

Giant cell (temporal) arteritis in Singapore: an occult case and the rationale of treatment

Cullen J F, Chan B M J, Wong C F, Chew W C I

ABSTRACT

Further observations in respect of giant cell arteritis (GCA) as encountered in a local neuro-ophthalmology service established in Singapore ten years earlier are reported. The rarely seen occult form of the disease is described along with an illustrative case report concerning an 80-year-old woman. The overall management of GCA is discussed in respect of four clinical scenarios and their treatment.

Keywords: arteritic anterior ischaemic optic neuropathy, giant cell arteritis, ischaemic optic neuropathy, occult giant cell arteritis, temporal arteritis

Singapore Med J 2010; 51(1): 73-77

INTRODUCTION

Temporal arteritis, now termed giant cell arteritis (GCA), was first defined by Horton et al⁽¹⁾ from the Mayo Clinic in 1932, but Hutchinson in 1890⁽²⁾ recorded the case of an employee at the London hospital, who had such severe pain and swelling in his temples that he was unable to wear his official hospital headgear. The literature was reviewed by Whitfield et al in 1963,⁽³⁾ and along with their own cases, an incidence of up to 70% of visual loss in GCA was reported. Occult or hidden GCA was first described in the USA by Simmons and Cogan⁽⁴⁾ and by Cullen⁽⁵⁾ in the UK. In contrast to the classical form of GCA, patients with occult disease present with sudden visual loss, no systemic symptoms, and an absence of signs or symptoms in their temples. Arteritic anterior ischaemic optic neuropathy (AAION) is the common ocular manifestation of the condition, and in a few cases, retinal vascular occlusions may occur.

CASE REPORT

An 80-year-old Chinese woman with no preceding medical history presented to the Emergency Department on March 20, 2009 with a three-week history of visual loss in the left eye. The visual loss was painless, and three days prior to presentation, she reported complete

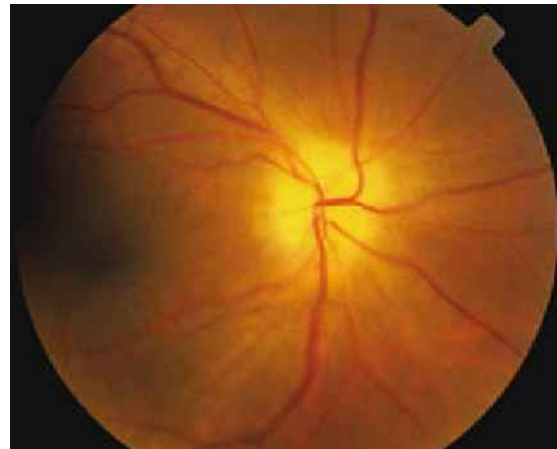


Fig. 1 Fundus photograph shows the optic disc appearance in acute anterior ischaemic optic neuropathy associated with giant cell arteritis. Note a pale, swollen infarcted optic disc with normal retinal circulation (It was not possible to reproduce a picture of the case reported because of the presence of substantial cataract).

loss of light perception in that eye, although this may have been discovered because she rubbed or closed her good eye. There was no associated headache, scalp pain or tenderness, and no jaw claudication or constitutional symptoms such as fever or loss of weight. The patient said she felt well. On examination, the visual acuity in the affected eye was no perception of light (NPL) with an afferent pupillary defect. Ocular examination revealed the presence of significant nuclear sclerosis cataract and a pale, slightly swollen optic disc (Fig. 1). The swelling was mainly below and nasally with a peridisc "exudate", all these signs suggesting resolving ischaemia. Based on these findings and particularly with NPL, a provisional diagnosis of AAION was made.

Visual acuity in the other eye was 6/15, explained by the presence of a significant nuclear sclerosis cataract. There were no other pathological findings in this right eye. Her erythrocyte sedimentation rate (ESR) was 84 mm/hr. An urgent biopsy of the left superficial temporal artery was performed, which showed a pronounced inflammatory infiltrate with epithelioid histiocytes and lymphocytes in the vessel wall, particularly over the intima but also involving the tunica media (Fig. 2). Scattered giant cells were also noted. Elastic staining

Neuro-
Ophthalmology
Service,
Singapore National
Eye Centre,
11 Third Hospital
Avenue,
Singapore 168751

Cullen JF, FRCS,
FRCSE
Senior Consultant

Chan BMJ, MRCSE
Registrar

Department of
Pathology,
Singapore General
Hospital,
Outram Road,
Singapore 169608

Wong CF, MBBS
Registrar

Chew WCI, MRCPath
Associate Consultant

Correspondence to:
Dr James Finbarr Cullen
Tel: (65) 6227 7255
Fax: (65) 6226 3395
Email: jbarrycullen@
yahoo.com

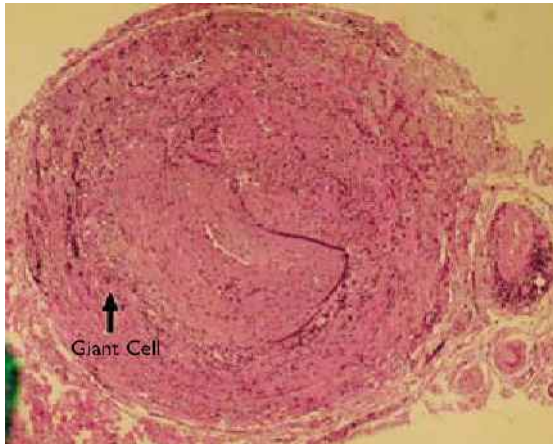


Fig. 2 Photomicrograph of the cross-section of the biopsied superficial temporal artery shows transmurular infiltrate of lymphocytes and histiocytes and a single giant cell (arrow) (Haematoxylin & eosin, $\times 4$).

highlighted the internal and external elastic laminae, which were shown to be discontinuous and fragmented (Fig. 3). The diagnosis of AAION was thus confirmed.

On completion of the biopsy, because the vessel appeared grossly abnormal, she was started on oral corticosteroid medication. Such treatment (see below), generally commencing with 60–80 mg oral prednisolone daily, is designed to prevent similar visual loss in the good eye which can be expected to develop in all positive cases without treatment. Sequential visual loss occurs in about one-third of cases within 24 hours, and the further thirds within one week and one month.⁽⁶⁾

As expected, there was no visual improvement in the affected eye, and the fellow eye remained unaffected. Her ESR fell to 60 mm after three days, and to 49 mm after a further week, and to 5 mm at one month following presentation when the dose of oral corticosteroid medication was reduced to 20 mg daily. She has now been followed up for nine months; her ESR has remained in single figures and the dosage is down to 5 mg prednisolone daily.

DISCUSSION

Table I gives the details of the seven cases discussed here. There have only been two papers from Singapore, both published in this journal, reporting visual loss associated with biopsy-proven GCA. The first case (Case 5), reported in the year 2000, was from another hospital and described a patient with bilateral sequential AAION with complete blindness and having a history of classical GCA.⁽⁷⁾ The second (Case 6), reported in 2003, recorded a case with central retinal artery occlusion that had been treated in a medical unit earlier, also with classical biopsy-proven GCA.⁽⁸⁾ This patient died suddenly five months later from a dissecting thoracic aortic artery

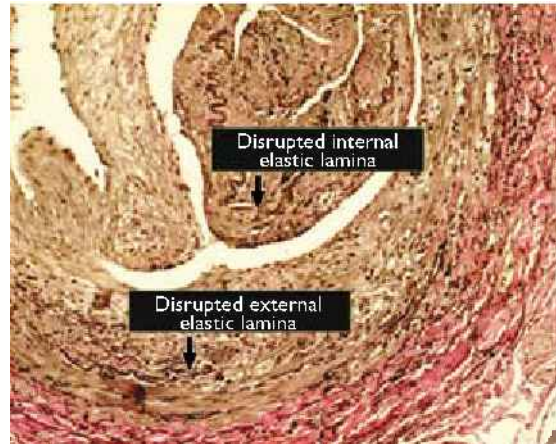


Fig. 3 Section of the arterial wall shows disruption of both internal and external elastic laminae (arrows) (Elastic van Gieson, $\times 10$).

aneurysm, which is a known complication of GCA.

Occult GCA is accepted as a common cause of visual loss in the elderly Caucasian population,⁽⁹⁾ and temporal artery biopsies are regularly performed in eye departments in Europe and the USA. Since our formal neuro-ophthalmology service was established ten years ago at the Singapore National Eye Centre (SNEC), only six positive temporal artery biopsies (Cases 1–4 & 6–7), including two (Cases 6 & 7) with visual loss, have until now been encountered. The case described above (Case 7) was the first biopsy-proven instance of occult GCA with visual loss seen here. In all, therefore, only seven biopsy-proven cases of GCA have been reported from Singapore, with all seven patients being Chinese and five female. No patient had evidence of polymyalgia, and all were treated with oral prednisolone.

It is important that all ophthalmologists who encounter an elderly patient with sudden severe visual loss remember that GCA must be considered and excluded in all such patients. Urgent ESR and C-reactive protein (CRP) tests should be performed and a temporal artery biopsy (TAB) carried out as soon as possible, if either is significantly elevated. It is also essential that all trainee ophthalmologists are able to perform a TAB and find the vessel, which can prove extremely difficult. The temporal artery looks more like a vein when normal and patent, but a diseased one can look like a thin white solid cord 1–2 mm in diameter, or it can be thickened and tortuous. The biopsy is usually taken from an anterior branch vessel at brow level or in front of the tragus of the ear; this latter position may prove easier for the less experienced surgeon, the vessel being larger and more constant in position, although quite deep and lying on the temporal fascia. Usually, when the biopsy is positive, the operative field is virtually bloodless.

Table I. Demographics, ESR levels, ocular involvement, period of follow-up and outcomes of the seven biopsy-proven GCA patients.

Patient no.	Age (years)	Gender	Ethnicity	Type	ESR	Ocular involvement	Treatment	Follow-up (mth)	Outcome
1	84	Female	Chinese	Classical	109	None	OP	84	No ocular involvement
2	73	Female	Chinese	Classical	125	None	OP	60	No ocular involvement
3	68	Male	Chinese	Classical	118	None	OP	24	No ocular involvement
4	77	Female	Chinese	Classical	92	Transient visual obscurations	OP	7	No subsequent visual loss
5	83	Female	Chinese	Classical	92	Sequential AAION ⁽⁷⁾	OP	No record	Bilateral blindness
6	86	Male	Chinese	Classical	72	Central retinal artery occlusion ⁽⁸⁾	OP	5	Died 5 months after presentation
7	80	Female	Chinese	Occult	84	Unilateral AAION*	OP	9	No involvement of the fellow eye

* Present case report

GCA: giant cell arteritis; ESR: erythrocyte sediment rate; AAION: arteritic anterior ischaemic optic neuropathy; OP: Oral prednisolone

In Singapore, AAION must be distinguished from the nonarteritic variety (NA-AION), which is the commonest cause of optic neuropathy in our elderly patients. This subject has also been discussed earlier in this journal.⁽¹⁰⁾ To make matters more difficult, some patients with GCA and visual loss have been found to have a normal ESR,⁽¹¹⁾ hence, the diagnosis has to be made on clinical grounds alone. It is also essential in this part of the world to state that the diagnosis of GCA should not be made without a positive biopsy. In the SNEC, a number of temporal artery biopsies have been performed on patients with visual loss associated with ischaemic optic neuropathy, and where there was a high ESR—often over 100 mm—which have proven to be negative, so these are non-arteritic cases. This is very important because only patients with proven AAION require immediate corticosteroid treatment, often for many years, while cases of commonly-occurring NA-AION are not given such treatment.

In order to understand this issue, the underlying pathology of AAION must be considered. GCA is a diffuse inflammatory disease mainly involving large- and medium-sized arteries, in particular the external carotid artery and its branches, especially the superficial temporal artery. There is also a predilection for involvement of the ophthalmic artery (which conversely is a branch of the internal carotid artery) and its branches, especially the ciliary vessels supplying the optic nerve head. When these latter vessels are involved, the optic nerve head is usually completely infarcted (Fig. 4), and vision is permanently lost. The detailed ocular and orbital pathology in a case of GCA has recently been reported elsewhere.⁽¹¹⁾

In contrast, the pathology of the much commoner nonarteritic disease, NA-AION, as reported earlier in this journal,⁽¹⁰⁾ is a similar optic nerve head infarction, usually incomplete and noninflammatory, and associated



Fig. 4 Pathology of AAION shows the infarcted optic nerve head in areas supplied by the posterior ciliary circulation with a clear line of demarcation (large arrow) between the normal more posterior optic nerve supplied from the pial plexus. The surrounding ciliary vessels (small arrows) show inflammatory arteritic occlusion.

with a drop in perfusion pressure and hypotension in the posterior ciliary vessels. This also usually occurs on awakening or rising in the morning in patients with vascular risk factors, and as mentioned before, these patients are not treated with corticosteroids, and it is very important that their anti-hypertension treatment should not be taken at nighttime.

Four different modalities of treatment of GCA arise in the following clinical scenarios where the diagnosis has been made following a positive biopsy:

Scenario 1: The commonest scenario, as with the case described above, where the ESR and/or CRP are

raised, and where one eye is already involved, with vision lost, and where there is a high risk of a second eye involvement. Treatment must be instituted at once, with oral medication being sufficient at a commencing dose of 60–80 mg prednisolone daily, and tapered until the ESR remains down on attempted withdrawal, which may take up to two years, the less corticosteroid sensitive ESR being more useful in our experience for long-term assessment of activity.

Scenario 2: Where both eyes are already involved and blind, and ESR and/or CRP elevated treatment is required only to control general symptoms and to get the ESR/CRP readings down to normal. Clearly, less frequent monitoring is required here, but oral corticosteroids will be required for one year or longer.

Scenario 3: Where the ESR and CRP are normal, and one eye is already involved. This is the most difficult scenario because of the long-term danger of a second eye involvement; treatment must again be continued for up to two years in smaller dosage at the outset, and a more rapid tapering and long-term follow-up is required. The patient must be carefully counselled to return immediately to the eye department in the event of any new ocular or general symptoms, in particular an episode of transient visual loss which can precede the actual development of a disastrous second AAION. A repeat biopsy should be considered in such cases, for repeated biopsies have in fact demonstrated active disease more than two years from the initial diagnosis, although most repeat biopsies have been negative after one year.⁽¹²⁾ However, false-negative biopsy results have been known to occur in 3%–9% of Caucasian patients with GCA due to the possibility of discontinuous arterial involvement and/or missed lesions.⁽¹³⁾

Scenario 4: In cases of classical GCA with raised ESR/CRP but without ocular symptoms, corticosteroid treatment is again required as above, with regular monitoring for up to two years, and the patient instructed to return at once in the event of visual loss or exacerbation of general symptoms, when the dosage will probably need to be increased and more frequent monitoring instituted.

As can be seen in all these scenarios, corticosteroid treatment is required for 1–2 years or even indefinitely. A patient has been described where an optic neuropathy developed after seven years of corticosteroid treatment for classical GCA,⁽¹²⁾ and more recently, a case of sequential AAION developing after five years when treatment had been discontinued earlier, aptly described as “Can lightning strike twice?”⁽¹⁴⁾ In acute cases with actual or threatened visual loss, the ESR/CRP should

be checked initially after three days and then weekly until it is within the normal range for an elderly patient. Once stabilised, it should be checked monthly for at least one year, when withdrawal may be attempted, but with more frequent monitoring of the ESR level at this stage. Because the CRP is more responsive to treatment than the ESR, repeated ESR readings are more useful and cheaper to perform. In our service, we have the patient attend on the day before the clinic visit for the blood test, so that the result is available when the patient is seen and the corticosteroid dosage adjusted as required. Two recent reports from rheumatologists in Israel⁽¹⁵⁾ and the USA⁽¹⁶⁾ have suggested that the prescription of aspirin may also be beneficial in the treatment of GCA. The evidence has, however, been reviewed by Edwards and Plant⁽¹⁷⁾ from the National Hospital in London, who found that there is no clear evidence to support this contention.

In conclusion, although GCA appears to be a rarely-encountered condition in this region as compared to elsewhere, it can have disastrous consequences; for if missed or mismanaged, it can result in total bilateral blindness. Thus, not only our ophthalmologists but general physicians and rheumatologists who may encounter such patients should, in our opinion, have these patients supervised in a specialist neuro-ophthalmology clinic. They require long-term follow-up, and a disastrous loss of vision can be prevented with early diagnosis and appropriate treatment. It should also be understood that the diagnosis of GCA must not be made without biopsy confirmation. It is surprising that despite the increasing age of our local population, there has apparently been no real increase in the incidence of GCA in Singapore since our earlier case report published in 2003.⁽⁸⁾ We presume that it is just a coincidence that two of our cases (Cases 4 & 7) presented within a two-month period in 2009.

NOTE

Since this paper was submitted for publication, another 73-year-old Chinese female patient with classical GCA, an ESR of 130 and a positive biopsy has been encountered in our clinic at SNEC, making an unexpected total of three GCA cases seen in 2009.

REFERENCES

- Horton BT, Magath TB, Brown GE. An undescribed form of arteritis of the temporal vessels. *Mayo Clinic Proc* 1932; 7:700-1.
- Hutchinson J. Diseases of the arteries. On a peculiar form of thrombotic arteritis of the aged which is sometimes productive of gangrene. *Arch Surg* 1890; 1:323-9.
- Whitfield AGW, Bateman M, Cooke WT. Temporal arteritis. *Br J Ophthalmol* 1963; 47:555-66.
- Simmons RJ, Cogan DG. Occult temporal arteritis. *Arch*

- Ophthalmol 1962; 68:38-48.
5. Cullen JF. Occult temporal arteritis. *Trans Ophthalmol Soc UK* 1963; 83:725-36.
 6. Jonasson F, Cullen JF, Elton PA. Temporal arteritis: a 14-year epidemiological, clinical and prognostic study. *Scott Med J* 1979; 24:111-7.
 7. Goh KY, Lim TH. Giant cell arteritis causing bilateral sequential anterior ischaemic optic neuropathy- a case report. *Singapore Med J* 2000; 41:32-3.
 8. Cullen JF, Chan CML, Chuah KL. Giant cell arteritis (temporal arteritis, cranial arteritis) and a case from Singapore. *Singapore Med J* 2003; 44:306-8.
 9. Cullen JF. Occult temporal arteritis. A common cause of blindness in old age. *Br J Ophthalmol* 1967; 51:513-25.
 10. Cullen JF, Por YM. Ischaemic optic neuropathy: the Singapore scene. *Singapore Med J* 2007; 48:281-6.
 11. Cullen JF. Temporal arteritis 50 years on. *Br J Ophthalmol* 2009; 93:833-4
 12. Cullen JF. Temporal arteritis. Occurrence of ocular complications 7 years after diagnosis. *Br J Ophthalmol* 1972; 56:584-8.
 13. Hayreh SS. Anterior ischaemic optic neuropathy. Differentiation of arteritic from non-arteritic type and its management. *Eye (Lond)* 1990; 4(Pt 1):25-41.
 14. Bendo E, Gilbert M, Foroozan R. Can lightning strike twice? *Surv Ophthalmol* 2008; 53:296-300.
 15. Neshet G, Berkun Y, Mates M, et al. Low-dose aspirin and prevention of cranial ischemic complications in giant cell arteritis. *Arthritis Rheum.* 2004; 50:1332-7.
 16. Lee MS, Smith SD, Galor A, Hoffman GS. Antiplatelet and anticoagulant therapy in patients with giant cell arteritis. *Arthritis Rheum.* 2006; 54:3306-9.
 17. Edwards MJ, Plant GT. Should we prescribe aspirin for patients with giant cell arteritis? A review of the evidence. *Neuro-Ophthalmology* 2009; 33:1-4.