

## Temporal artery biopsy in the management of giant cell arteritis with neuro-ophthalmic complications

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Giant cell arteritis (GCA) with neuro-ophthalmic complications requires treatment with systemic steroids, initially in high dose and continued at a gradually reducing dose for at least 6 months and usually for 1 year or longer.<sup>1</sup> There is a high risk of complications from the steroid therapy and thus the diagnosis of GCA needs to be as certain as possible. Histopathological evidence, usually by temporal artery biopsy, is the definitive investigation.<sup>2</sup> However, patients are still being treated with systemic steroids without a biopsy being performed.

Three actual cases are presented and discussed to illustrate the role of temporal artery biopsy in the management of possible GCA with neuro-ophthalmic complications.

### Case 1: "Occult GCA"

A 75 year old white woman presented with sudden visual loss in her left eye. She denied any headache, scalp tenderness, jaw claudication, muscle pains, or systemic disturbance. The left eye was blind with a relative afferent pupillary defect and a pale, swollen, optic disc (Fig 1), consistent with anterior ischaemic optic neuropathy (AION). The left temporal artery was not tender, but was cord-like and pulseless. The right temporal artery was pulsatile and not tender. Erythrocyte sedimentation rate (ESR) was 80 mm in the first hour. High

dose systemic steroid therapy was instituted. Left temporal artery biopsy showed granulomatous inflammation with giant cells.

Despite the absence of classic systemic symptoms of GCA the index of suspicion for arteritic AION in this patient must be very high. The objective pointers to the diagnosis were (a) pallid swelling of the optic disc in a blind eye, (b) pulseless temporal artery, and (c) highly elevated ESR. "Occult GCA" has long been known to ophthalmologists.<sup>3-4</sup> Patients present with severe ischaemic ocular complications and no systemic symptoms or signs of GCA. ESR may not be elevated and the temporal arteries may be clinically normal only to show granulomatous inflammation on histological examination.<sup>5-8</sup> Diagnosis and management of patients with occult GCA are especially challenging. Hayreh *et al* found that out of 85 patients with ocular involvement from biopsy proved GCA more than one fifth did not show any systemic symptoms and signs of GCA at presentation.<sup>9</sup>

This patient is at great risk of blindness in the fellow eye if adequate high dose steroid treatment is not given immediately, if the dose is reduced too rapidly, and even in the first couple of days following initiation of high dose steroid treatment. In occult GCA irreversible visual loss in one eye is often inevitable because the patient does not seek medical attention before it occurs. Protection of the second eye becomes the real issue of concern to the patient, the ophthalmologist, and the physician. The risk of bilateral ocular involvement in GCA is estimated at 10-50%, depending on whether steroids have been given, and the interval between involvement of the two eyes is measured in days or weeks.<sup>10</sup> In our experience of 21 consecutive patients with arteritic AION, 10 developed visual loss in the second eye mainly because of delayed diagnosis, but occasionally due to rapid reduction of steroid dose in the course of the disease.<sup>11</sup>

When systemic side effects arise in a patient who lost vision in one eye from GCA, the general physician may be inclined to reduce or stop treatment, and is more ready to do so if no initial temporal artery biopsy was performed. This is an important reason to perform temporal artery biopsy in every case of suspected

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Figure 1 Case 1. Pallid swollen left optic disc.

GCA, including those with a very strong clinical suspicion. Both the patient and the physician will be more willing to cope with the difficulties involved with long term steroid treatment if they are certain that the initial diagnosis was correct and the threat of blindness is real.

### Case 2: Repeat temporal artery biopsy

An 81 year old white woman presented with 3 weeks of headaches and vertical double vision. She denied any scalp tenderness, jaw claudication, or muscle pains. Her weight had fallen by 6 kg over 4 weeks. There was a partial, pupil sparing left third nerve palsy. Temporal arteries were pulsatile and not tender. ESR was 71 mm in the first hour. C reactive protein (CRP) was 218 g/l. Neuroimaging excluded an intracranial aneurysm. Left temporal artery biopsy, performed 5 days after institution of high dose systemic steroid therapy, showed no evidence of GCA (specimen length 18 mm) (Fig 2A). Right temporal artery biopsy, performed 1 week later, showed granulomatous inflammation with giant cells (specimen length 22 mm) (Fig 2B).

This elderly woman presented with a pupil sparing third nerve palsy, neuroimaging having excluded an aneurysm. There were clinical features consistent with a systemic disease—namely, the headache, weight loss, elevated ESR, and CRP.

After visual loss, diplopia is the second most common ocular manifestation of GCA.<sup>12</sup> A pupil sparing third nerve palsy is the most common sign; however, the pupil can be involved and other eye movement abnormalities including internuclear ophthalmoplegia have been recorded.<sup>13</sup>

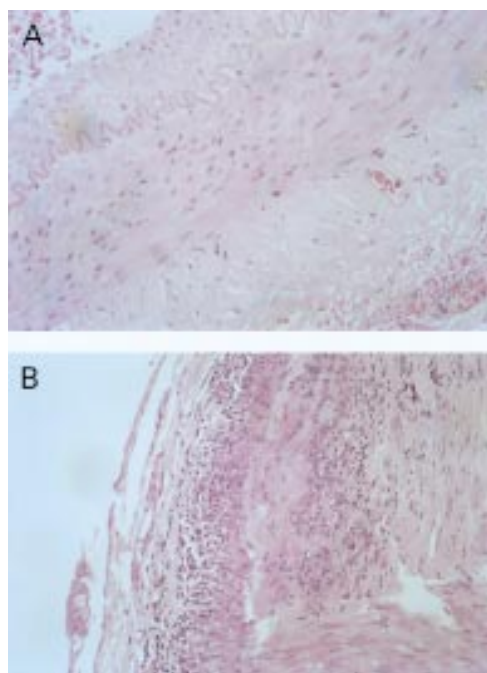


Figure 2 Case 2. (A) First temporal artery biopsy showing arteriosclerotic changes only. (B) Second temporal artery biopsy showing granulomatous inflammation with giant cells. (Courtesy of Dr Debbie Hopster, Department of Histopathology, King's College Hospital, London, UK.)

When there is a high index of suspicion of GCA clinically and the temporal artery biopsy is negative, the appropriate investigation is a contralateral temporal artery biopsy.<sup>14</sup> There is up to a 5% chance of the contralateral biopsy being positive when the first biopsy was negative.<sup>15-18</sup> There are three possible approaches to the second biopsy: (a) do both together as a routine, (b) do a frozen section on the first and if negative do a second biopsy, (c) wait until the results of the first biopsy are known and if negative then take a second biopsy if there is a high clinical index of suspicion.<sup>19-21</sup>

GCA is reported to last from 6 months to 14 years. The dose of steroids is gradually reduced according to resolution of systemic symptoms and reduction of the ESR and CRP. Disease recurrence, with the risk of further visual loss, will be associated, primarily, with recurrence of systemic symptoms and, secondarily, a confirmatory increase in the ESR and CRP, and necessitates increase in the steroid dose. If there is doubt as to whether there is uncontrolled disease activity, such as (a) recurrence of symptoms but no elevation of ESR, (b) elevated ESR in the absence of systemic symptoms, (c) failure of the symptoms to resolve or ESR to fall with increase in steroid dose, or (d) further vascular event without symptoms or elevation of the ESR, and particularly if there is concern about steroid side effects, then a repeat temporal artery biopsy can help determine appropriate clinical management.<sup>22</sup> It is important to remember that systemic symptoms or elevated ESR unresponsive to increased steroid dose may be due to opportunistic infections such as cryptococcal meningitis.<sup>23</sup>

Cerebrovascular accident has been described after temporal artery biopsy when the temporal artery provided an essential collateral circulation because of severe carotid artery disease.<sup>24</sup> Caution is required if cerebral ischaemic symptoms occur with digital occlusion of the temporal artery to be biopsied. If there is suspicion of severe carotid disease, Doppler ultrasonography of the carotid vessels should be performed.<sup>25</sup> Large haematomas may occur if the arterial ligature slips. A prominent eyebrow droop may result from damage to branches of the facial nerve if the incision is taken too close and parallel to the eyebrow. The risk of these complications is low, however.<sup>26</sup>

### Case 3: Exclusion of GCA

An 80 year old Caribbean, diabetic, hypertensive, woman presented with a 3 week history of right periorbital pain and loss of vision in her right eye. She was uncertain as to the duration of the visual loss and whether she had experienced any scalp tenderness. She denied any jaw claudication but had been generally unwell for 2 months with poor appetite, loss of weight, and hip pain. The right eye was blind with a relative afferent pupillary defect and a pale optic disc. Both temporal arteries were pulsatile and not tender. There was a normocytic, hypochromic anaemia (Hb 9.6 mg/dl).



Figure 3 Case 3. Coronal head magnetic resonance image showing dural enhancement over both frontal lobes.

ESR was 110 mm in the first hour. CRP was 187. Rheumatological opinion was that she had polymyalgia rheumatica. Treatment was begun with high dose systemic steroids for presumed GCA, with considerable adverse effects on blood glucose control. The patient reported improvement in her headache within 48 hours of initiation of steroid therapy.

Right and then left temporal artery biopsies showed no evidence of GCA. Brain and orbital magnetic resonance imaging revealed enhancement of the dura over both frontal lobes (Fig 3) and in the right orbital apex. Left frontal burr hole meningeal biopsy revealed a granulomatous pachymeningitis, for which no cause was identified on further investigation.

The patient was diagnosed as having idiopathic chronic granulomatous cranial pachymeningitis, with involvement of the right orbital apex. This is a rare condition that characteristically presents with headache, cranial neuropathies including optic neuropathy, and markedly elevated ESR. The response to systemic steroids, other immunosuppressants, and radiotherapy is variable. In this case there was a poor symptomatic response to systemic steroids, and thus they were discontinued. One year later no further neurological complications had developed and the headaches were controlled with simple analgesics.

The triad of age more than 50 years, new headache, and ESR greater than 50 mm in the first hour, fulfils the American College of Rheumatology traditional format classification for GCA, which is reported to have a sensitivity of 93.5% and a specificity of 91.2%.<sup>27</sup> The criteria of Ellis and Ralston for a clinical diagnosis of GCA were also fulfilled.<sup>28</sup> Hayreh identified jaw claudication, CRP greater than 24.5 g/l, and ESR of 47 mm in the first hour or more as the clinical criteria most strongly suggestive of biopsy positive GCA, with elevated ESR and CRP having a specificity of 97%.<sup>29</sup> Other authors have highlighted the usefulness of jaw claudication and clinical abnormality of the temporal arteries, both absent in this case, as predictors of a positive temporal artery biopsy.<sup>26 30 31</sup> Conversely, Martinez *et al* reported that no pattern of clinical features

reliably predicts a positive temporal artery biopsy.<sup>32</sup>

Initially it might have seemed reasonable to have accepted the clinical diagnosis of GCA in this patient and continued with systemic steroid therapy, with its inevitable consequences on her diabetic control. However, subsequent events demonstrated how the presence of seemingly specific clinical criteria may be misleading and do not provide sufficient certainty about the diagnosis of GCA to justify long term systemic steroid therapy. It is important to bear in mind that criteria, such as those formulated by the American College of Rheumatology are designed for use in research studies to classify patients with a diagnosis of vasculitis rather than as diagnostic criteria for clinical practice.<sup>33</sup>

Do two normal temporal artery biopsies adequately exclude giant cell arteritis? Temporal artery biopsy is reported to have a 5–10% false negative rate for the diagnosis of giant cell arteritis.<sup>34 35</sup> In these studies contralateral biopsies were not performed and in many instances the diagnosis of giant cell arteritis was based upon a clinical suspicion of the need for long term steroid therapy rather than a subsequent clinical event or other histological proof. There is up to 5% chance of a positive contralateral biopsy when the first biopsy is negative (see above). Thus, two normal temporal artery biopsies probably do exclude giant cell arteritis, as long as both specimens are of adequate length (more than 20 mm) and have undergone careful examination of serial sections, and the pathologist is sensitive to atypical features if the biopsies have been taken more than 2 weeks after institution of systemic steroid therapy.<sup>36–39</sup> In such cases, clinical features will determine the pattern of investigation, such as whether neuroimaging is required. Investigations should be particularly directed towards excluding malignancy and other types of systemic vasculitis.<sup>26 34</sup>

## Conclusions

Temporal artery biopsy should be performed in all patients with neuro-ophthalmic disease suspected of being due to GCA. It provides a tissue diagnosis to justify long term systemic steroid therapy and ensures that other diagnoses are not missed.

Contralateral temporal artery biopsy should be undertaken when the first biopsy is negative and there is a high clinical suspicion of GCA.

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