

Lessons of the month 2: Retinal vasculitis: a first presentation of Takayasu's arteritis

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ABSTRACT

Takayasu's arteritis is a chronic, systemic, large-vessel vasculitis affecting the aorta and its primary branches. However, coronary, renal and pulmonary arteries and small vessel involvement has been documented. We describe a rare case of Takayasu's arteritis with extensive supra-aortic arch disease, manifesting with bilateral occlusive retinal vasculitis as a first presentation. This is elicited by fundus findings of vascular sheathing and fundus fluorescein angiography evidence of retinal vessel occlusion and peripheral capillary non-perfusion.

KEYWORDS: retinal vasculitis, Takayasu's arteritis

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Case presentation

A 39-year-old woman presented with sudden left visual loss preceded by a 1-week history of headache. Systemic enquiry revealed a syncopal episode 3 months previously, and a 1-month history of unintentional weight loss. Past medical history included psoriasis and a hospital admission aged 16 years, with a flu-like illness associated with a rash and hypertension. Around the same time, she had right nephrectomy for refractory hypertension. She had a caesarean section performed at 27 weeks for poor fetal growth. She was not taking any regular medications and had no known allergies.

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On examination, blood pressure was 135/85 mmHg. Unaided visual acuities were 6/6 in the right eye and 6/36 in the left eye. Intraocular pressure (IOP) was normal bilaterally. The left pupil was fixed and dilated, and there was no relative afferent pupillary defect. Left fundus examination showed multiple cotton-wool spots and vascular sheathing in the posterior pole, and microaneurysms and small blot haemorrhages in all four quadrants (Fig 1a). Right eye examination showed sparse dot retinal haemorrhages in the superotemporal fundus (Fig 1b). Wide-field fundus fluorescein angiography showed bilateral (mainly left) occlusive vasculitis involving retinal arteries and arterioles (Figs 1c and 1d).

Results of laboratory investigations demonstrated mild hypercholesterolaemia and hypertriglyceridaemia. Autoimmune and infection screens were negative (supplementary material S1).

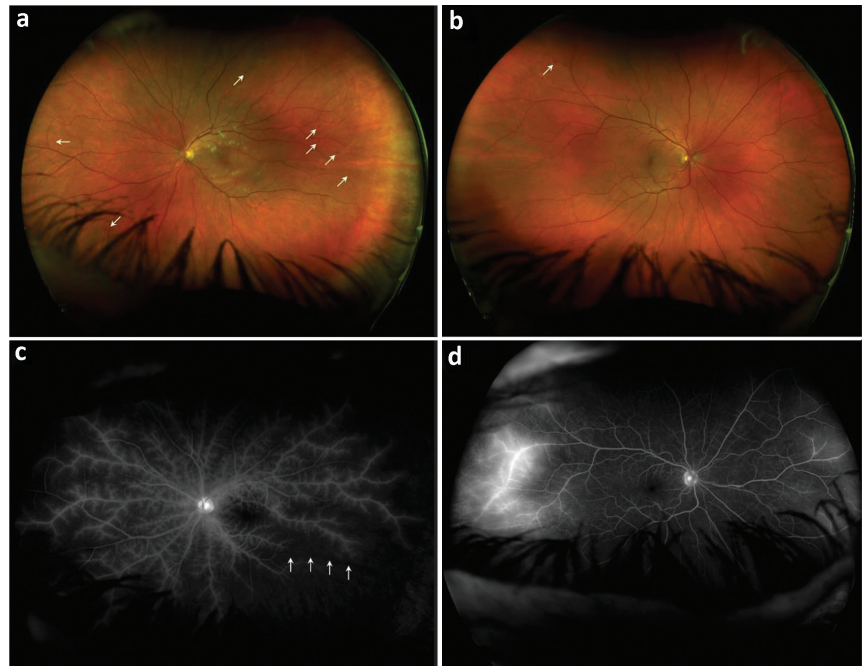
Treatment with high-dose oral prednisolone (1 mg/kg per day) was initiated and the patient was referred urgently to a vasculitis specialist. Contrast magnetic resonance imaging and magnetic resonance angiography of the brain (Fig 2) showed multiple old watershed and deep white matter infarcts, and an acute left cortical infarct. There was no significant abnormal contrast enhancement to suggest active vasculitis.

She experienced two subsequent episodes of collapse and an episode of right amaurosis fugax. Further evaluation demonstrated differential arm blood pressure measurements (right 111/60 mmHg; left 94/61 mmHg). Her pulse was absent over the left carotid artery and in both feet, and bruits were audible bilaterally over carotid, vertebral and subclavian arteries, and over the abdominal aorta and left renal artery.

Subsequent assessment by the vascular team with carotid duplex and computed tomography angiography of the aortic arch and supra-aortic vasculature (Fig 3) demonstrated complete occlusion of the left carotid artery and 90% stenosis of the right internal carotid artery (ICA). Before right ICA endarterectomy, induction immunosuppression with intravenous cyclophosphamide (800 mg) and intravenous pulsed methylprednisolone (3 g) was administered. This was followed by three doses of intravenous tocilizumab infusion (8 mg/kg), 4 weeks apart, which covered the peri-operative period. Tocilizumab was converted to weekly subcutaneous dosing, 28 days after the last infusion, continuing for 1 year. Methotrexate was started for maintenance immunosuppression.

During follow-up in uveitis clinic 3 weeks after surgery, left IOP was raised (42 mmHg), associated with a closed

Fig 1. Bilateral fundus photography and fundus fluorescein angiography at presentation. a) Left fundus showing multiple cotton-wool spots and vascular sheathing in the posterior pole, and microaneurysms and small blot haemorrhages in all four quadrants (arrows). b) Right fundus showing sparse dot retinal haemorrhages in the superotemporal fundus. c and d) Wide-field fundus fluorescein angiography showing bilateral occlusive vasculitis, widespread in the left retina with peripheral capillary non-perfusion, the arrows indicate an occluded retinal vessel (c) and localised in the right temporal and nasal peripheral retina (d).



iridocorneal angle, but there was no visible iris or angle neovascularisation. She was treated with a combination of IOP-lowering eye drops. Eight months later, she presented with left neovascular glaucoma: eye pain, raised IOP, total peripheral anterior synechiae and hyphaema. She was treated with left intravitreal bevacizumab injection, followed by peripheral

retinal photocoagulation, and trans-scleral cyclodiode laser. At follow-up 18 months after her first presentation, she was still experiencing episodes of left ocular pain associated with IOP spikes, for which she had aqueous shunt implantation surgery. Visual acuity in the left eye was perception of light and 6/9 in the right eye.

Fig 2. Contrast magnetic resonance imaging (MRI) and magnetic resonance angiography of the brain. a) Coronal MRI SENSE sequence demonstrating irregularity of the posterior brain circulation with occluded left V4 branch (arrow). b and c) Axial brain MRI diffusion-weighted imaging / apparent diffusion coefficient sequences showing an acute left precentral gyrus cortical infarct, seen as restricted diffusion (circles).

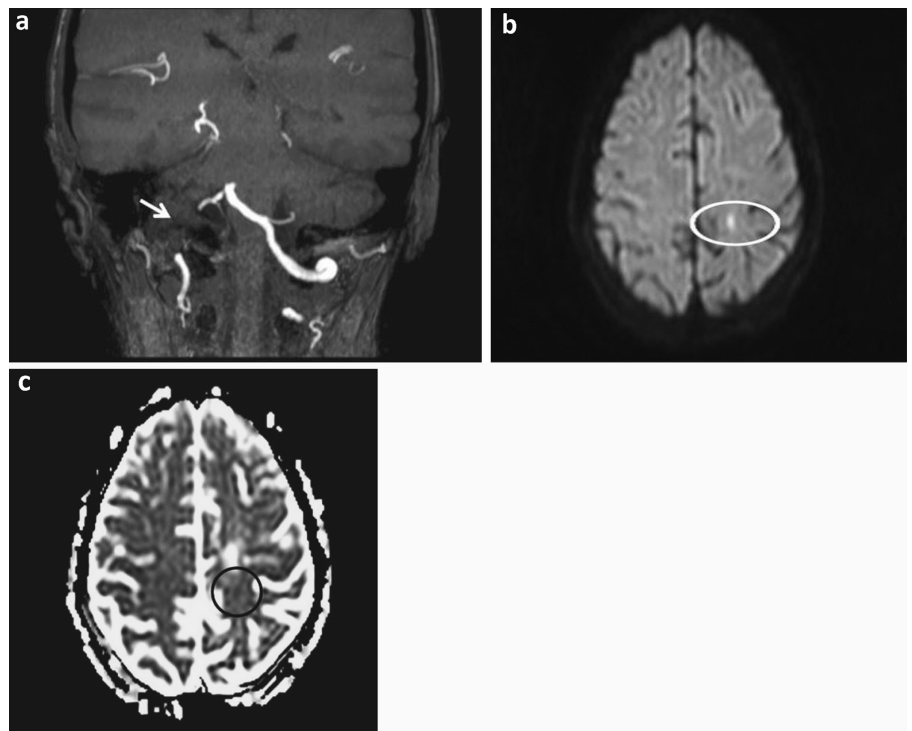




Fig 3. Computed tomography angiography of the aortic arch and supra-aortic vasculature. a, b and c) Axial (a), coronal (b) and sagittal (c) images demonstrating occluded left common carotid artery from its origin at the aortic arch (arrows). d) Coronal image showing occluded right external carotid artery (arrow), left common carotid artery (lower dashed arrow) and left internal carotid artery (upper dashed arrow). e) Sagittal reformatted computed tomography demonstrating 90% stenosis of the right internal carotid artery (arrow).

Discussion

Takayasu's arteritis (TA) is a chronic systemic large vessel vasculitis affecting the aorta and its primary branches; however, coronary, renal and pulmonary arteries and small vessel involvement has been documented.^{1–3} The major pathology is granulomatous panarteritis with intimal proliferation and defects of the elastic lamina, leading to thickening, fibrosis, stenosis, aneurysm and thrombus formation.^{1,2} Patients may present initially with constitutional symptoms and later develop ischaemic symptoms.

Ocular involvement can be part of TA in up to 45% of cases.⁴ The most common manifestation is Takayasu's retinopathy (TR), classified into four stages: dilatation of small vessels capillary, microaneurysm formation, arteriovenous anastomoses and ocular ischaemic syndrome.⁵ Other reported manifestations include central or branch retinal artery or vein occlusion; anterior ischaemic optic neuropathy; vitreous haemorrhage secondary to neovascularisation; neovascular glaucoma; or uveitis.⁶

We report the first case of TA diagnosed following initial presentation with bilateral occlusive retinal vasculitis. This rare manifestation of TA was reported in one other case of a patient with a diagnosis of TA referred to the ophthalmology clinic.⁷ The patient we present had features of stage 1 and 2 TR, with an

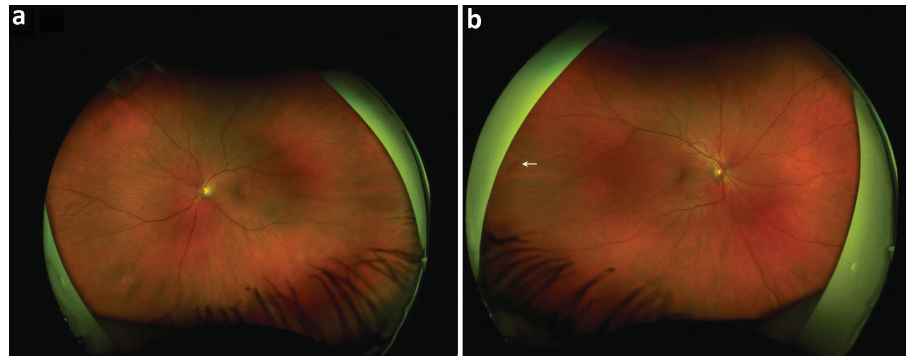
improvement in appearance 24 weeks from treatment initiation (Fig 4). The subsequent ophthalmic sequelae of left ocular ischaemia and neovascular complications in the left eye is in line with the more frequently reported late ophthalmic presentation of ocular ischaemia.^{6,8}

According to the American College of Rheumatology, the presence of at least three of six characteristics is diagnostic of TA.¹ In this case, the patient fulfilled four characteristics: age ≤ 40 years; systolic blood pressure difference greater than 10 mmHg between two arms; audible bruit over subclavian arteries and abdominal aorta; and arteriographic narrowing of primary branches of the aorta.

The aim of medical treatment is to reduce inflammation. The history of multiple syncopal episodes and radiological evidence of watershed cerebral infarcts suggested haemodynamic cerebral ischaemia. The resultant high risk of stroke meant that early surgical intervention to the stenosed right ICA was necessary. Immunosuppression with high-dose corticosteroids and tocilizumab (an interleukin-6 receptor inhibitor) was administered peri-operatively in order to reduce inflammation at surgical anastomosis sites and improve surgical outcome.⁹

Interestingly, histological analysis of the right ICA endarterectomy revealed exclusively atherosclerotic plaques.

Fig 4. Bilateral fundus photography showing an improvement in retinal signs 24 weeks from treatment initiation.



A higher rate of atherosclerotic plaques in patients with a confirmed diagnosis of TA compared with healthy controls has been previously reported due to premature accelerated atherosclerosis.¹⁰

The rare ocular presentation of retinal vasculitis in this case allowed prompt diagnosis of TA. This case highlights the important role of timely retinal and radiological imaging. TA is a morbid and potentially life-threatening condition that has a significant effect on quality of life. Involvement of specialist teams early and a multidisciplinary approach to management are necessary to improve clinical outcomes and reduce risk of complications. ■

Supplementary material

Additional supplementary material may be found in the online version of this article at www.rcpjournals.org/clinmedicine:
S1 – Results of laboratory measurements at time of presentation to emergency eye clinic.

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