CLINICAL PRACTICE GUIDELINE: Emergency Department

Giant Cell Arteritis

Disclaimer: This Clinical Practice Guideline ('CPG') was written for use in The Royal Victorian Eye and Ear Hospital Emergency Department. It should be used under the guidance of an Ophthalmology or ENT registrar. If clinical advice is required, please contact the Eye and Ear Admitting Officer for assistance: EYE: +61 3 9929 8033; ENT: +61 3 9929 8032. Links to internal Eye and Ear documents cannot be accessed from the website CPG.

Description:

Giant Cell Arteritis (GCA), also known as Temporal Arteritis, is a systemic vasculitis affecting medium and large arteries with significant ocular and systemic morbidity.

Red Flags:

- This is an ocular emergency with a risk of bilateral blindness if not diagnosed and treated immediately
- The patient can present with transient visual loss, diplopia or any cranial nerve palsy
- Do not wait for temporal artery biopsy (TAB) before initiating steroid treatment if suspicion of GCA high
- Rarely is GCA possible with a normal ESR and CRP. Also remember that not every patient with an elevated ESR and CRP has GCA.
- GCA is possible without systemic symptoms (incidence of "occult GCA" can be up to 20%)

Background:

- More common in Caucasian women
- Average age of onset: 71 years old. Most patients are over 60, and very rarely younger than 50 years old

How to Assess:

History:

- Systemic symptoms
  - Symptoms of systemic inflammation such as fever, night sweats, fatigue and weight loss are present in the vast majority of patients and often precede ophthalmic symptoms

    Headache (usually temporal), scalp tenderness*, jaw claudication*, tongue pain, proximal limb girdle pain and stiffness (polymyalgia rheumatica)

    (* most specific symptoms)
  - in the presence of jaw claudication-like symptoms, exclude denture/tooth

pain and temporomandibular joint pain

History of transient ischemic attack, stroke, myocardial infarction

- Ocular/ENT symptoms
    - Acute loss of vision (arteritic anterior ischemic optic neuropathy (AAION)), central retinal artery occlusion (CRAO))
    - Amaurosis fugax (precedes AAION in 10-30% of patients)
    - Diplopia
    - Ocular pain

Examination:

- Complete ophthalmic examination must be performed
- Loss of vision: VA is usually less than 6/60 in cases of AAION.
- AAION is the cause of permanent visual loss in 90% of patients with GCA.
- Signs of optic nerve dysfunction: afferent pupil defect, loss of colour vision.
- Optic nerve: chalky white oedema is specific for GCA. However, there may be disc oedema without a chalky white appearance or even a normal optic disc.
- Examine for CRAO
- Less common: posterior ischemic optic neuropathy, cilioretinal artery occlusion, anterior segment and ocular ischemia
- Ocular motility deficit: any pattern is possible. This is caused by any cranial nerve palsy, brain stem or orbital ischemia. Clinically, it can mimic myasthenia gravis.
- Palpate superficial temporal arteries (STA). In GCA, STA can be tender, firm, nodular, and pulseless.
- Consider:
    - Auscultation for carotid, and subclavian bruits
    - Assess for upper limb BP discrepancies

Investigations

- Immediate ESR, CRP, FBE, UEC, LFT.
    - Normal ESR can be expected in up to 22% of patients with GCA and can be elevated by anaemia and other inflammatory/infectious diseases.
    - An elevated CRP is probably more specific.
    - Thrombocytosis is associated with GCA.
- Consider: fluorescein angiography for delayed choroidal perfusion after ED attendance if indicated. Can help discriminate AAION from non-arteritic AION.

Acute Management:

- Discuss with neuro-ophthalmology consultant if there is uncertainty as to the requirement for TAB and advice regarding steroid treatment before biopsy.
- Initiate treatment immediately when suspicion for GCA is high as the fellow eye can become involved within 24 hours in 1/3 of patients and within 7 days in 2/3 of patients.
- **Systemic steroid treatment:**
- **Intravenous (IV) steroids** are indicated in patients with recent visual loss, myocardial infarction, cerebrovascular ischemia
    - Admit
    - Dosage: 1000 milligrams (mg) methylprednisolone daily for 3 days. This can be given as a once daily dose. In high-risk patients, consider divided doses (twice or three times daily) or a reduced dose.
        - High-risk patients include patients with diabetes, heart failure, uncontrolled hypertension, cardiac disease, renal failure, suspected peptic ulcer disease, acute, chronic or latent infections, and concurrent immunosuppression.
        - Change in dose should be discussed with the neuro-ophthalmology consultant and, in some cases, St Vincent's medical registrar.
        - Medically unstable or high-risk patients may require transfer to a medical unit (e.g. at St Vincent's) for appropriate supervision during high-dose IV steroid therapy.
    - Monitoring whilst an in-patient must occur daily and include assessment of pupils, visual acuity and intraocular pressure (IOP).
    - Notify the neuro-ophthalmology consultant on-call about any change in clinical status and visual function.
    - Discharge on oral prednisolone 1mg/kg until neuro ophthalmology clinic review.
    - For further information, see Methylprednisolone Inpatient Procedure and Appendix 1 (Further management after initial ED presentation)
- **Oral prednisolone** (without IV methylprednisolone) is indicated if there are no sight threatening symptoms or if IV methylprednisolone is a relative contraindication, e.g., frail/diabetic patient.
    - Dosage: 1 mg/kg up to 70 mg daily.
    - Admission may be required based on the patient's other co-morbidities.
- **Organise Temporal Artery Biopsy (TAB)**
    - See Temporal Artery Biopsy Procedure for booking details
    - TAB must occur within seven days of assessment to minimise false negative histopathology due to steroid treatment.

- Contact Neuro-ophthalmology Registrar with patient details. Complete the consent form and forward it to Surgical Booking Unit immediately.
- Indicate 'right or left' TAB on consent. The preferred side for TAB may be indicated on the consent form but final decision on side to biopsy will be determined by surgeon. If the surgeon cannot detect a pulse/ palpate the artery or identify it by ultrasound, they may elect to biopsy the fellow side to increase likelihood of a successful biopsy.
- TAB is usually performed in Day Surgery Treatment Room on the afternoon list every Monday (Thursdays, if Monday is a public holiday).
- See the TAB teaching package for pre, intra, and post-operative information and learning resources
- It is not necessary to routinely discontinue anticoagulants or antiplatelets for TAB. If these medications have been stopped by a medical practitioner, they can be resumed post-operatively on the day of surgery.
- If unable to find pulse (and no palpable 'cord'), please organise for patient to have the superficial temporal artery mapped (ultrasound) by St Vincent's radiology department. Book radiology on morning before biopsy scheduled.

Appendix 1: Further management after initial ED presentation

Additional Investigations

Before commencement of long-term high dose corticosteroids, suspected and confirmed GCA patients should have the following investigations. These can be ordered on admission for systemic steroids or by the neuro-ophthalmology clinic. These tests can be found on Cerner under Neuro-Ophthalmology Pathology & Radiology Orders →Giant Cell Arteritis. Steroids will need to be started before the results of these tests are known but the results should in all cases be followed up at the first outpatient attendance.

- Glucose level
- Calcium level
- CRP
- HbA1c
- UEC
- ESR
- FBE
- Hepatitis B: Surface Ab (HBsAb), Surface antigen (HBsAg), Core Ab (HBcAb)
- Hepatitis C serology
- HIV serology
- VZV IgG
- Syphilis Serology
- Strongyloidiasis serology – serum IgG (only if commencing DMARDS)
- Quantiferon TB Gold
- CXR
- Bone mineral density scan
- CTBrain/ CT angiogram or MRI Brain/MRA if there is concern for intracranial involvement

Prophylactic medical treatments:

- GCA Patients on long-term high dose corticosteroids need to be treated with the following:
    - Bactrim (trimethoprim/sulfamethoxazole) DS 800/160mg three times weekly – ensure the renal function is normal prior to starting
    - Omeprazole 20 mg daily
    - Calcium and vitamin D supplementation as required in consultation with their GP
- The following should also be arranged in consultation with their GP:
    - Bone density testing
    - Blood glucose monitoring

NOTE: COVID precautions: all suspected GCA patients given high-dose steroids should consider self-isolation for 2 weeks, with the exception of hospital attendance for TAB or neuro-ophthalmology appointments. All patients on high-dose corticosteroids are eligible for antiviral therapy if they test positive for COVID and should be advised to contact their GP / local hospital service to discuss as soon as possible after testing positive.

Follow up:

- Follow-up options must be offered to the patient after the TAB has been performed and include the following. Please consider patient's usual home address in helping determine the most appropriate follow-up location.
    - **Eye and Ear Neuro-ophthalmology clinic**
        - Wednesday pm 2 days after TAB to review TAB results and management
    - **Alfred Neuro-ophthalmology clinic**
        - Thursday pm, 3 days after TAB to review TAB results and management
        - The patient must agree to be followed-up at the Alfred Hospital and provided with the Alfred Hospital neuro-ophthalmology information sheet
        - Referral via Specialist clinic referral pathway, indicating possible GCA and date of biopsy.
        - DO NOT refer the following patients to Alfred Neuro-ophthalmology:
            - Other ophthalmological problems and/or an existing relationship with services at Eye and Ear
            - Patients that are already linked to St Vincent's hospital for management of comorbid medical problems

- Private Ophthalmologist or Rheumatologist if the original referral came from this specialist

Referral to Rheumatology or Neuroimmunology (to be arranged by Neuro-ophthalmology Clinic at Eye and Ear or Alfred)

- Patients with a previous diagnosis of GCA who have been unable to successfully wean off steroids without relapse, or have developed significant steroid toxicity should be considered for steroid sparing agents
  - Consider referral to a rheumatologist, immunologist or neurologist (with expertise in this area) for Tocilizumab If f the temporal artery biopsy is positive and the patient had ESR ≥ 50 mm/hr OR CRP ≥ 24.5 mg/L at diagnosis
  - Referral should be made within the first six weeks after diagnosis to be eligible for tocilizumab PBS eligibility.
  - Not all patients are suitable for tocilizumab and alternative agents may need to be considered such as methotrexate.
- Referral should be done urgently if the patient has multiple comorbidities, particularly if diabetic, obese, has previously had difficulty tolerating steroids, has a history of significant osteoporosis, severe depression or delirium.
- Please contact a member of the rheumatology department (EORC at the Eye and Ear) or Neuroimmunology at the Alfred Hospital (Fax: 90762850/ email: msniadmin@alfred.org.au)

Other referral options include:

- A private rheumatologist/immunologist/ neuroimmunologist locally – this is preferable for patients who find it difficult to attend in-person appointments at Eye and Ear
- Referral to Eye and Ear rheumatologist (EORC Clinic) with appropriate referral paperwork and investigations as listed above performed. Discussion with our rheumatologist is preferable to facilitate timely access.
- Referral to Alfred Neuro-ophthalmology clinic. This will then prompt referral to the Alfred neuroimmunology clinic (NIC), where a qualified Immunologist (also employed by Eye and Ear EORC) and Neuroimmunologists are available.
- Rheumatology/ Immunology or Neuroimmunology at their local tertiary hospital, to centralise care especially if already receiving care. This will allow multidisciplinary care with geriatricians, endocrinologists etc.

Additional notes:

- Patients given systemic steroids need to be advised of potential side effects
- Give the patient a copy of the Giant Cell Arteritis Patient Information and Temporal Artery Biopsy Patient Information sheets available on the Policy Centre or Eye and Ear website and patient information hub.

Evidence Table

Author(s)	Title	Source	Level of Evidence (I – VII)
W Rahman, FZ Rahman	Giant cell (temporal) arteritis: an overview and update	Surv Ophthalmol. 2005 Sep-Oct; 50(5):415-28	I
Hellmich B, et al.	Update of the EULAR recommendations for the management of large vessel vasculitis	Annals of the Rheumatic Diseases 2020;79:19-30 George Spaeth Ophthalmic Surgery, Principles and Practice, Chapter 52, Temporal Artery Biopsy	VII
Nesher G	The diagnosis and classification of giant cell arteritis	J Autoimmun. 2014 Jan 21, epub	VII
Colin CK Chan, Mark Paine, Justin O'Day	Steroid management in giant cell arteritis	Br J Ophthalmol 2001:85:1061-1064	VI
Helen V. Danesh-Meyer, Peter J. Savino	Giant cell arteritis	Curr Opin Ophthalmol, 2007:18:443-447	VII
Thomas RG Poole, Elizabeth M Graham, Sebastian B Lucas	Giant cell arteritis with a normal ESR and CRP	Eye 2003;17:92-93	VII
SS Hayrey, PA Podhajsky, B Zimmerman	Occult Giant Cell Arteritis: Ocular Manifestations	Am J Ophthalmol 1998;125:521-526	IV
M Haq et al	Is it Necessary to Hold Anticoagulation Prior to Temporal Artery Biopsy	Poster Abstract, Number 2782. 2018 American Rheumatology Annual Meeting, October 2018	VI

The Hierarchy of Evidence

The Hierarchy of evidence is based on summaries from the National Health and Medical Research Council (2009), the Oxford Centre for Evidence-based Medicine Levels of Evidence (2011) and Melynk and Fineout-Overholt (2011).

I) Evidence obtained from a systematic review of all relevant randomised control trials.

II) Evidence obtained from at least one well designed randomised control trial.

III) Evidence obtained from well-designed controlled trials without randomisation.

IV) Evidence obtained from well-designed cohort studies, case control studies, interrupted time series with a control group, historically controlled studies, interrupted time series without a control group or with case series.

V) Evidence obtained from systematic reviews of descriptive and qualitative studies.

VI) Evidence obtained from single descriptive and qualitative studies.

VII) Expert opinion from clinician, authorities and/or reports of expert committees or based on physiology.

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