In association with

Giant cell arteritis

Giant cell arteritis is a medical emergency. Early detection and prompt treatment are potentially sight saving, and reduce the risk of complications. We will see it relatively rarely in primary care but it needs to be on our radar.

The British Society for Rheumatology has produced NICE-accredited guidance to support primary and secondary care in working together to provide best practice care for people with giant cell arteritis (Rheumatology 2020;59:e1-e23); this guidance is the main reference for this article. In addition, we refer to a BMJ Clinical Review (BMJ 2019;365:l1964).

What is giant cell arteritis?

- A large vessel vasculitis.
- Affects older people, most commonly between age 70 and 79y. It is very rare in those aged <50y.
- Inflammation is seen in the walls of medium and large-sized arteries, including the aorta and its branches, and can result in ischemia in the end organs they serve.
- This gives rise to the characteristic symptoms of giant cell arteritis, which can be divided into:
  - **Cranial manifestations:** headache, jaw claudication, scalp tenderness, visual loss and stroke may be seen.
  - **Large vessel manifestations:** inflammation of the aorta and/or its branches is common is GCA *(presumably, we are now more aware of this because of more extensive vascular imaging)*. This may be asymptomatic or have non-specific symptoms such as fever and weight loss; limb claudication symptoms may also be seen.

Role of primary care in GCA: the headlines

We have an important role in primary care:

- **Spotting GCA** and recognising it as a medical emergency.
- **Taking bloods and starting high-dose prednisolone** 40–60mg if we have a high degree of clinical suspicion (defined in this guideline as "in the assessing clinician's judgement, GCA is a more likely explanation for the patient's symptoms than any other diagnosis").
- **Referring urgently** for further diagnostic evaluation and definitive testing:
  - Patients with visual disturbance should be seen that same day by ophthalmology.
  - All other patients should be discussed and ideally seen by a specialist with appropriate experience (usually rheumatologist), ideally the same day but definitely within 3 working days.
- **Shared-care follow-up** for the duration of treatment and management of comorbidities, e.g. diabetes, hypertension and osteoporosis commonly impacted by the long-term glucocorticoid therapy.

This will not be a quick consultation!

Suspecting GCA: symptoms and signs

There is no one symptom, sign or blood test that offers a definitive marker for GCA. Many of the symptoms and signs can have multiple causes in the undifferentiated primary care population. There is no validated primary care scoring tool. *This all makes it rather tricky!*

So, we need to think, could this be GCA? And then, are other diagnoses more or less likely?

What makes GCA more likely?

In people aged >50y, if you consider a diagnosis of GCA is possible:

Ask about	Look/feel for
• New headache. • Visual disturbance or diplopia. • Scalp tenderness when brushing hair. • Pain in jaw on chewing. • New/recent limb claudication.	• Tenderness over scalp. • Tenderness, thickening or loss of pulse in temporal arteries. • Check vision and look for: abnormal visual acuity or visual fields (*though if people report a change in their vision and other symptoms sug-*

• Systemic symptoms including fever/weight loss (if very significant, consider infection/malignancy). • Proximal muscle pain and stiffness *(may suggest co-existing polymyalgia rheumatica).*	*gestive of GCA, refer regardless of what our primary care visual assessment finds).* • Carotid or subclavian bruits (will only be present if large vessel involvement). • Difference in BP between 2 arms may be present if there is large vessel involvement (15–20mmHg is probably significant).

Then have a low threshold for doing bloods.

Remember: **headache is not universal**; it is present in about 75% at first presentation but, if there are other features, the absence of headache should not put us off considering the diagnosis.

The positive predictive value of these symptoms and signs in a primary care population is not known, and much of the data we do have relates to patients seen in secondary care settings (so once we have already referred them!).

THINK: could it be something else?

If so, does it need to go down an alternative referral pathway or should it be managed in primary care (this is less likely as usually these people are relatively sick)? (BMJ 2019;365:l1964):

Headache dominant
Headache of alternative cause (migraine, trigeminal neuralgia, cluster headache, sinusitis, TMJ dysfunction; if acute and severe, also consider SAH, etc.).
Shingles before the rash appears.
Skull metastases.
High ESR/systemically unwell
Polymyalgia rheumatica.
Endocarditis.
Malignancy, e.g. lung cancer, myeloma.
Deep-seated infection, e.g. intra-abdominal collections, discitis.
Other vasculitides, e.g. polyarteritis nodosa.

How can we decide which diagnosis is more likely?

A recent systematic review and meta-analysis evaluated the diagnostic accuracy of a range of symptoms, signs and tests; again, the studies were mainly from those people we have already referred to secondary care. It identified symptoms, signs and test results that were consistently associated with an increased chance of a diagnosis of GCA, but the positive likelihood ratios were modest.

Symptoms, signs and test results that make a diagnosis of GCA <u>more likely</u>	**Symptoms, signs and tests that make a diagnosis of GCA <u>less likely</u>**
Jaw claudication (*pain on chewing).*	ESR <40mm/h
Limb claudication (*this may surprise some of us!).*	CRP <25mg/L
Temporal artery thickening on palpation.	Age <70y
Temporal artery loss of pulse.	
Platelet count >400x10^3/μL.	
ESR >100mm/h.	

It concluded that **no single symptom, sign or laboratory test performs well enough to rule GCA in or out**, so if we suspect it in primary care, it is likely that further investigations (vascular imaging and/or temporal artery biopsy) will be necessary and we will need to refer (JAMA Int Med 2020, 180(10):1295).

What does this all mean in practice?

The guideline talks about "estimating the probability of GCA based on symptoms, signs and laboratory tests", and separating patients into low (<20%), medium (20–50%) and high (>50%) pre-definitive test probability. This is targeted at the secondary care audience and I think is difficult to apply in primary care.

The key message for us is:

- If we have a **high degree of clinical suspicion** and there is no ***more likely*** explanation for the patient's symptoms, we should take immediate bloods, start treatment and refer.

- If we have a **low to medium clinical suspicion** (GCA is one of a number of possibilities), we should take immediate bloods and discuss the case with secondary care to make a treatment and investigation plan.

The bottom line is, generally these patients will be unwell and need further rapid assessment somewhere!

Testing and starting treatment

- **Take bloods for FBC, ESR (or plasma viscosity if not available) and CRP before or, if this is not possible, immediately after, commencing high-dose steroids.** *This is a situation where we should be squeezing patients in for a same-day blood test.*

When we are doing blood tests, it is reasonable to test more widely in this scenario because of the potential wide differential.

The BSR guidance suggests we should request:

Bloods to support diagnosis/inform prognosis	Bloods to offer baseline for important general health/comorbidities
Always take before or immediately after starting steroids: • CRP. • ESR (or plasma viscosity if not available). • FBC (platelets may be elevated). Consider: • *Myeloma screen (protein electrophoresis/light chains/urine Bence-Jones protein).*	• Renal function. • Liver function. • HbA1c (if no recent assessment; try to take before starting steroids if possible) as steroid therapy may push pre-diabetes to diabetes. • Lipids (if no recent assessment). Consider: • *Assessing risk of serious infection, e.g. urine dipstick, CXR and tests for latent tuberculosis – this is more likely to be done in secondary care).* • *Calcium/ALP/vitamin D/TSH if clinically relevant in the assessment of osteoporosis risk (this is discussed further below).*

Should we wait for results before starting treatment/referring?

The BSR 2020 guidelines state that:

- If GCA is ***strongly suspected*** (no other diagnosis is more likely) then steroids can be commenced without waiting for results.

Having said this, the situation is rarely this black and white in primary care, and 'certainty' is rare! UK data suggests that only 10–20% of patients referred from primary care to secondary care GCA pathways actually end up with a diagnosis of GCA.

So, in reality, many of us will discuss these patients with rheumatology on the day we see them (even if secondary care assessment is delayed for a few days) and formulate a shared management plan.

Secondary care service provision and speed of assessment varies significantly around the country. The publication of the BSR 2020 guidelines, with clear benchmarks of what good care and appropriate speed of secondary care assessment looks like, may reduce this national variation.

Comorbidities

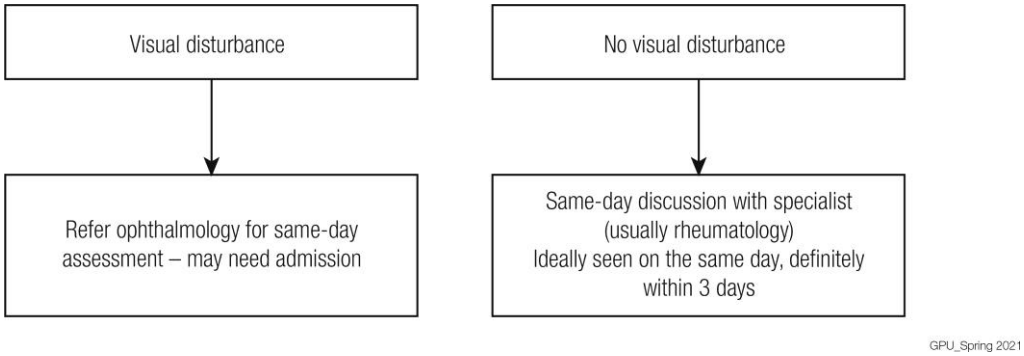
Primary care has a valuable role in assessing and communicating potential comorbidities that may impact on treatment and outcomes as we refer these patients to secondary care. We are particularly thinking about conditions which may increase the risk of steroid adverse events, e.g.:

- Hypertension.
- Diabetes.
- Osteoporosis/history of fragility fracture.
- Dyslipidaemia.
- Chronic infection, e.g. TB.
- Peptic ulcer disease.
- Glaucoma.
- History of psychiatric adverse events with steroids.

Referral

GCA is a medical emergency and requires urgent assessment.

The BSR 2020 guidance states that where we suspect GCA, we should **refer urgently** for further diagnostic evaluation and definitive testing:



Local pathways may vary, though – do you know your local referral pathway? If not, ask colleagues and find out.

Confirming the diagnosis

GCA diagnosis should be confirmed by temporal artery biopsy or vascular imaging, or both. This will be determined by secondary care and local availability of testing.

- **Temporal artery biopsy**:
  - Involves taking a 1cm segment of the temporal artery under local anaesthetic.
  - It is not a perfect test and patients with a negative biopsy can still have GCA.
  - Treatment should not be delayed waiting for the result. Biopsies can remain positive for 2–6 weeks after initiation of steroids but the sooner it is done, the more likely it is that an accurate result will be obtained.
- **Vascular imaging (usually duplex ultrasound)** of temporal and axillary arteries:
  - Increasingly used.
  - Typical appearances of oedema of the vessel wall (halo) may be seen but this starts to fade within a day or two of starting steroids.
  - If ultrasound is positive, in some centres no biopsy will be performed.
  - If there is too long a delay between starting steroids and getting an ultrasound, some patients who have a negative ultrasound may go on to have a biopsy which might have been avoidable.
  - **If ultrasound is available at your local hospital, it is particularly important to discuss with the specialist team whether starting steroids in low-probability cases is advisable.**

Vascular MRI/CT may also be used to look at the aorta and its branches.

If secondary care does not make a diagnosis of GCA, it may undertake further investigations or simply refer back to us as "Not GCA, consider other diagnoses". Depending on the clinical situation and how sick the person is, we may need to consider more holistic rapid assessment routes, and this may be where local rapid diagnostic centres (if you have one) or a friendly general medic or geriatrician may be helpful.

Management

This will be guided by secondary care but, in high probability cases, we will start treatment as soon as the condition is suspected and we have taken bloods:

Drug	Dose	Notes
Prednisolone	40–60mg per day (single daily dose)	Symptoms usually improve significantly within 1 week – rethink diagnosis if not. One possible tapering regimen is as follows (there is an absence of evidence of one optimal regimen and they will be individualised for the patient). • **High dose (40–60mg) maintained for 3–4 weeks** or until resolution of all symptoms, then tapered: o Reduce by 10mg every 2 weeks to 20mg then o Reduce by 2.5mg every 2–4 weeks to 10mg then o Reduce by 1mg every 1–2 months until stopped. Patients with visual symptoms may be given IV methylprednisolone for 3 days before starting oral medication, although the evidence for this is uncertain.

Proton pump inhibitor	Standard dose	Consider whether gastroprotection is required based on age, comorbidities and other medication. It is usual to offer gastroprotection for higher doses >20mg.
Bone protection: usually a bisphosphonate + calcium/vitamin D if needed	Standard dose for preparation	These are very high doses of steroid and most patients are elderly, so it is very likely they will need bone protection. See the *Osteoporosis* article for more details. *The rheumatologists may make a specific recommendation when the patient is seen – whether we wait for a DXA scan result will depend on how long they are taking in our area as bone loss occurs quickly on steroids.*

Aspirin is no longer recommended as an adjunctive treatment for GCA; there is an absence of evidence of its efficacy and it may increase risk of harms, e.g. gastrointestinal bleeding.

All patients should receive a steroid card AND a steroid emergency card, as per NPSA guidance, because of the risk of iatrogenic adrenal insufficiency (Clinical Medicine 2020;20 (4):371). Further information can be found in our article on *Adrenal insufficiency and Addison's disease.*

Follow-up and shared care

Patients with GCA should remain under secondary care for the duration of their illness. They will be seen in secondary care regularly at first, and then less frequently.

Shared care arrangements exist in many areas, and primary care will be asked to support follow-up in the same way we do for other rheumatological conditions.

How often should people with GCA be seen?

A follow-up schedule is proposed in the BSR 2020 guidance, and suggests that people with GCA should be seen by a clinician with appropriate expertise:

Suggested follow-up schedule for GCA (BSR 2020)
• Every 2–8 weeks for the first 6 months. • Every 12 weeks for the second 6 months. • Every 12–24 weeks for the second year. • Additionally, as indicated by symptoms of relapse.

What should be done at follow-up visits?

- Assess symptoms (of GCA and PMR – both should be absent) and do a targeted physical examination.
- Discuss stage of tapering – the aim is to taper steroids to zero over 12–18 months, providing there is no return of signs or symptoms, or a significant rise in inflammatory markers.
- Consider complications, e.g., diabetes, hypertension and osteoporosis.
- Ask about mood.
- Promote self-care to improve wellbeing, e.g. improving sleep quality, physical activity, weight management.
- Bloods for FBC, ESR and/or CRP (and consider blood glucose monitoring if relevant – *HbA1c and a post-prandial random glucose* may be more useful than fasting as prednisolone particularly impacts post-prandial glucose).
- Patients with large vessel involvement *may* require ongoing vascular imaging to monitor for the development of aneurysms, though the clinical and cost effectiveness of this is uncertain. This will be determined and organised in secondary care.

What symptoms may suggest relapse?

Symptoms	**Action**
New visual loss or diplopia.	• Same-day assessment by ophthalmology.
Return of headache symptoms.	• Return to previous higher prednisolone dose.
Jaw or tongue claudication.	• **Discuss with secondary care.** • Consider returning to high-dose 40–60mg prednisolone +/- glucocorticoid-sparing agents.
Weight loss, fever, night sweats, anaemia, persistent raised ESR/CRP, new or recurrent PMR symptom, limb claudication, abdominal pain or back pain.	• Consider GCA-related inflammation of aorta and/or its proximal branches. • **Discuss with secondary care** – will require vascular imaging and possible increase of prednisolone and/or addition of glucocorticoid-sparing medication.

Do small fluctuations in inflammatory markers matter?

The BMJ review reminds us that small fluctuations in inflammatory markers during steroid tapering are common and should not be used alone to guide treatment. They need to be correlated against symptoms.

Glucocorticoid-sparing agents for GCA

Patients who relapse should be considered by the specialist team for steroid-sparing treatment. Tocilizumab is licensed for this purpose. Methotrexate is not licensed but is sometimes used instead when tocilizumab cannot be used. Not all patients are suitable for steroid-sparing treatment, depending on their comorbidities.

Giant cell arteritis

- Think about it and, if suspected, refer immediately to specialist care.
- Start steroids in primary care if GCA is strongly suspected (there is no more likely diagnosis). Ensure bloods are sent **before** starting steroids.
- If there is visual disturbance at presentation, immediate ophthalmology review is required – admit!
- Once diagnosis confirmed in secondary care, shared-care follow-up will be required.
- Remember bone and gastroprotection, and to monitor for diabetes and hypertension.

Do you know your local pathway for the assessment of patients with possible giant cell arteritis? If not, find out.

QI project: Review your last 3 consultations with patients with GCA (and PMR):

- Are they taking the recommended medication?
- Have they got gastroprotection and bone protection?
- Do they have a written tapering regimen?
- Are they being monitored for long-term complications?
- Do they know the symptoms of GCA to watch out for (headache, jaw claudication) that should prompt them to seek urgent medical advice?

Could you develop a template to support these reviews? This would be a great job for your clinical pharmacists to provide support and to look more widely at long-term prednisolone prescribing across your practice.

Patient information from Versus Arthritis: https://tinyurl.com/Red-Whale-GCA-leaflet

Treatment:

Steroids advice: https://www.versusarthritis.org/about-arthritis/treatments/drugs/steroids/

Living well:

Managing fatigue: https://www.versusarthritis.org/about-arthritis/managing-symptoms/managing-fatigue/

Exercising with arthritis: https://www.versusarthritis.org/about-arthritis/exercising-with-arthritis/

Let's move with Leon: https://www.versusarthritis.org/about-arthritis/exercising-with-arthritis/lets-move-with-leon/

Patient support group: https://pmrgca.org.uk/get-support/