon angioplasty and for deployment of stents. The technique, however, is invasive, involves use of iodinated contrast, and a substantial dose of radiation is given to the patient. It shows arterial mural thickness poorly, and luminal abnormalities are generally a late feature.<sup>35</sup> There are cases where arterial puncture would be difficult because of extensive stenosis or calcification. In one report, the frequency of ischemic complications resulting from angiography was found to be high because blood coagulation is increased in patients with Takayasu's disease.<sup>40</sup>

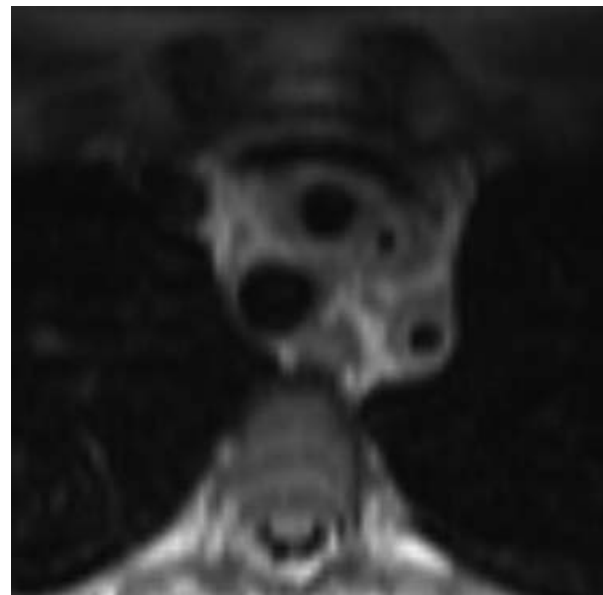
### Cross sectional imaging

Computed tomography and magnetic resonance imaging are important tools for investigating patients, because they can assess luminal and mural

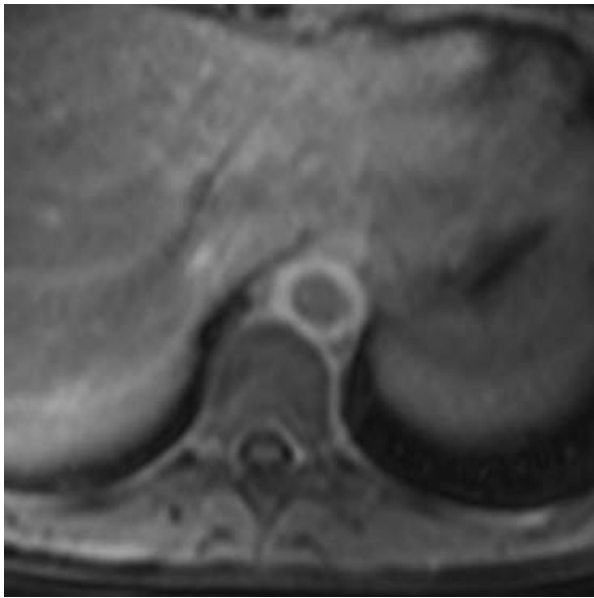
changes, as well as angiographic appearances. In the acute inflammatory stage, the wall becomes thickened, a feature not seen in normal adults (Figs 5 and 6).<sup>41</sup> A decrease in mural thickness following



**Figure 5.** Axial computerised tomogram after administration of contrast at the level of the origin of the arch vessels. Soft tissue thickening surrounding all branches can be seen. Note the normal luminal calibre at this stage.



**Figure 6.** Axial T1-weighted magnetic resonance image at the level of the origin of the arch vessels. Soft tissue thickening surrounding all branches can be seen. The lumen of the left common carotid is now narrowed however.

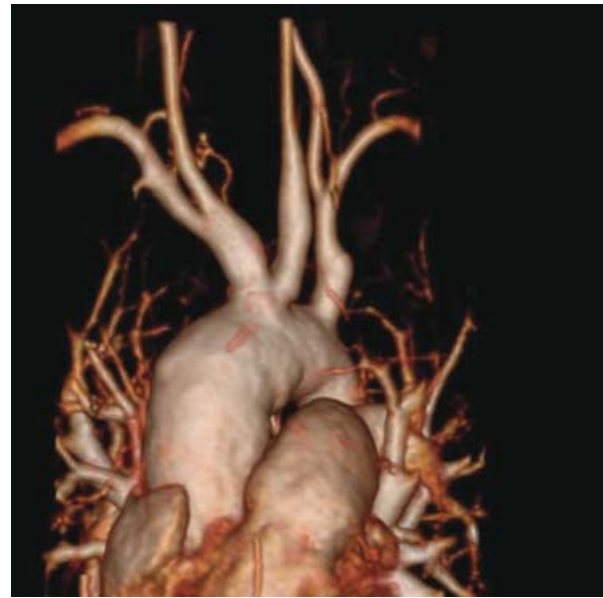


**Figure 7.** Delayed gadolinium enhanced magnetic resonance image. Axial image of the aorta at the level of the diaphragm, showing persisting enhancement at 20 minutes.

treatment with steroids has also been demonstrated with both modalities.<sup>42–43</sup>

Following administration of contrast, there is both early and delayed enhancement. On computed tomography, early mural enhancement is heterogeneous, whereas delayed enhancement is extremely pronounced. An inner concentric ring of low attenuation may also be seen on both arterial phase and delayed imaging in between the opacified blood and outer wall of the aorta, which most likely represents the intima. On magnetic resonance imaging, patterns of aortic mural enhancement are variable.<sup>44</sup> In the acute phase, the aortic wall and surrounding adventitia enhance more than the myocardium, suggesting active disease. Using an inversion recovery prepared gradient echo sequence to null the signal from blood and the arterial wall, it is possible to show delayed mural enhancement (Fig. 7). The mechanism of enhancement using this technique is unknown. Delayed gadolinium enhancement is also seen with myocardial necrosis, fibrosis, myocarditis, and in atherosclerotic plaques.<sup>45</sup> Some authors have not found the presence or absence of gadolinium enhancement of the arterial wall to be a reliable tool for assessing disease activity.<sup>46</sup>

In chronic disease the wall becomes calcified, best appreciated on computed tomography. This calcification may be intimal, or more commonly full-thickness, reflecting the trans-mural nature of the inflammatory process. In addition, the arterial wall in chronic disease does not enhance on early or delayed imaging with iodinated contrast media.<sup>41</sup>



**Figure 8.** Volume rendered magnetic resonance image subsequent to administration of gadolinium showing the aortic arch and its branches, and demonstrating mild tapering of the distal carotid arteries.

Computed tomography also demonstrates parenchymal change within the lungs. Areas of low attenuation reflect arteritis and hypoperfusion,<sup>15</sup> while wedged shaped areas of high attenuation suggest pulmonary infarction.<sup>47</sup>

Cross sectional imaging is of particular importance in follow-up. New lesions can be demonstrated in patients with clinical remission (Figs 8 and 9). Therapeutic effectiveness of medical and surgical intervention can be assessed, including treatment with steroids, the patency of bypass grafts, and any restenosis after percutaneous transluminal angioplasty. Magnetic resonance imaging has several advantages over computed tomography. Paramagnetic contrast media is not as nephrotoxic, and allergic reactions even rarer. There is no ionizing radiation, and hence it can be used safely for long term follow up. Soft-tissue contrast resolution is better, with improved visualisation of mural edema, and cine magnetic resonance imaging can be used to evaluate vascular and valvar flow, along with ventricular function.

#### *Positron emission tomography*

Recently, [<sup>18</sup>F] fluorodeoxyglucose positron emission tomography has been investigated as a tool for diagnosing and monitoring disease activity in large vessel vasculitides. [<sup>18</sup>F] fluorodeoxyglucose identifies areas of high glucose metabolic activity.<sup>46</sup> Several reports have shown the value of this



**Figure 9.** Volume rendered magnetic resonance image after administration of gadolinium of the aortic arch and branches, demonstrating a severe long segment stenosis of the left common carotid artery involving its origin, and mild narrowing of the other arch vessels. Figure 9 was obtained in the same patient 5 months after Figure 8, and shows progression of disease despite normal inflammatory markers, and no symptoms.

technique in the diagnosis of large vessel arteritis. In one study, 28 positron emission tomography scans were performed on 18 patients suspected of having Takayasu's disease. All patients were evaluated with a full clinical and laboratory assessment, cross-sectional imaging and angiography, and all but 2 satisfied the criteria of the American College of Rheumatologists for Takayasu's disease. In another study, the technique achieved a sensitivity of 92%, a specificity of 100%, and negative and positive predictive values of 85% and 100% respectively, in the initial assessment of active vasculitis in Takayasu's disease.<sup>48</sup> The signal is not always strong enough to diagnose inflammation, and sensitivity can be improved by co-registering with enhanced computed tomography.<sup>49</sup> Accumulation of [<sup>18</sup>F] fluorodeoxyglucose has been shown to correlate with levels of activity of the disease, suggesting that it may be a potential tool for estimating the extent of disease and its response to medical treatment.<sup>46,49</sup>

[<sup>18</sup>F] fluorodeoxyglucose has also been shown to accumulate in atherosclerotic plaques.<sup>50</sup> It should be noted that, as with other chronic inflammatory diseases such as systemic lupus erythematosus and rheumatoid arthritis, one-quarter of patients with Takayasu's disease have an increased incidence of

atherosclerosis.<sup>51</sup> Interpretation of positive results, therefore, should be undertaken cautiously, and used in conjunction with clinical findings. Positron emission tomography with or without co-registration with computed tomography carries a high radiation dose. There is also limited availability, making it unsuitable for long-term follow up.

## Treatment

### Medical

Treatment is divided into those therapies designed to induce remission, and those that manage the complications of Takayasu's disease. Glucocorticoid therapy is often the first line treatment. In one North American series,<sup>7</sup> glucocorticoid therapy alone achieved initial remission in over half the patients, with children and adults achieving comparable levels of remission, but with shorter times to remission in children. Second-line agents, including cyclophosphamide, azathioprine, and methotrexate, can be added if the patient is unresponsive to glucocorticoids alone. This produces remission in up to four-fifths of patients, children as well as adults.<sup>7,52</sup> Increasingly, second line agents are being added early as steroid-sparing drugs, as opposed to waiting for relapse when steroids are weaned.<sup>53</sup> Minocycline combined with prednisolone has also been used with success in patients with active disease.<sup>54</sup> Use of anti-tumour necrosis factor therapy, with etanercept or infliximab, also produced an improvement in all but 1 patient with active relapsed disease over an age range of 17 to 48 years, and sustained remission in two-thirds of patients, who were able to discontinue glucocorticoid therapy.<sup>55</sup>

Hypertension can be difficult to treat, and is exacerbated by glucocorticoid therapy. The use of inhibitors of angiotensin converting enzyme needs particular care because of the high frequency of associated renal arterial stenosis.<sup>37</sup> Thrombosis is a further problem, with patients often requiring antiplatelet therapy and anticoagulation. Prophylaxis against *Pneumocystis carinii* pneumonia may be required with immunosuppressant therapy. In one study, one-fifth of patients had strongly positive skin tests for tuberculosis, and had been started on anti-tubercular therapy.<sup>11</sup>

### Endovascular and surgical

For patients who require interventional revascularisation, both endovascular and surgical procedures can be performed safely, with low morbidity and mortality. The best long-term outcomes however are achieved with conventional bypass grafts.<sup>56</sup> Interventional procedures are indicated for hypertension associated with critical renovascular stenosis, ischemia when

extremely limiting activities of daily living, clinical features of cerebrovascular ischaemia or critical stenosis of at least three cerebral vessels, moderate aortic regurgitation, cardiac ischaemia with proven coronary arterial stenosis,<sup>7</sup> and aneurysmal dilation of the aorta.

Bypass surgery, and the use of interposition grafts, with the exception of selected pulmonary arterial reconstructions, is the preferred technique for arterial reconstruction. This is because of disappointing early results with patch angioplasty and endarterectomy in areas of inflammation and transmural fibrosis. For bypass surgery, areas of the arterial tree that are unaffected by disease are the preferred anastomotic sites. Autologous grafts are more successful than synthetic grafts. Long-term rates of patency are good for both, but can be compromised by poor flow, if extensive collaterals divert large volumes of blood.<sup>57</sup>

Whenever possible, surgery should be done when the disease is quiescent, since there is an increased risk of failure for surgical procedures undertaken during active disease. Surgical bypass is the preferred treatment of longer segment stenoses and occlusions. Complications include restenosis, thrombosis, haemorrhage, infection,<sup>7</sup> and anastomotic aneurysms.<sup>57</sup>

Percutaneous transluminal angioplasty with or without placement of stents has been described in the aorta, brachiocephalic, carotid, subclavian, coeliac trunk, mesenteric, iliac and femoral arteries. The success rate of angioplasty in total occlusion is comparatively low. Short-segment occlusions may be initially opened by angioplasty,<sup>58</sup> and can be successfully reattempted with recurrent stenosis. Endovascular stenting is performed following arterial dissection, and suboptimal results after angioplasty.

Initial success rates of angioplasty are high. In contrast to the results in treating atherosclerosis, nonetheless, a number of series report a high proportion of vessels restenosing.<sup>59,60</sup> Other authors,<sup>61</sup> in contrast, are more optimistic about the long-term efficacy of angioplasty. Coronary arterial stenting deserves particular attention, because of the seriousness, in terms of major adverse cardiac events, of occlusion of stents. There have only been a few reports regarding angioplasty and stenting of the coronary arteries resulting from Takayasu's disease. The most likely reason is that lesions are usually sited at the orifices of the arteries, such as the main stem of the left coronary artery, which in the past have often been considered unsuitable for percutaneous treatment.<sup>62</sup> There are promising early results, nonetheless, in the use of sirolimus-eluting stents. Sirolimus has immunosuppressive properties, which may have a beneficial synergistic effect with its anti-proliferative action on vascular

smooth muscle cells in the prevention of occlusion after stenting the coronary arteries in Takayasu's disease.<sup>63</sup> The surgical treatment of aortic regurgitation caused by Takayasu's disease is difficult because of the need to manipulate friable tissue. Complications, such as valvar detachment after replacement of the aortic valve, or anastomotic aneurysm after composite graft repair, may still occur as a result of fragility of the aortic wall or the hingelines of the leaflets. There is also further concern about late dilation of the remaining ascending aorta in the long-term follow up.<sup>64</sup>

## Conclusions

The investigation and management of Takayasu's disease can prove difficult. The initial symptoms and signs are non-specific, and a high index of suspicion is needed if the diagnosis is to be made. The disease is associated with a high incidence of morbidity, and a significant risk of premature death. The presence of one or more severe single complications, including retinopathy; secondary hypertension; aortic regurgitation, and aortic or arterial aneurysms, are useful in predicting outcome. Serological tests have proved unreliable in distinguishing active from quiescent disease. Recent work suggests that monitoring inflammatory cytokines such as interleukin-18 may prove useful in the future.

The clinical challenge is to diagnose the disease early during active inflammation. Subtle signs may be apparent on plain radiography, but computed tomography is likely to be the most effective, widely available, tool for patients. Angiography has traditionally been the gold standard, but only provides information relating to luminal change. Magnetic resonance imaging is preferred for long-term follow up, as it visualises the vessel lumen, shows mural thickening, and enhancement, and can therefore provide information relating to activity of the disease and unrecognised complications. Positron emission tomography co-registered with computed tomography can also demonstrate active inflammation, but the availability is currently limited and requires a high radiation dose.

Medical treatment involves high dose steroids, with immunosuppressants. Newer agents, including anti-tumour necrosis factor drugs, have been used with some success. Surgical and endovascular procedures provide symptomatic relief from ischaemic complications, but suffer from late vascular occlusion. Future treatment may involve targeting both inflammation and myointimal hyperplasia associated with the disease in the form of medical therapy and drug-eluting endovascular stents.



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