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Giant cell arteritis

Emphasis on the temporal artery biopsy

Giant cell arteritis (GCA) – also known as temporal arteritis or cranial arteritis – is the most common of the arteritides. It is characterised by segmental acute and chronic (most often granulomatous) vasculitis involving primarily the elastic tissue-rich medium to large sized arteries of the head and neck[1-5].

GCA has a predilection for the temporal arteries and the terminal branches of the ophthalmic artery, frequently leading to vision loss and blindness. Other vessels that may be affected include the aorta and arteries to the brain. Involvement of these vessels can have severe systemic consequences, including stroke and death[1]. Histological changes that occur in GCA include panarteritis with intimal proliferation, destruction of the internal elastic lamina, and thickening of the media. There is an inflammatory infiltrate consisting of mononuclear cells, multinucleated giant cells (classically described in GCA, but not necessary for diagnosis), and occasional eosinophils. Obstruction of the lamina of the arteriole ensues, due to a combination of oedema, thickening of the intima and thrombosis[1-5].

Profile of a GCA patient

GCA occurs in patients over the age of 50, with the peak occurrence in older Caucasian individuals between the ages of 60 and 70[5]. It has a greater predilection for women, with a 2:1 or 3:1 female-to-male ratio[6]. In about half of cases, the arteritis develops on a background of polymyalgia rheumatica (a flu-like illness in elders marked by pain and stiffness in the proximal muscles of the hip and shoulder girdles, neck and buttocks)[1].

Classic symptoms of GCA include jaw claudication (i.e. pain whilst chewing), generalised scalp or especially temporal scalp tenderness (often first noticed as pain when combing hair over the temporal region), localised headache, severe visual loss, amaurosis fugax, diplopia, weight loss and myalgia (muscle pain) (**Table 1**)[4-7].

Table 1
Symptoms of GCA

Jaw claudication (pain with chewing)
Scalp or temporal region tenderness/pain
Headache
Recent weight loss
Low-grade fever
Myalgias and arthralgias
Generalised malaise
Polymyalgia rheumatica
Visual loss or transient visual loss
Diplopia
Throat or ear pain
Altered mental status

Table 2 lists the signs associated with GCA in order of decreasing sensitivity. Laboratory tests, including the Westergren erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), are valuable tools in the diagnosis of GCA. Although elevated ESR and CRP are highly indicative of GCA, a positive temporal artery biopsy is required for definitive confirmation[5,6].

Arteritic AION versus NAION

Anterior ischaemic optic neuropathy (AION) is a segmental, or generalised, infarction within the prelaminar or laminar portion of the optic nerve. It is caused by occlusion of the short posterior ciliary arteries[2-4]. The occlusion occurs in the absence of demyelinisation, compression by cranial mass lesions, or non-vascular systemic inflammatory disease[2].

A challenge faced by eyecare professionals is differentiating between arteritic and non-arteritic forms of AION. Both of these conditions cause sudden, unilateral, painless vision loss (frequently in the form of an altitudinal visual field defect). Both also result in the development of an afferent pupillary defect and a pale, swollen disc, often with flame-shaped hemorrhages[2,3]. However, only arteritic AION is secondary to GCA,

Table 2
Signs of GCA

• Caucasian male or female over 50 years
• Elevated Westergren erythrocyte sedimentation rate (ESR)
Men: normal ESR = age/2
Women: normal ESR = (age+10)/2
• Elevated C-reactive protein (CRP)
Over 2.45mg/dL are considered abnormal
• Tender or non-pulsatile temporal artery
• Scalp tenderness
• Anterior ischaemic optic neuropathy
• Posterior ischaemic optic neuropathy
• Choroidal ischaemia
• Central retinal or branch retinal artery occlusion
• Ischaemic cranial nerve palsy
• Visual field defects
• Anaemia
• Acute or subacute dementia
• Temporal scalp ischaemia

requiring immediate intervention with corticosteroids and a temporal artery biopsy. This course of action would be inappropriate in NAION. Moreover, patients with arteritic AION are at an increased risk of early death from systemic vascular disease, while those with NAION are not[3]. How then does one proceed when differentiating between these two, similar-presenting, conditions?

The patient's age, a thorough history, and review of systems is imperative when making the differential diagnosis between arteritic and NAION. As artertic AION is secondary to GCA, patients will fall into the profile described above. In addition to vision loss, these patients commonly present with headache, temporal tenderness, jaw claudication and myalgia[1-7]. The patient's age is important in the diagnosis; very few researchers believe that GCA occurs in anyone younger than 50. Therefore, it follows, that arteritic AION will occur only in patients older than 50 years of age. When differentiating between AION and NAION, laboratory tests are of the utmost importance. Tests that should be ordered include: complete blood count (CBC), ESR and CRP. The ESR and CRP are likely to be significantly elevated in a patient with arteritic AION, while in NAION these laboratory results are most often normal to only slightly elevated. A CBC should be ordered because anaemia is common in temporal arteritis and its presence affects the ESR[6].

NAION is defined as AION in the absence of GCA. NAION is the result of an acute loss of perfusion to the optic nerve head. A balance of intraocular pressure, blood pressure and cerebral spinal fluid pressure maintains nerve head perfusion. An acute alteration of this pressure-perfusion ratio compromises nerve head tissue and can lead to NAION. The most common causes of this compromised system include systemic hypertension, diabetes, hyperlipidaemia and severe, sudden blood loss known as 'shock-induced NAION'. Other causes of altered pressure perfusion include Lyme disease, complications from cataract surgery or general surgery, radiotherapy, relapsing polychondritis, and tamoxifen therapy[2].

Laboratory testing

Before a temporal artery biopsy is performed, several haematological tests should be ordered to determine the appropriate level of clinical suspicion for GCA. As mentioned previously, tests that should be ordered include a CBC, ESR and CRP. A CBC is a group of tests which provides a great deal of information about the blood and organ systems[4]. Patients

with GCA often have an associated mild anaemia and varying degrees of leukocytosis. A CBC should be ordered to evaluate for these conditions[8].

The ESR is a non-specific test used to detect inflammatory conditions, infections, neoplasms, and necrotic processes. It measures the rate at which red blood cells (RBCs) settle in a sample of anticoagulated blood in one hour. Inflammatory conditions, such as GCA, can cause an increase in the amount of fibrogen and globulins in the plasma. As a result, the repellant forces between the RBCs break down and the RBCs stack on top of each other. The increased weight of the adherent cells causes them to sediment faster than single cells, effectively increasing the ESR[4,8]. There are two methods of testing the ESR – Westergren and Wintrobe. Because a longer tube is utilised, underlying anaemia does not confound the results as much using the Westergren method, making it the preferred method. It is important to note that the ESR is a manual test; the results vary with the skill of the technician and the technique used at individual laboratories.

The procedure is preformed by first drawing 7-10ml of venous blood and placing it into a tube containing an anticoagulant (e.g. ethylenediamine tetracetic acid, EDTA, or an oxalate). It is then taken immediately to the haematology laboratory. The test must be preformed at room temperature. The blood is drawn into the Westergren tube, placed on a vertical rack and left undisturbed (**Figure 1**). After one hour, the height of clear plasma above the red column is measured. This height represents the distance the RBCs settled in one hour[4,8] (**Table 4**).

CRP is one of the physiologically active compounds referred to as 'acute phase reactants' produced by the liver in response to inflammation, tissue damage, infection, malignancy and immunologic reactions. CRP rises with advancing inflammation and normalises as the body responds to therapy more acutely than ESR[8]. As a result, CRP is useful both in the diagnosis and continued monitoring of the disease process[4,8]. The CRP test is an automated procedure and the results are quantifiable. This is advantageous, as it removes the potential for technician error and increases its reproducibility and sensitivity[8]. Another advantage is that the CRP test uses serum, allowing it to be stored and tested in the future without compromising results. Also the factors that falsely influence the results of the ESR (anaemia, temperature, tube placement) do not affect CRP[4,8] (**Table 5**). Nevertheless, there is a good correlation between ESR and CRP. Both tests should be ordered immediately whenever there is suspicion for GCA. The tests should also be performed periodically after treatment has begun, to monitor the patient's response to therapy and to detect disease relapse[8].

When to perform the temporal artery biopsy

The decision to do a TAB is made based on clinical suspicion. In 1990, the American College of Rheumatology analysed diagnostic criteria for GCA, ranking the criteria according to both sensitivity and specificity[9]. These results were then used to develop a step-wise evaluation pathway for determining the level of clinical suspicion for GCA[9] (**Table 3**).

Table 3
Index of clinical suspicion for GCA[10]

High index of clinical suspicion
- Any one of the following clinical features demonstrating a high specificity for GCA in a patient over 50 years of age with an elevated ESR: jaw or tongue claudication; visual abnormalities; temporal artery abnormalities (e.g. decreased pulse, tenderness or nodules);

OR

- If three or more of the following are met: new localised headache; temporal artery abnormality; elevated ESR and/or CRP*; abnormal temporal artery biopsy

Medium index of clinical suspicion
- Meeting any one of the highest specific clinical features (see above)

OR

- Anterior ischaemic optic neuropathy (AION) present;

OR

- Any two of the following: elevated ESR and/or CRP*; new headache in an older patient; and/or clinical temporal artery abnormality

Low index of clinical suspicion
- Any of the above in a patient under age 50
- In a patient over 50, clinical suspicion is low with the following findings: absence of the highest specific clinical features listed by American College of Rheumatology (*see above*)

AND

- Normal ESR (or only slightly elevated); normal CRP*; negative bilateral TAB

* CRP was not included as a diagnostic criterion for GCA in the American College of Rheumatology study. However, recent data has shown CRP to be approximately 80% specific for GCA. As such, CRP should also be considered in the determination of level of clinical suspicion for GCA[5,9,10]

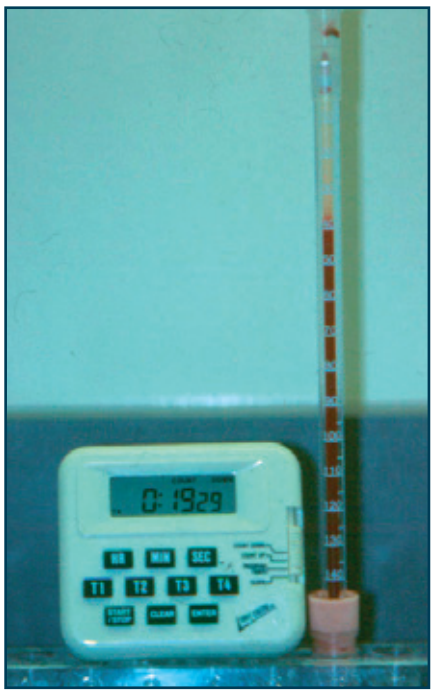

Figure 1
Columnated tube used to measure Westergren ESR

A clinician may decide to proceed with a TAB even when the index of suspicion is not high. The procedure is relatively straightforward and poses little risk to the majority of patients. When one considers the potential ramifications of GCA, including blindness, stroke and death, the minimal risk associated with TAB is warranted if there is any suspicion of GCA[5,9,10].

The clinician must also decide whether to perform a unilateral or bilateral biopsy. Most clinicians opt to perform TAB on the symptomatic side, and reserve a second biopsy on the contralateral side if the index of suspicion remains high in spite of initial negative results[5].

Table 4
ESR[4,8]

- Whole blood
- Cannot be stored
- Easily done in local lab
- Manual procedure
- Faster turnaround time
- More technician error
- Factors affect value (anaemia, temperature, tube placement)
- Non-specific quantitation

Table 5
CRP[4,8]

- Serum can be frozen
- Usually sent to reference lab
- Automated procedure
- Slower turnaround time
- Consistent, reproducible results
- Less prone to interference
- Acute phase reactant quantitation

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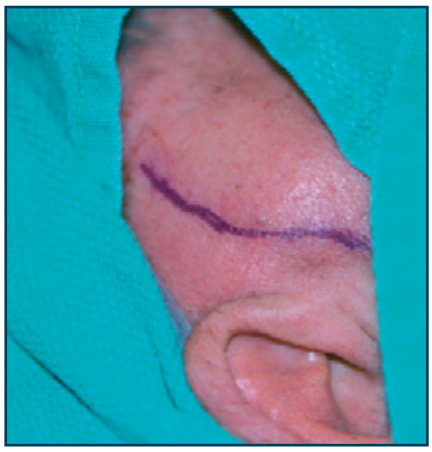

Figure 2
After shaving the temple and sideburn hair, the course of the STA is marked

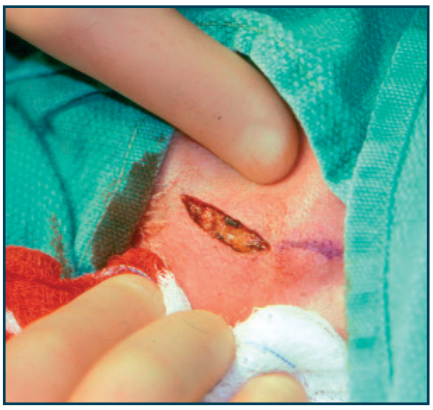

Figure 3
Initial incision of skin and subcutaneous layers

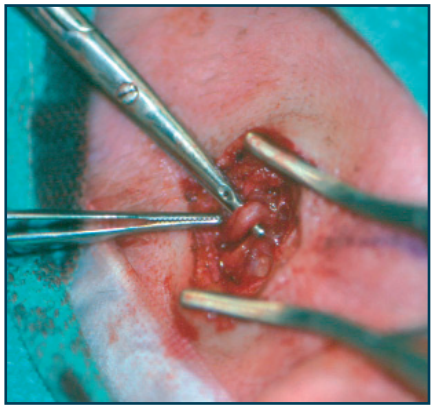

Figure 4
The STA has been isolated

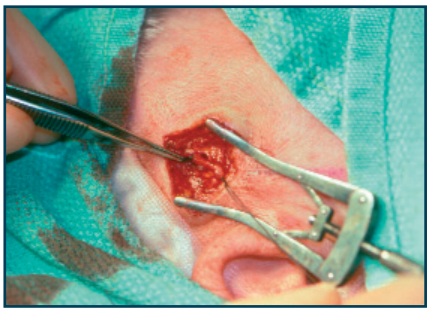

Figure 5
Both distal and proximal ends of the STA are ligated with suture

When TAB should be avoided
TAB should not be preformed when the patient does not meet the typical profile of GCA, or when a patient has a presentation that is obvious for GCA but to whom the procedure poses a significant risk. For example, TAB should be avoided in individuals with bleeding abnormality; a large amount of subcutaneous fat, precluding the ease of surgical approach; or when scalp ischaemia is imminent or present[5].

Surgical procedure

The frontal branch of the superficial temporal artery (STA) is the one most often chosen for biopsy. This branch is preferred for its high degree of involvement in GCA, its accessibility and expendability[6].

The most critical and time-consuming step in the TAB process is selecting the biopsy site. The site should be in the temporal fossa on the patient's symptomatic side. The area should be evaluated for temporal artery tenderness, skin erythema, absent pulsation and arterial nodularity. If these signs are present, the biopsy should be attempted at that site, as it will be of the highest yield in making the diagnosis[5,6,11].

The facial nerve runs in close proximity to the STA. Care must be taken to avoid damaging the facial nerve when doing the biopsy. The surgeon should avoid performing the biopsy from the area where the facial nerve is in closest proximity to the STA. This area of close proximity is delineated by the following four points[10]:

1. The tragus of the ear
2. The junction of the zygomatic arch and the lateral orbital rim
3. 2cm above the level of the superior and orbital rim and in a line directly superior to #2
4. Superior to the tragus and in horizontal alignment with #3

The surgical site should be shaved intraoperatively. Marking the site begins with the surgeon carefully palpating the area and tracing the course of the temporal artery with a gloveless hand. Doppler ultrasound can be used to aid in identification, especially if the pulse is weak or non-existent. The area immediately superficial to the STA is then marked with a surgical pen. The overlying area is sterilised with Betadine solution (povidone-iodine, Purdue Frederick) and draped (**Figure 2**). The area is anaesthetised with a local injection of 5cc of 2% lidocaine longitudinally on either side of the markings. Care should be taken to avoid puncturing the artery, thus avoiding a subcutaneous haematoma that would greatly add to the difficulty of the procedure. Lidocaine with epinephrine should be avoided as it can result in arterial spasm, making it more difficult to locate the vessel[6].

After the anaesthesia has taken effect, the skin and subcutaneous layers are incised directly over the skin markings using a No.15 Bard Parker surgical blade (**Figure 3**). Care should be taken to avoid incising the vessel; this is particularly true in thin, older patients where the superficial artery can lie just below the skin. Cautery is used as necessary to control bleeding[6].

Palpation and watching for vessel pulsation should be done throughout the procedure to help differentiate the artery from its accompanying vein (**Figure 4**). Once the artery has been identified and isolated, it should be digitally compressed prior to biopsy. During compression, the patient is asked to move his or her feet and hands. This step mimics the loss of blood flow that will result after the biopsy. It ensures that there is no potential collateral circulation between the external and internal carotid artery systems, thus avoiding a stroke if the vessel is removed. Both the distal and proximal ends of the artery can then be safely ligated with 4-0 silk suture (**Figure 5**)[6].

The surgeon then cuts the artery with scissors 2mm or 3mm inside the ligatures to prevent the suture knots from slipping off (**Figure 6**). The biopsy should consist of a sufficiently large section of the artery (minimum of 1.5cm). Without an adequate specimen, there is a greater likelihood of a false negative result secondary to skip lesions (areas of histologically normal artery between areas of chronic or active inflammation). The incision is closed with subcutaneous dissolvable chromic suture, and the skin edges are approximated with non-dissolvable silk or nylon interrupted sutures[6].

Antibiotic ointment is applied over the closed incision. The incision is then covered with a Telfa pad and cotton gauze. A tight head wrap pressure dressing is applied and can be removed in 24 hours. The antibiotic ointment is used twice a day, and the skin sutures are removed in one week[6].

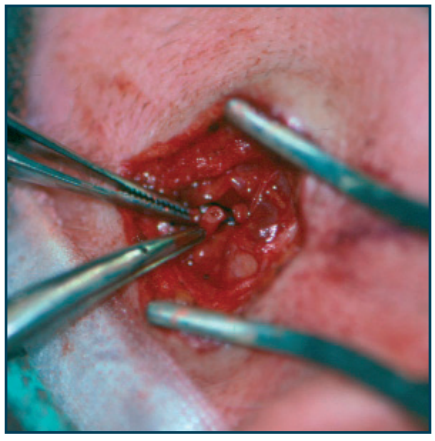

Figure 6
Cut end of STA

Complications

The most common complication of TAB is a haematoma. As with any surgery, bleeding, infection and scarring may also occur. Partial paralysis of the facial muscles due to incidental damage to a branch of the seventh cranial nerve may occur. Less commonly, scalp necrosis, loss of vision in the ipsilateral eye, or stroke can occur if the artery is part of a collateral flow to the eye or between the external and internal carotid arteries[5,6,11].

Treatment

Untreated GCA may result in significant (frequently bilateral) vision loss and severe systemic complications. Therefore, it is imperative that corticosteroid therapy begins immediately upon clinical suspicion of GCA. The standard approach is an initial dose of oral prednisone of 1-1.5mg/kg/day (60-100mg/day). Treatment with intravenous (IV) corticosteroids has been recommend for GCA in the presence of visual loss. The recommended IV therapy for these patients is 250mg methylprednisonlone, four times daily for three to five days. Prebiopsy treatment with corticosteroids may alter the biopsy results, but the biopsy remains positive in most cases even after 14 days of corticosteroid therapy. If the treatment effectively heals the inflammation within the arterial wall, transmural scarring may still be suggestive of GCA[4,5,9].

Steroid-sparing immunosuppression may be used in patients who cannot tolerate steroids, have had a serious adverse reaction to steroids, or do not respond to steroid treatment. Clinicians, in these cases, have used methotrexate, cyclophosphamide, azathioprine and dapsone. These medications may take longer than one month to take effect. Steroid therapy should be continued until the immunosuppression agent begins to take effect. If steroid-sparing medications are indicated, a rheumatologist or oncologist should also participate in the management of the patient[5].

Summary

Prompt diagnosis and early treatment of GCA can often prevent irreversible (often bilateral) blindness, and reduce or eliminate other symptoms of the disease. TAB is the gold standard in the diagnosis of GCA. The decision to biopsy should be based on clinical suspicion. In most cases, the risk associated with performing TAB is much lower than the consequences of failing to diagnose GCA.

About the authors

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