SURVEY OF OPHTHALMOLOGY 65 (2020) 218–226

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/survophthal

Diagnostic and surgical techniques

The role of vascular ultrasound in managing giant cell arteritis in ophthalmology

Jared Ching, MB, ChB, MPharm, MRPharmS, FRCOphth[a,b,c],
Sonja Mansfield Smith, MB, ChB, MRCP(UK) (UK)[a],
Bhaskar Dasgupta, MBBS, MD, FRCP, Professor[d],
Erika Marie Damato, MBBS, BA, MA (Cantab), MRCP(UK), MRCOphth[a,*]

[a] *Department of Ophthalmology, Addenbrookes, Hospital, Cambridge, UK*
[b] *John Van Geest Centre for Brain Repair, Cambridge, UK*
[c] *MRC Mitochondrial Biology Unit, Keith Peters Building, Cambridge Biomedical Campus, Cambridge, UK*
[d] *Southend University Hospital NHS Foundation Trust and Anglia Ruskin University, Southend on Sea, UK*

ARTICLE INFO

Article history:
Received 14 May 2019
Received in revised form 14 November 2019
Available online 24 November 2019
Neelakshi Bhagat and **Mohammad Dastjerdi**, Editors

Keywords:
vascular ultrasound
giant cell arteritis
fast track clinic
large vessel vasculitis

ABSTRACT

Giant cell arteritis is the most common systemic vasculitis in the elderly and is a potentially life-threatening ophthalmic emergency that can result in irreversible blindness. Blindness is most commonly associated with acute onset, irreversible arteritic ischemic optic neuropathy. Without treatment, second eye involvement may occur, resulting in bilateral blindness. Patients with established visual loss are treated with high-dose steroids and generally undergo a temporal artery biopsy to confirm their diagnosis. A significant number of patients are, however, referred for urgent ophthalmology assessment from concerns about "incipient" arteritic ischemic optic neuropathy. Before visual loss, patients may experience a range of ocular symptoms related to ischemia. This generally leads to treatment with high-dose systemic steroid and an urgent request for a temporal artery biopsy. Temporal artery biopsy is considered as the standard investigation for confirmatory diagnosis. It is generally arranged as soon as possible, although it is often not carried out for several days, and there may also be delays in histopathological reporting. It is often perceived that the patient is "safe" while on corticosteroids, in that they are being treated to avoid visual loss. What is not acknowledged, however, is that, if patients do not have giant cell arteritis and are being treated "just in case," they will often require a tapering of oral steroids over several weeks, exposing them to unnecessary and significant side effects. In the rheumatology setting, vascular ultrasound has emerged as a safe and reliable alternative to temporal artery biopsy as a point of care diagnostic tool in the management of giant cell arteritis. Given an experienced sonographer and optimal equipment, a rapid diagnosis can be established in a fast-track clinic setting, taking into consideration clinical assessment, scoring, and ultrasound findings. A huge advantage of ultrasound is that it provides immediate information that can be used to inform treatment decisions. We explore the evidence that supports the incorporation of vascular ultrasound into the ophthalmology repertoire to make a more efficient diagnosis that is cost-effective and

* Corresponding author: Dr. Erika Marie Damato, Department of Ophthalmology, Addenbrookes, Hospital, Hills Road, Cambridge CB2 0QQ, UK.
E-mail address: erika.damato@addenbrookes.nhs.uk (E.M. Damato).

https://doi.org/10.1016/j.survophthal.2019.11.004

associated with better patient outcomes, including a potential reduction in loss of sight and avoidance of unnecessary long-term steroid treatment by early exclusion of mimics.

1. Introduction

Giant cell arteritis (GCA) is the most common systemic vasculitis in the elderly[8] and predominantly occurs in whites.[50] Those of Scandinavian descent are at an increased risk, and familial aggregations of GCA have been observed.[18] GCAis a potentially life-threatening ophthalmic emergency that can result in irreversible blindness without prompt treatment.[39] Advancing age, peaking at 70–79 years, female gender, and an underlying diagnosis of polymyalgia rheumatica are associated risk factors in British populations.[37] Visual loss can occur unilaterally or bilaterally, occurring in 20% of patients as partial or complete presentations.[48]

The diagnosis of GCA is challenging owing to its protean manifestations of cranial and extracranial disease, difficulties in interpretation of blood results, and nonspecific ophthalmic symptoms. Very often, the ophthalmic examination is completely normal until catastrophic visual loss from anterior ischemic optic neuropathy. Sudden-onset unilateral visual loss, associated with a relative afferent pupillary defect and a pale, swollen optic nerve, is a classic presentation of arteritic ischemic optic neuropathy, which is typical of GCA. Patients often experience other symptoms, however, including transient monocular blindness, transient visual blurring, double vision. These symptoms are not specific to GCA; however, they may raise the suspicion of the diagnosis, especially in the context of headaches, jaw claudication, raised inflammatory markers, and advanced age.

Challenges arise when elderly patients present with vague symptoms, are poor historians, or may have other reasons for their ocular symptoms, such as carotid artery disease, early *Herpes zoster ophthalmicus*, or general malaise from systemic infection or malignancy. In some cases, blurred vision is attributed to vitreous detachment. Nonarteritic anterior ischemic optic neuropathy is another condition that may lead to a false diagnosis of GCA. In this case, cardiovascular risk factors and fluctuations in blood pressure are thought to lead to a watershed infarct of the optic nerve, leading to sectoral ischemia and consequent field loss, which is typically, but not always, altitudinal.

The treatment of GCA with ocular involvement is high-dose systemic corticosteroids, starting with either intravenous methylprednisolone or high-dose oral prednisolone, tapering slowly over several months to years. Although high-dose steroids are justified in confirmed cases where the diagnosis is clinically evident, a significant proportion of patients are treated for suspected GCA on the basis of nonspecific visual symptoms, headaches, and elevated inflammatory markers. This is the result of the great difficulty in confirming a diagnosis based on symptoms, history, examination, and blood results in the acute setting and the concern about the possibility of visual loss. This group of patients with ocular symptoms is generally referred to the emergency eye services, where, in the United Kingdom, they are often managed by the "on-call" ophthalmology team.

In view of the challenge of diagnosis, patients with a suspected diagnosis are commonly started on high doses of systemic steroid while awaiting a definitive histological diagnosis. After being on such treatment for more than 2–3 weeks, steroids are then tapered slowly over 18–24 months, resulting in a high cumulative dose. Commonly, even when a diagnosis is excluded with a negative biopsy, steroid taper is often required, leading to unnecessary steroid exposure.

American College of Rheumatology (ACR) guidelines include temporal artery biopsy (TAB) as one of the five diagnostic criteria, of which at least three must be present to make a diagnosis of GCA.[23] In the past, TAB has been considered the gold standard for the diagnosis of GCA, and the consensus has been that this should always be performed without delaying treatment.[22,27,39] This practice has been supported by the guidelines from the British Society of Rheumatology, British Health Professionals in Rheumatology, and the 2014 National Institute of Clinical Excellence.[11,34]

Vascular ultrasound (US) is shown to be a well-tolerated, safe, and cost-effective investigation with a proven role in the diagnosis of GCA.[7,27,41] The recent 2018 EULAR recommendations advocate US examination of the temporal arteries with or without axillary artery examination as a first-line investigation in patients with suspected predominantly cranial GCA.[13] As such, there is a clear need to incorporate vascular US examination into ophthalmic practice as patients with suspected cranial GCA are regularly referred to ophthalmologists. We review the literature to date and the rationale to incorporate vascular US into the ophthalmology repertoire.

2. Temporal artery biopsy

TAB has an established role in confirming GCA and is regarded by many as the "reference standard," providing histological evidence for the diagnosis. TAB is performed under local anesthetic by surgical specialists, including ophthalmologists, general surgeons, vascular surgeons, and neurosurgeons.[17,30] The temporal artery is a terminal continuation of the external carotid artery that begins in the parotid gland posterior to the neck of the zygomatic process of the temporal bone and divides approximately 5 cm superior to this point into the frontal and parietal branch.[29] The frontal branch is identified and ligated at two points to permit excision of a portion of the artery and sent for histological analysis. The suggested length of artery required to confirm the diagnosis varies in the literature from 5.0 mm,[28] 10.0 mm,[52] 15.0 mm,[35] 20.0 mm[47] to 40.0 mm,[9] while British Health Professionals in

Rheumatology guidelines advocate biopsy lengths of no less than 10.0 mm.[11]

A "positive biopsy" is hugely valuable and supports the use of prolonged systemic steroids and sometimes immunosuppression and now tocilizumab therapy. In the acute setting, high-dose steroid treatment is rarely questioned; however, in the later stages of treatment, when patients may encounter side effects from prolonged systemic steroids, a positive biopsy is important in justifying ongoing treatment and avoiding inappropriate cessation of treatment, which may carry the risk of relapse.

Problems associated with TAB may include false-negative results or surgical complications. False-negative results may occur for a number of reasons. Owing to the discontinuous nature of the vascular changes within the arterial lumen, "skip" lesions may be present, and biopsies meeting the specified length may still be negative for pathological changes, resulting in false negatives.[38] Inadequate sample from a too short section may also result in false-negative results. Histological features of GCA are known to vary from florid accumulations of giant cells to subtle pockets of non-granulomatous inflammation, which may cause a degree of uncertainty in the histological diagnosis.[49] The recent TABUL study found the sensitivity of TAB as only 40%, with considerable difference of opinion between histopathologists regarding biopsy interpretation.[27] Though the protocol followed did not reflect typical clinical practice and this low sensitivity cannot be extrapolated into real-life clinical practice.

TAB can rarely be associated with complications including facial nerve injury,[5,51] wound infection,[21] scalp necrosis,[39] and stroke.[19] In addition to such risks, the surgical procedure may be more challenging in patients taking anticoagulants, medications, resulting in difficulty with hemostasis, time required for wound healing, and hair regrowth in shaved areas.

The absolute need for a TAB in all patients suspected of having GCA has been questioned, given that an ACR score of 3 of more has a sensitivity of 93.5% and specificity of 91.2%. Davies and coworkers demonstrated that avoiding TAB in patients with an ACR score of ≤ 2 was feasible[12]; however, the latest British Society of Rheumatology guidance (2019) makes a strong recommendation to obtain a confirmatory test in all cases. The NHSE eligibility criteria for tocilizumab in relapsing/refractory disease require confirmation of diagnosis with either US or TAB.

3. Overview of vascular US in the assessment of patients with suspected large vessel vasculitis

US examination is a noninvasive, safe, and efficient imaging modality that can take cross-sectional images of vessels and evaluate vascular flow dynamics.[41] Rheumatologists routinely employ US as a useful tool to facilitate diagnoses.[42] Four pathological lesions are evident on US when assessing vessels. These include arterial wall thickening depicted as a "halo" on longitudinal imaging, noncompressible arteries on transverse imaging, stenosis, and vessel occlusion.[41]

In patients with GCA, it has been shown, using a Delphi exercise, that the most relevant of these are the "halo" sign and noncompressibility of affected arteries.[10]

3.1. *The noncompressible halo sign*

The presence of an inflammatory infiltrate and edema of the tunica media with possible spread to the intima and adventitia is responsible for this sign[43] defined as a hypoechoic rim of vascular wall swelling around the artery lumen that is visible in 2 planes and does not disappear on compression.[2,43] Multiple meta-analyses to date have supported the role of vascular US in the management of GCA.[1,4,25] In 2005, Karassa and coworkers reported on 2036 patients from 23 heterogeneous studies, finding weighted sensitivity and specificity of the halo sign to be 69% and 82%, respectively, compared with TAB, and presence of vessel occlusion or stenosis was 82% sensitive and 92% specific compared to TAB.[25] Ball and colleagues reported in 2010 on 998 patients from 17 similar studies, a finding that US was 75% specific and 83% sensitive when compared to TAB, advocating US as a first-line investigation for GCA in light of these results.[4] Arida and colleagues in 2010 reported on 575 patients from 8 studies and found that a unilateral positive halo sign was 68% sensitive and 91% specific, and bilateral positive halo sign was 43% sensitive and 100% specific for GCA.[1]

More recently, the role of ultrasound, especially regarding the significance of the halo sign and compression sign, has been strengthened. Specific protocols,[10] aimed at clarifying the definition and imaging settings required to interpret a Halo, have been proposed. In addition, Aschwanden and coworkers[3] have reported a high interobserver agreement in using the compression sign to diagnose GCA.

Such findings have led to the recommendation by the EULAR group[13] that temporal artery ultrasound should be a first-line imaging investigation in patients referred with a suspected diagnosis of GCA. Such guidelines do not explicitly advice against TAB but rather support initial use of US due to availability, reliability, cost, and noninvasiveness.

Detailed clinical workup for each GCA suspect is still a prerequisite[14] taking into consideration patient presentation, risk factors, and blood workup. A recently published probability score may aid the initial triage of referrals of suspected GCA to a fast-track clinic.[26]

3.2. *Compression sign*

Aschwanden and colleagues first reported the compression sign as persistence of a visible vessel wall on compression of the vessel lumen with the US wall in the presence of wall thickening secondary to inflammation was associated with a sensitivity of 75–79% and 100% in GCA.[2,3] The same authors found that this sign was robust with excellent interobserver agreement.[3]

3.3. *Stenosis and occlusion signs*

Arterial stenosis and occlusion have been shown to be neither specific nor sensitive and should therefore be avoided in the specific evaluation of GCA.[1,10,24]

Table 1 – Gray scale settings to assess arteries in GCA

Setting	Function	Recommended setting
Frequency	Regulates beam penetration	18 MHz
Focus	Level of depth of focus	Temporal artery: 5 mm Axillary artery: 2–3 cm
Depth	Determines penetration depth	Temporal artery: 1–2 cm Axillary artery: 3–4 cm
B-mode gain	Brightness (important to avoid false halo readings with excess/inadequate brightness)	35–45 dB
Line density	Adjusts number of scan lines and thus spatial resolution (higher line density increases image quality but decreases frame rate)	3
Frame rate	Adjust acquisition frame rate and thus temporal resolution	>15 images per second
Dynamic range	Adjusts intensity between shades of gray	40–66 dB

GCA, giant cell arteritis.
Adapted from Monti et al.[32]

3.4. *Which vessels?*

Shäfer and colleagues compared vascular US findings between GCA patients and control subjects, determining cutoff measurements for normal intima-media thickness in the common temporal artery and its branches and the axillary artery.[40] There is evidence that examining the temporal and axillary arteries in suspected GCA cases are most pertinent, where Schmidt and colleagues found that 98% and 62% of large-vessel GCA patients had characteristic axillary and temporal artery changes on US, respectively.[46] A recent meta-analysis by Duftner and colleagues who defined the reference standard for GCA diagnosis clinical assessment or TAB demonstrated a pooled sensitivity and specificity of 77% and 96%, respectively, when examining the superficial temporal artery with US.[16]

4. Technical aspects of vascular US for GCA

4.1. *Equipment requirements and settings*

Modern US machines equipped with linear probes with a gray scale frequency of at least 15 MHz and color Doppler mode of at least 6 MHz are appropriate for investigating GCA.[32] Probes of 20 MHz or more permit visualization of the intima-media complex in normal subjects.[41] Such equipment is not routinely found in the eye department, where a standard ophthalmic ultrasound does not include high frequency probes or color Doppler; however, the high frequency probes will enable good resolution for standard ophthalmic use.

Temporal artery examination ideally with frequency probes of at least 15 MHz would be necessary to detect small changes in arterial vessel wall thickness in temporal arteries using a linear or hockey stick–type probe.[41] For axillary, vertebral, subclavian, carotid, and femoral arteries, a linear probe with a lower gray scale frequency can be used. Tables 1 and 2 summarizes the settings for gray scale and color Doppler recommended by Monti et al.[32]

4.2. *Examination technique*

Performing temporal artery ultrasound and axillary artery ultrasound takes about 20 minutes and can be performed with the patient in the recumbent or semirecumbent position in either the supine or lateral positions. The common superficial temporal artery is identified adjacent to the tragus and is then followed to its bifurcation into frontal and parietal branches, which are also explored. This is repeated on both sides. Images are saved in longitudinal and transverse sections, and findings are reported in a standardized fashion.

Imaging of the axillary artery has also been shown to be valuable in diagnosing large vessel vasculitis. This can be carried out in the same setting, with the patient's arm elevated, elbow flexed, with the hand resting under the head to expose the axillary area.

4.3. *US signs and measurements*

When the halo sign is positive, the maximal thickness in the longitudinal plane should be recorded. The measurement is made by marking the first reference point at the outer limit of the vessel wall and as close to the outer limit of the color Doppler flow. A pathological cutoff in temporal artery US has been reported as >0.3 mm and measurements >0.7 mm correlate well to a positive TAB.[1] Axillary artery wall thickness of >1.0 mm has been correlated with patients at risk of vasculitis, and >1.5 mm diagnostic.[46]

Recently, Shafer and colleagues found that when comparing 40 GCA patients with 40 matched controls, intima-media thickness cutoff measurements can be used to reliably differentiate between vasculitic and normal vessels with very high levels of sensitivity and specificity (see Table 3).[40] These reference values have now been compiled into a quantitative halo score that informs the extent and severity of sonographic abnormalities and may form an outcome marker in the follow-up of GCA on treatment.

4.4. *Timing and follow-up*

Once treatment with systemic steroids has been initiated, the duration for which the halo sign in the temporal arteries

Table 2 – Color Doppler settings to assess arteries in GCA

Setting	Function	Recommended setting
Frequency	Regulates beam penetration	Approx. 10 MHz
Pulse repetition frequency	Doppler sampling frequency (needs to be dynamically adjusted during examination according to flow velocity of vessel to avoid artifact)	Temporal artery: 2–3 kHz Axillary artery: > 3 kHz (depends on machine and flow velocity)
Wall filter	Removes noise from moving vessel walls	Low values (need to be increased to assess axillary artery)
Color box	Requires an angle steer to correction to obtain an angle between scan lines and direction of flow ≤60° to avoid inaccurate readings	≤60°
Color flow gain	Needs to be dynamically adjusted to precise filling of the vessel lumen with color, otherwise misinterpretation of halo ensues	2–18
Flow direction	Red if flow toward transducer and blue if away. Conventionally red is arterial and blue venous; however, transducer orientation determines this.	Invert function off

GCA, giant cell arteritis.
Adapted from Monti et al.[32]

remains positive has been reported to vary from 2 days to a number of weeks.[33] Muratore and colleagues found that the sensitivity of US reduces with treatment, where 85% demonstrated resolution within 24 hours of starting treatment and 50% resolved within 2–4 days or more than 4 days from the initiation of steroids.[20] Schmidt and colleagues found that of the 22 patients with a positive halo sign, the sign disappeared at a mean of 16 days, with a wide range of 7 to 56 days.[44] De Miguel and colleagues examined 30 GCA patients with US biweekly for the first month from diagnosis, then four weeks once until resolution of the halo sign.[31] They found that in 95% of patients, the halo sign disappeared at an average of 11 weeks from the initiation of treatment. In the TABUL study, it was found that of the 312 patients included, following more than 4 days of treatment resulted in a significantly smaller halo sign.[27]

The halo sign and intima-media thickness increase in axillary arteries can, by contrast, persist for weeks, months, or years after steroid treatment.[45] With such variability after treatment, vascular US assessment should ideally be instigated as soon as possible either before treatment initiation or within 3 to 4 days of initiation or corticosteroids.

Table 3 – Ultrasound cutoff for intima-media thickness in GCA

Artery	Intima-media thickness pathological cutoff (mm)	Sensitivity (%)	Specificity (%)
Common superficial temporal	0.42	100	100
Frontal branch	0.34	100	100
Parietal branch	0.29	97.2	87.5
Axillary artery	1.0	100	100

GCA, giant cell arteritis.
Adapted from Schafer et al.[40]

4.5. *Training and certification in US*

To widely implement the use of ultrasound into ophthalmic services, the appropriate training, supervision, validation, and certification is required. There is currently no formal certification in ultrasound for ophthalmologists or indeed rheumatologists; however, there are proposals to introduce such regulation into clinical practice in the UK. At present, within our region, it is proposed that a minimum of 50 ultrasounds should be performed and supervised or validated before an individual being recognized as "certified," and this has been how rheumatologists have established their fast-track services. In addition, when introducing US into clinical services, ultrasounds have initially been compared with TAB findings and prospectively evaluated. In some centers, such validation has led to US becoming the investigation of choice, with TAB being reserved for those cases where ultrasound findings are not in keeping with the clinical picture.

Although US has been successfully implemented into clinical fast-track settings in some centers, with robust validation and a reported high specificity and sensitivity, there are studies that are not supportive of its use and report low specificity and sensitivity. Bilyk and coworkers reported minimal value of incorporating US into GCA assessment,[6] in contrast to other authors such as Schmidt and Dasgupta. The need for an "expert," highly trained ultrasonographer, variation in technology, lack of standardized values, different ultrasound machines and ultrasound settings, and lack of a standardized procedure may be the explanation for such discrepancy. This highlights the need for robust certification and training specifically in temporal artery ultrasound in order for such an investigation to be reliably incorporated into ophthalmic services.

The OMERACT large-vessel vasculitis working group[10] has carried out a systematic literature review on ultrasound definitions of normal and abnormal temporal arteries and provides definitions of both normal appearances and key elementary lesions of vasculitis based on international expert consensus.

5. TAB versus vascular US

Vascular US has become the first choice in a number of centers, where the need for TAB has subsequently been reduced.[41] In cases where clinical suspicion is high but the ultrasound is nonconfirmatory, TAB is still indicated. A GCA probability score developed by Laskou and coworkers has outlined an algorithm that best utilizes US, TAB, and other imaging modalities in the context of individual clinical presentations.[26]

The key benefits of US over TAB relate to cost and time savings. The TABUL study identified cost-effectiveness of £485 in favor of US, indicating that providing a service that incorporates vascular US is likely to result in cost savings by reducing the number of TABs.[27] Time is saved as there is no diagnostic delay with the need to wait for a histological report and additional theater time is not required at short notice.

6. The role of GCA "fast-track" clinics in rheumatology

Inspired by other fields in medicine including stroke and cardiology, the introduction of GCA fast-track clinics (FTCs) into rheumatology has been shown in two separate studies to significantly reduce visual loss compared to the conventional approach.[15,36] The GCA FTC approach uses the immediate use of US on the temporal, axillary, and carotid arteries alongside a history, physical examination, and laboratory tests. Treatment is instated without delay where there is a high clinical suspicion and positive US findings. Where clinical suspicion and US findings are negative, the GCA diagnosis is aborted and other diagnoses are considered. In cases where clinical suspicion is high for GCA but US findings are negative, further investigation on TAB or other imaging modalities such as computerized tomography angiography and magnetic resonance angiography is required.

The role of US as a primary investigation in such clinics has been justified by the speed of availability, low invasiveness, and completeness of examination of multiple vessels where expertise in vascular US is a prerequisite.[13,32] Given that GCA is an emergency frequently presenting to ophthalmologists, incorporating the FTC approach may have a role in improving outcomes and improving the efficiency of diagnosis and management.

7. Incorporating vascular US into ophthalmology practice

TABs are generally added onto elective operating lists or performed outside of normal working hours, given the likely importance of timing and detection on pathological analysis. Ophthalmologists routinely perform B-scan ultrasound in the eye casualty or retinal clinics for assessment of retinal detachment, vitreous hemorrhage, or ocular tumors, among other diagnoses. Incorporating vascular US as a new diagnostic test into the ophthalmologists' skill set would complement anterior segment, A-scan, B-scan, and orbital US techniques. Adopting vascular US in an ophthalmic setting is highly anticipated to lead to improved patient assessment at the initial consultation and could reduce the diagnostic

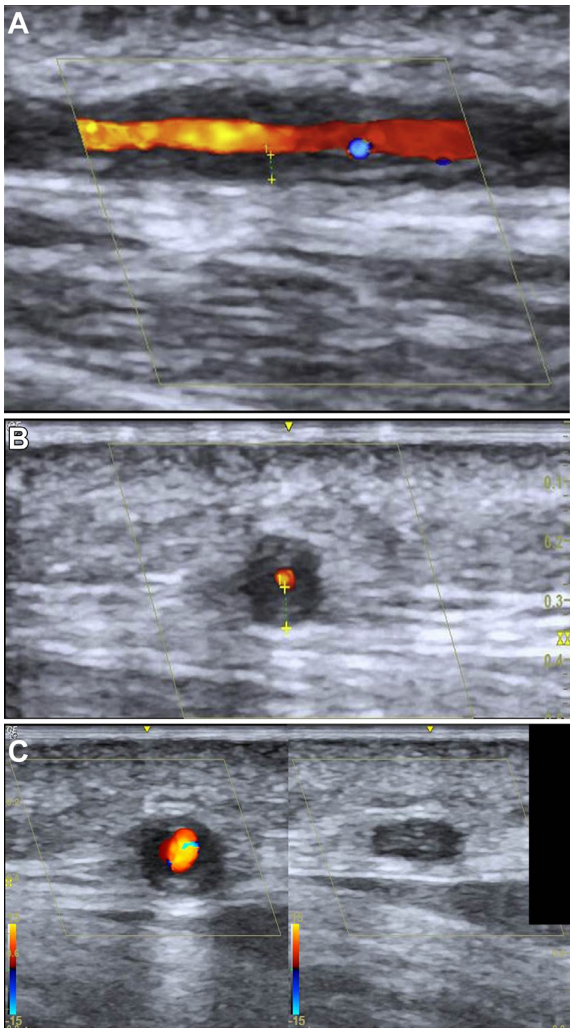

Fig. 1 – A: Longitudinal view of the frontal branch of temporal artery showing intima-media thickening as a dark hypoechoic area around the artery lumen measurement of intima-media thickness: 0.4 mm. B: Cross-sectional view of frontal branch of temporal artery showing a positive halo sign, intima media thickness: 0.7 mm. C: Demonstration of positive compression sign which shows persistence of hypoechoic halo (attached image).

uncertainty and ambiguity for patients referred with suspected GCA.

There is an argument for US for all patients referred to the ophthalmologist with suspected GCA.

1. The patient with "classic" GCA, raised inflammatory markers, jaw claudication, arteritic anterior ischemic optic neuropathy, and established visual loss. This patient is highly likely to have GCA, likely to have a positive TAB, and likely to be treated with high-dose oral steroids, tapering over several months. An ultrasound at presentation should confirm the diagnosis, avoiding the need for a TAB. A positive ultrasound is regarded as a confirmatory test and can justify the use of high-dose steroid, second-line immunosuppression, and tocilizumab therapy down the line if indicated.
2. The patient without established visual loss, but with suspicious symptoms, for example, amaurosis, raised inflammatory markers, headache, and jaw claudication. This patient is suspected to have GCA. An US carried out in the fast-track setting showing characteristic findings will support this diagnosis and justify high-dose steroid treatment.
3. The patient with ophthalmic symptoms who is assessed and felt to be at low risk for GCA, with low inflammatory markers, no headaches, or presence of other ophthalmic diagnosis. Such patients lead to significant dilemma for the ophthalmologist due to the possibility of GCA. Although perceived to be at "low risk," such patients may still be started on treatment dose steroid due to concerns about the risk of visual loss. An ultrasound scan at this point showing normal arteries would be reassuring and could avoid such patients being treated with high-dose systemic steroid unnecessarily.

In all cases, TAB may still be carried out if there is uncertainty, if the ultrasound is delayed, if the ultrasound does not show expected findings based on clinical scores, or if there is a strong clinical suspicion or contradictory findings. Such an approach requires further study in the eye clinic setting. Close collaboration with rheumatologists and established FTC providers as well as a robust training in vascular US would be required.

8. Conclusions

Suspected GCA remains a highly challenging diagnosis presenting to the ophthalmologist. Despite existing guidelines, patients are still at risk of visual loss given ambiguity in clinical presentation, difficulties in interpretation of blood results, and often delays in obtaining TAB. The role of ophthalmologist in delivering US in the workup of GCA should be investigated in the acute ophthalmic setting, given its proven effectiveness as a diagnostic test, safety profile, cost-effectiveness, and time savings. The FTC approach should be explored in ophthalmology with dedicated clinics incorporated into services to investigate GCA suspects. Ophthalmologists should be encouraged to gain certification in US, in the same way rheumatologists in the UK are doing, as they are first to review patients with suspected GCA and visual symptoms in the acute setting.

9. Methods of literature search

A search was performed using the search terms "giant cell arteritis" and "ultrasound" inputted into Embase and Embase Classic (1947 to January 2017) and Ovid Medline In-Process & Other Non-Indexed Citations (1946 to Present). Further relevant articles were handpicked and included if they alluded to the use of vascular ultrasound as a diagnostic adjunct for giant cell arteritis.

10. Disclosures

There are no disclosures to report.

Acknowledgments

The authors would like to thank Dr Chetan Mukhtyar, MBBS, MSc, MD, FRCP (Edin), a consultant rheumatologist in Norfolk and Norwich University Hospital, who kindly provided images of the halo sign as shown in Fig. 1.

REFERENCES

1. Arida A, Kyprianou M, Kanakis M, Sfikakis PP. The diagnostic value of ultrasonography-derived edema of the temporal artery wall in giant cell arteritis: a second meta-analysis. BMC Musculoskelet Disord. 2010;11:44
2. Aschwanden M, Daikeler T, Kesten F, et al. Temporal artery compression sign - a novel ultrasound finding for the diagnosis of giant cell arteritis. Ultrashall Med. 2013;34:47–50
3. Aschwanden M, Imfeld S, Staub D, et al. The ultrasound compression sign to diagnose temporal giant cell arteritis shows an excellent interobserver agreement. Clin Exp Rheumatol. 2015;33:S113–5
4. Ball EL, Walsh SR, Tang TY, et al. Role of ultrasonography in the diagnosis of temporal arteritis. Br J Surg. 2010;97:1765–71
5. Bhatti MT, Goldstein MH. Facial nerve injury following superficial temporal artery biopsy. Dermatol Surg. 2001;27:15–7
6. Bilyk JR, Murchison AP, Leiby BT, et al. The utility of color duplex ultrasonography in the diagnosis of giant cell arteritis: A prospective, Masked Study. (An American Ophthalmological Society Thesis). Trans Am Ophthalmol Soc. 2018;115:T9
7. Bley TA, Reinhard M, Hauenstein C, et al. Comparison of duplex sonography and high-resolution magnetic resonance imaging in the diagnosis of giant cell (temporal) arteritis. Arthritis Rheum. 2008;58:2574–8
8. Borg FA, Salter VL, Dasgupta B. Neuro-ophthalmic complications in giant cell arteritis. Curr Allergy Asthma Rep. 2008;8:323–30
9. Chambers W, Bernadino V. Specimens in Temporal Artery Biopsies. J Clin Neuro-ophthalmology. 1988;8:121–5
10. Chrysidis S, Duftner C, Dejaco C, et al. Definitions and reliability assessment of elementary ultrasound lesions in giant cell arteritis: a study from the OMERACT Large Vessel Vasculitis Ultrasound Working Group. RMD Open. 2018;4:e000598

11. Dasgupta B, Borg FA, Hassan N, et al. BSR and BHPR guidelines for the management of giant cell arteritis. Rheumatology (Oxford). 2010;49:1594–7
12. Davies C, Frost B, Eshan O, et al. Temporal artery biopsy…who needs one? Postgrad Med J. 2006;82:476–8
13. Dejaco C, Ramiro S, Duftner C, et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. Ann Rheum Dis. 2018;77:636–43
14. Diamantopoulos AP, Haugeberg G, Hetland H, et al. Diagnostic value of color Doppler ultrasonography of temporal arteries and large vessels in giant cell arteritis: a consecutive case series. Arthritis Care Res (Hoboken). 2014;66:113–9
15. Diamantopoulos AP, Haugeberg G, Lindland A, Myklebust G. The fast-track ultrasound clinic for early diagnosis of giant cell arteritis significantly reduces permanent visual impairment: towards a more effective strategy to improve clinical outcome in giant cell arteritis? Rheumatology (Oxford). 2016;55:66–70
16. Duftner C, Dejaco C, Sepriano A, et al. Imaging in diagnosis, outcome prediction and monitoring of large vessel vasculitis: a systematic literature review and meta-analysis informing the EULAR recommendations. RMD Open. 2018;4:e000612
17. Galloway GD, Klebe B, Riordan-Eva P. Surgical performance for specialties undertaking temportal artery biopsies: who should perform them? Br J Ophthalmol. 2002;86:250
18. Gonzalez-Gay MA, Martinez-Dubois C, Agudo M, et al. Giant cell arteritis: epidemiology, diagnosis, and management. Curr Rheumatol Rep. 2010;12:436–42
19. Haist SA. Stroke after temporal artery biopsy. Mayo Clin Proc. 1985;60:538
20. Hauenstein C, Reinhard M, Geiger J, et al. Effects of early corticosteroid treatment on magnetic resonance imaging and ultrasonography findings in giant cell arteritis. Rheumatology (Oxford). 2012;51:1999–2003
21. Hayreh SS, Podhajsky PA, Raman R, Zimmerman B. Giant cell arteritis: validity and reliability of various diagnostic criteria. Am J Ophthalmol. 1997;123:285–96
22. Hayreh SS, Podhajsky PA, Zimmerman B. Occult giant cell arteritis: ocular manifestations. Am J Ophthalmol. 1998;125:521–6
23. Hunder GG, Bloch DA, Michel BA, et al. The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. Arthritis Rheum. 1990;33:1122–8
24. Karahaliou M, Vaiopoulos G, Papaspyrou S, et al. Colour duplex sonography of temporal arteries before decision for biopsy: a prospective study in 55 patients with suspected giant cell arteritis. Arthritis Res Ther. 2006;8:R116
25. Karassa FB, Matsagas MI, Schmidt WA, Ioannidis JP. Meta-analysis: test performance of ultrasonography for giant-cell arteritis. Ann Intern Med. 2005;142:359–69
26. Laskou F, Coath F, Mackie SL, et al. A probability score to aid the diagnosis of suspected giant cell arteritis. Clin Exp Rheumatol. 2019;37:104–8
27. Luqmani R, Lee E, Singh S, et al. The role of ultrasound compared to biopsy of Temporal Arteries in the Diagnosis and Treatment of Giant Cell Arteritis (TABUL): a diagnostic accuracy and cost-effectiveness study. Health Technol Assess. 2016;20:1–238
28. Mahr A, Saba M, Kambouchner M, et al. Temporal artery biopsy for diagnosing giant cell arteritis: the longer, the better? Ann Rheum Dis. 2006;65:826–8
29. Meyers A, Said s. Temporal artery biopsy: concise guidelines for otolaryngologists. Laryngoscope. 2015;114:2056–9
30. Micieli JA, Micieli R, Margolin EA. A review of specialties performing temporal artery biopsies in Ontario: a retrospective cohort study. CMAJ Open. 2015;3:E281–5
31. De Miguel E, Roxo A, Castillo C, et al. The utility and sensitivity of colour Doppler ultrasound in monitoring changes in giant cell arteritis. Clin Exp Rheumatol. 2012;30:S34–8
32. Monti S, Floris A, Ponte C, et al. The use of ultrasound to assess giant cell arteritis: review of the current evidence and practical guide for the rheumatologist. Rheumatology (Oxford). 2018;57:227–35
33. Muratore F, Boiardi L, Restuccia G, et al. Comparison between colour duplex sonography findings and different histological patterns of temporal artery. Rheumatology (Oxford). 2013;52:2268–74
34. NICE: Giant Cell Arteritis. https://cks.nice.org.uk/giant-cell-arteritis - !diagnosissub. 2014. Accessed December 10, 2019.
35. Oh LJ, Wong E, Gill AJ, et al. Value of temporal artery biopsy length in diagnosing giant cell arteritis. ANZ J Surg. 2018;88:191–5
36. Patil P, Williams M, Maw WW, et al. Fast track pathway reduces sight loss in giant cell arteritis: results of a longitudinal observational cohort study. Clin Exp Rheumatol. 2015;33:S103–6
37. Petri H, Nevitt A, Sarsour K, et al. Incidence of giant cell arteritis and characteristics of patients: data-driven analysis of comorbidities. Arthritis Care Res (Hoboken). 2015;67:390–5
38. Poller DN, van Wyk Q, Jeffrey MJ. The importance of skip lesions in temporal arteritis. J Clin Pathol. 2000;53:137–9
39. Rahman W, Rahman FZ. Giant cell (temporal) arteritis: an overview and update. Surv Ophthalmol. 2005;50:415–28
40. Schäfer VS, Juche A, Ramiro S, et al. Ultrasound cut-off values for intima-media thickness of temporal, facial and axillary arteries in giant cell arteritis. Rheumatology (Oxford). 2017;56:1632
41. Schmidt WA. Ultrasound in the diagnosis and management of giant cell arteritis. Rheumatology (Oxford). 2018;57:ii22–31
42. Schmidt WA. Role of ultrasound in the understanding and management of vasculitis. Ther Adv Musculoskelet Dis. 2014;6:39–47
43. Schmidt WA, Kraft H, Volker L, et al. Colour doppler sonography to diagnose temporal arteritis. Lancet. 1995;345:866
44. Schmidt WA, Kraft HE, Vorpahl K, et al. Color duplex ultrasonography in the diagnosis of temporal arteritis. N Engl J Med. 1997;337:1336–42
45. Schmidt WA, Moll A, Seifert A, et al. Prognosis of large-vessel giant cell arteritis. Rheumatology (Oxford). 2008;47:1406–8
46. Schmidt WA, Seifert A, Gromnica-Ihle E, et al. Ultrasound of proximal upper extremity arteries to increase the diagnostic yield in large-vessel giant cell arteritis. Rheumatology (Oxford). 2008;47:96–101
47. Sharma NS, Ooi JL, McGarity BH, et al. The length of superficial temporal artery biopsies. ANZ J Surg. 2007;77:437–9
48. Soriano A, Muratore F, Pipitone N, et al. Visual loss and other cranial ischaemic complications in giant cell arteritis. Nat Rev Rheumatol. 2017;13:476–84

49. Stacy RC, Rizzo JF, Cestari DM. Subtleties in the histopathology of giant cell arteritis. Semin Ophthalmol. 2011;26:342–8
50. Watts RA, Robson J. Introduction, epidemiology and classification of vasculitis. Best Pract Res Clin Rheumatol. 2018;32:3–20
51. Yoon MK, Horton JC, McCulley TJ. Facial nerve injury: a complication of superficial temporal artery biopsy. Am J Ophthalmol. 2011;152:251–5.e1
52. Ypsilantis E, Courtney ED, Chopra N, et al. Importance of specimen length during temporal artery biopsy. Br J Surg. 2011;98:1556–60