Giant cell arteritis: not just a stroke in the eye

Giant cell arteritis is a large vessel vasculitis with predilection for the cranial arteries. However, as illustrated by two case reports in this month's issue (p. 650 and 651), involvement of large vessels, such as the aorta, is increasingly recognized. It is the commonest systemic vasculitis of the elderly, almost exclusively seen in those of over 50 years of age. There is a female preponderance and geographical variation in prevalence, with higher frequency in Caucasians than in other ethnicities. The incidence in the UK is 2.2/10 000 person-years.

Cranial giant cell arteritis

The best recognized manifestation of giant cell arteritis is temporal arteritis. Visual loss occurs early in disease. Once established, visual recovery is rare. Therefore early detection and immediate treatment of giant cell arteritis is paramount, and features predictive of neuro-ophthalmic complications must be recognized and sought.

In meta-analysis, the following features were found to be most predictive of temporal artery biopsy positivity (which is associated with neuro-ophthalmic complications): jaw and tongue claudication, visual disturbance, especially diplopia, and physical abnormalities of the temporal artery (including diminished pulse, thickening and beading) (Smetana and Shmerling, 2002). It should be noted that features commonly sought when evaluating patients for giant cell arteritis, such as headache, scalp tenderness and raised erythrocyte sedimentation rate, did not correlate to biopsy positivity.

Large vessel giant cell arteritis

As illustrated in this month's cases, patients with giant cell arteritis can suffer ischaemic complications in extracranial vascular territories. In a 50-year follow-up cohort, 27% of patients experienced large artery complications of giant cell arteritis, with an incidence of 30.5/1000 person-years at risk (Nuenninghoff et al, 2003) (Makkuni et al, 2008). Of these, 18% suffered aortic aneurysm or dissection, and 13% developed large artery stenosis. Large vessel involvement was less likely in patients with cranial symptoms (hazard ratio 0.1) and high erythrocyte sedimentation rate (hazard ratio 0.8). Thoracic artery dissection was associated with an excess of deaths. A recent study (Blockmans et al, 2008) using fluorodeoxyglucose-positron emission tomography (FDG-PET) in early giant cell arteritis showed that patients with uptake around the aortic root developed greater dilatation at this site later on.

Patients with giant cell arteritis may also present with a systemic picture, with constitutional upset, weight loss and unexplained high inflammatory markers.

Temporal artery biopsy and imaging

Temporal artery biopsy should be performed in all patients suspected to have giant cell arteritis, given the potential for serious toxicity from high-dose steroid therapy. The degree of intimal hyperplasia on temporal artery biopsy correlates well with the likelihood of neuro-ophthalmic complications, therefore temporal artery biopsy has a prognostic as well as a diagnostic role (Makkuni et al, 2008). The likelihood of biopsy positivity is sensitive to technical issues, and biopsy may be difficult to obtain because of logistic issues. Therefore it is very important to establish local referral pathways for temporal artery biopsy. Histology can remain positive for up to 4 weeks after institution of steroids, so treatment should not be delayed pending biopsy. However, a negative biopsy does not exclude giant cell arteritis if the clinical suspicion is high.

Although Doppler ultrasound shows promise for the non-invasive detection of cranial giant cell arteritis (Schmidt et al, 1997), it is operator-dependent and requires a high level of expertise, so cannot be recommended for general use. Outline proposals are being evaluated for a study of duplex ultrasonography *vs* temporal artery biopsy in diagnosis of patients with suspected giant cell arteritis.

Imaging modalities such as magnetic resonance imaging (MRI) and PET are sensitive in detecting large vessel giant cell arteritis. Assessment of the cranial involvement pattern of giant cell arteritis has also been reported using 3 Tesla MRI. Indeed, a number of cases of giant cell arteritis have been identified through imaging, when alternative diagnoses were suspected. Routine screening of patients with cranial giant cell arteritis with PET or MRI is not indicated.

Treatment

Early treatment with high-dose glucocorticoids is paramount, as delays in treatment cause blindness (Proven et al, 2003). In uncomplicated giant cell arteritis, prednisolone 40–60 mg should be started (at least 0.75 mg/kg/day), together with bone and gastrointestinal protection. Low-dose aspirin decreases the rate of visual loss and ischaemic complications, and should be used in all patients (Nesher et al, 2004). In patients with visual disturbance, intra-venous steroids may be used.

Although there is no consensus in the literature, it is generally recommended that 3 days of intravenous methylprednisolone 500 mg–1 g/day should be used, followed by prednisolone 60 mg daily. Alternate day regimens are associated with visual loss, and should not be used. High-dose steroids should be maintained for 4 weeks, with a gradual dose reduction after this, provided that patients remain clinically in remission with normal inflammatory markers. Most patients can discontinue steroids within 1–2 years. If remission cannot be maintained, adjuvant disease-modifying therapy may be required (Mahr et al, 2007). Although promising in uncontrolled case series, biological therapies remain unproven in systematic studies.

Table 1. Recommendations for management of giant cell arteritis

Clinical	Increased vigilance to allow prompt diagnosis of giant cell arteritis
	Predictors of ischaemic complications, including jaw and tongue claudication and visual disturbance, must always be sought
	Immediate institution of high-dose corticosteroid when giant cell arteritis is suspected
	Urgent temporal artery biopsy in all patients with suspected giant cell arteritis, which should not delay commencement of steroid therapy
	Use of positron emission tomography or magnetic resonance imaging in assessment of suspected large vessel disease, but not cranial disease
	Low-dose aspirin in all patients
	Bone and gastrointestinal protection with commencement of steroids
Organizational	All patients with suspected giant cell arteritis should be referred for specialist assessment and management. However, this should not delay steroid initiation
	Local processes need to be developed to allow prompt access to specialist management, including temporal artery biopsy
	Widespread education and training in the early detection and management of giant cell arteritis is necessary

Outcomes

Once visual loss is established, recovery is rare. Although this does not impact on mortality, it has major implications for quality of life and independent living. Patients with total monocular visual loss, faced with the prospect of visual loss in the second eye, would trade three quarters of their remaining years for perfect vision in each eye.

Although higher mortality rates may be expected with large vessel complications of giant cell arteritis, in longitudinal follow up survival was the same for patients with and without large vessel complication, and also the general population. The only large vessel complication with excess mortality was thoracic aortic dissection.

Conclusions

Giant cell arteritis is a medical emergency, with permanent vision loss in up to 20% patients, resulting mainly from failure of prompt recognition and treatment. It should be viewed as a 'stroke of the eye' with features of impending visual loss being considered its 'transient ischaemic attacks', with similar urgency in approach as cerebral and coronary ischaemia.

Widespread education is needed to ensure prompt diagnosis and especially recognition of predictors of visual loss (*Table 1*). Pathways for referral for urgent management, including temporal artery biopsy, need to be established locally. National guidelines for the management of giant cell arteritis are being produced by the British Society of Rheumatology and a national group for polymyalgia rheumatica and giant cell arteritis is being formed to increase patient involvement in education, training and research. BJHM

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KEY POINTS

- Giant cell arteritis is a medical emergency with rapid irreversible visual loss if untreated. Early disease recognition and immediate initiation of high-dose steroid therapy saves sight.
- Giant cell arteritis does not always present with headache.
- Jaw claudication is a cardinal 'red flag' warning of imminent visual loss.
- Patients at highest risk of visual loss often do not have very high levels of inflammatory markers.
- Temporal artery biopsy is indicated in all patients with suspected giant cell arteritis and can remain positive for some days after initiation of steroids. Treatment should not be delayed awaiting biopsy.
- Giant cell arteritis may also involve intracranial and other large arteries elsewhere in the body.
- Consider giant cell arteritis in older patients with unexplained high inflammatory response or constitutional symptoms.