Review

A Proposed Pathway For The Treatment of Giant Cell Arteritis: Experience From a District General Hospital in The United Kingdom

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Abstract

Introduction: Giant Cell arteritis can be difficult to diagnose clinically. In those cases, where there is no certainty, there is more reliance on a temporal artery biopsy and radiological imaging to confirm the diagnosis. The purpose of this article was to identify the standard of care in individuals with suspected Giant Cell Arteritis in a typical district general hospital and to offer a proposed pathway for treatment.

Methods: Darent Valley Hospital has been managing Giant Cell Arteritis for many years but there has always been a need for an outlined pathway to identify those at risk of cranial complications like visual loss to improve patient care. We evaluated the management of 70 individuals that had a temporal artery biopsy and followed their treatment journey. We extracted clinical specialist, emergency admission, operation theatre and histological data. We collected clinic follow up data over the following years to identify those that relapsed on treatment, stayed in remission or had complications. We propose a pathway to manage those individuals with Giant Cell arteritis in line with the new advances in treatment.

Results: Ten patients were identified that had a histologically positive biopsy. Reassuringly, most individuals with an obvious clinical diagnosis had high dose glucocorticoid treatment commenced before even being referred for a biopsy. Nine individuals had visual ischemia out of which five lost their vision.

Conclusion: The presentation of a pathway will help streamline best medical and surgical practice and ensure the availability of urgent specialist treatment and to identify those at risk of ischemic complications.

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Introduction

Presentation of Giant Cell Arteritis

Temporal Arteritis (TA) is a spectrum of signs and symptoms involving the neck and cranial arteries due to a chronic inflammatory disorder. This can cause headaches, tender scalp, jaw claudication and more importantly visual loss. A complication of Giant Cell Arteritis (GCA), it is a chronic granulomatous inflammation of medium to large sized arteries, which can involve the aorta, proximal upper limb, neck, and extra cranial arteries. Irreversible blindness can occur if this arteritis involves the branches of the ophthalmic artery. It is called Arteritic Anterior Ischemic Optic Neuropathy (AAION) if it involves the posterior ciliary branches and and/or the ophthalmic artery. It is important that the patient have high dose glucocorticoids commenced immediately to prevent the progression of visual loss. Some individuals are at risk of losing their vision because of delay in commencing glucocorticoids (1).

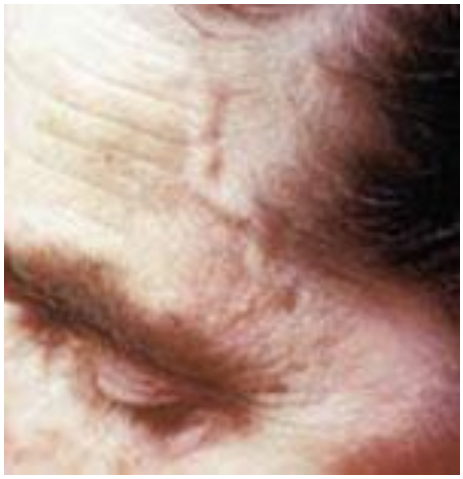

Figure 1. Clinical presentation of the patient with temporal arteritis (authors' photograph)

Clinical presentation

Classically the patient will present to the clinic or to an emergency unit with headache and a tender scalp on palpation and would be unable to comb his/her hair. Signs will be palpation of a prominent, thick and tender artery with or without a palpable pulse. Fundoscopy might reveal papilledema on ophthalmological review. The erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and platelet count rise as an acute phase response.

Constitutional symptoms

Arterial lesions may be widespread and causes nonspecific symptoms like fever, malaise and night sweats. The fever can reach 38˚C but fever of unknown origin is more common in GCA.

Other features like malaise and weight loss may lead to the suspicion of malignancy leading to further investigations to rule out sinister causes.

Myalgia and muscle stiffness

The proximal muscles involving the shoulder and pelvic girdle are involved but distal muscles can also be involved. Muscle stiffness occurs commonly in the morning and can be debilitating and difficult to treat. Muscles can be tender causing difficulty in examining the strength and tone. Disuse leads to contractures and atrophy of muscles. The duration of symptoms can vary from weeks to months.

Joint symptoms

Patients can develop tenderness over joints especially over shoulder and hip joints. Synovitis although uncommon, can occur in the knees, shoulders and wrists.

Vasculitis involving branches of the external carotid artery

Headache and scalp pain are 50-75 % of the presenting symptoms of GCA. The headache is characteristically extra-cranial, boring and dull in nature. The occipital or posterior auricular branches can be involved leading to varied symptoms like difficulty in combing hair, pain behind the ear and inability to sleep using a pillow.

Jaw pain and claudication has been shown to be a common symptom in GCA and can occur in almost 50% of patients (2). The involvement of lingual and maxillary arteries leads to pain in the buccinators, maxillary muscles and tongue on

chewing and talking. There have been reports of tongue gangrene although uncommon but a serious effect of ischaemia due to disease in the lingual artery. There have been cases of scalp necrosis secondary to GCA. This is caused by severe arteritis and occlusion of the branches of the superficial temporal artery (3).

Vasculitis involving branches of the ophthalmic artery

In patients with GCA, decreased vision secondary to arteritis is the most serious consequence. It appears that 40% of patients presenting with visual loss have headaches, constitutional symptoms and Polymyalgia Rheumatica (PMR). Partial visual field loss can progress to permanent blindness eventually. If unilateral visual loss is not treated, the second eye can be involved and can go blind in 1-2 weeks (4).

Involvement of the central retinal artery is about 10%. Retinal signs and symptoms like exudates, haemorrhage and vasculitis are seen. Amaurosis fugax occurs in 10% of patients with GCA. Eighty percent of patients with amaurosis develop blindness and hence treating the patients urgently is of fundamental importance. Branches of the ophthalmic artery also supply the muscles to the eye and can cause diplopia and ptosis (5).

Vasculitis of larger arteries

The symptoms may be due to the involvement of the aortic arch and descending aorta. The incidence varies from 9-18%. Thoracic aneurysms with the presence of giant cells in the arterial wall can occur after a decade of the successful treatment of GCA. It typically presents in a younger age group and mostly in women.

The majority of symptoms involve arm or lower limb claudication. Subclavian steal syndrome can occur due to narrowing of aortic arch roots. Aortic aneurysms and intestinal infarction can occur but renal vessel involvement is rare. GCA and Takayasu's disease have overlapping signs, radiological findings and symptoms (6).

Polymyalgia Rheumatica

PMR syndrome can occur alone or in conjunction with Giant Cell Arteritis. Forty percent of patients with GCA have PMR. Characteristically it starts with aching in the shoulder and hip girdles and morning stiffness. Muscle weakness and elevated muscle enzymes unrelated to PMR. The individual experiences intense fatigue and malaise. There is a raised Erythrocyte Sedimentation Rate (ESR) and C-reactive protein. It is a clinical diagnosis and is treated with low dose GC in contrast to GCA where high dose GC is given. PMR can present with distal synovitis that can mimic rheumatoid arthritis.

Patients with PMR should be warned to report new headaches or visual symptoms that could be the hallmarks of incipient GCA immediately (7).

Complications secondary to GCA

Cranial

1. There can be a long interval between the onset of symptoms and the occurrence of blindness. Temporal arteritis may not be apparent initially if the symptoms are subtle. Most commonly acute anterior ischemic optic neuropathy develops (8, 9, 10).

2. Vertigo, deafness and tinnitus.

3. The central or peripheral nervous system can be involved leading to strokes and transient ischemic attacks (9).

4. The extent of the involvement of the scalp vessels depriving one area of the scalp of an adequate blood supply can cause scalp necrosis. There have been studies describing scalp necrosis secondary to ischaemia. In some case reports there have been occasions where debridement and skin graft was required for the area of skin loss (3, 11).

Extracranial

1. Intermittent claudication and rest pain of upper and lower extremities due to

inflammation in more axial large vessels can lead to persistent symptoms despite GC treatment. This requires appropriate investigations like magnetic resonance imaging and colour Doppler imaging. If symptoms persist, Takayasu's aortitis needs to be ruled out as it can remain subclinical and quiescent despite being on GC therapy (12, 13).

2. Aortitis and aortic dissection needs to be high in the differentials if presenting with atypical symptoms, backache and renal failure due to dissection extending down to the renal vessels.

3. Cardiac murmurs like aortic regurgitation can lead to heart failure.

4. Individuals can present with constitutional and PMR like symptoms, fever of unknown origin and raised inflammatory markers with no obvious clinical evidence of any aortic branch involvement.

Incidence and epidemiology

Over a 50-year period in Olmsted County, Minnesota, there were 173 incident cases of GCA during the 50-year study. Of these, 79% were women. A cyclic pattern of annual incidence rates was apparent, with evidence of 6 peak periods the mean age at diagnosis was 74.8 years (14). There has been increasing interest in epidemiology of GCA where it was found to be more common in certain families particularly in the Scandinavian Countries (15).

Investigations and Diagnosis

Traditionally clinical suspicion from the usual unilateral throbbing headaches and a tender scalp lead to an ESR test and an immediate prescription of high dose oral steroids as soon as possible. Clinical suspicion is important with typical throbbing headaches, tenderness in the scalp and age over 50.

TAB (temporal artery biopsy) is still performed quite frequently for individuals with clinical findings of GCA. TAB has traditionally been the gold standard for a diagnosis (2, 16).

In 1990 The American College of Rheumatology after comparing 214 GCA individuals and 593 patients with other forms of vasculitis, identified criteria to diagnose GCA. For the traditional format classification, five criteria are:

1. age greater than or equal to 50 years at disease onset,

2. new headache localised to the temple,

3. temporal artery tenderness or decreased temporal artery pulse,

4. elevated erythrocyte sedimentation rate (Westergren) greater than or equal to 50 mm/hour,

5. Biopsy sample including an artery showing necrotizing arteritis (17).

Pathophysiology

It is known that the inflammatory cascade activates early in the pathological process of GCA. However, the initiating event (aetiology) remains uncertain. There are many suspected pathogens. Endothelial injury leads to the cell mediated immunity to be stimulated leading to the activation of the antigen presenting cells to the endothelium. This triggers vascular dendritic cells and monocytes to produce interleukin-6 (IL-6), IL-1 and pentraxin 3 (18). This leads to the stimulation of the liver to produce C- reactive protein (CRP). Constitutional symptoms as if fever and myalgia develop that are very responsive to glucocorticoid therapy, which effectively inhibits production of cells stimulated by Th17, which produces IL-6.

The arterial wall is infiltrated by Th1 and Th17 type 4p lymphocytes. Th1 lymphocytes produce interferon-g (IFN-g) and which result in formation of multinucleated giant cells from interaction with macrophages. Glucocorticoids have minimal effect on these cells showing why visual loss persists despite high dose applied (19). GC therapy can suppress mechanisms affected by the IL-6 like Th17 activity. The increasing number of circulating immune cells and the inability of dendritic cells to block access to the arterial wall via the PD-1 immune checkpoint suppress the natural defences. It is

known that the NOTCH 1 receptor on T cells and NOTCH-jagged 1 Ligand receptor on the vasa-vasorum in the endothelium allow permeability of T cells into the vessel wall (20).

Platelet derived growth factor (PDGF) is an important cytokine activating concentric intimal hyperplasia. PDGF comes from macrophages and giant cells differentiating it from other vasculopathies. The media of the vessel wall is the main site of injury. The medial macrophages secrete tissue destroying enzymes and cytokines like PDGF and vascular endothelial growth factor (VGEF) that also initiate repair. This results in a hyperplastic intima leading to occlusion of the vessel lumen. The intima and media is the centre of the pathological process. Cell adhesion molecules and endothelial cells play a pivotal role in the repair process and neovascularisation. Cell adhesion molecules might regulate how leukocytes and endothelial cells interact differently in different temporal arteries (21). Activated white cells and platelets cause vessel inflammation and vascular thrombo-embolic events, an important finding in diagnosing GCA.

The inflammatory changes are quite similar to polymyalgia rheumatica. However, PMR is more of a systemic disease. The symptoms are more constitutional like fever malaise and weight loss. More specifically, there is more proximal muscle pain and joint pain in the shoulder, neck and pelvis. There is considerable chance (50%) in patients of TA to have PMR.

Temporal Artery Biopsy Procedure

The individual is consented for the biopsy and then brought in to the operating theatre. Ideally, Duplex ultrasound helps in identifying the temporal artery. We infiltrate local anaesthetic under the skin. A sterile field is created using drapes. A transverse or longitudinal incision is made on the skin just over the artery. Both ends of the artery are ligated with absorbable or non-absorbable suture and a generous length is isolated. The artery is divided between the two ligatures. The skin is apposed after haemostasis with interrupted non-absorbable or continuous absorbable suture. A sterile dressing is applied to the wound. Non-absorbable sutures on the face or temple are removed in 5 days in the community.

There has been a suggestion that the intra-operative assessment can identify thickness, tortuosity, colour/pallor of the arterial wall, blood flow, and the lumen size. This gives enough evidence to confirm the macroscopic presence of TA and appropriate treatment can be commenced immediately. However, it depends on the experience of the surgeon. This was studied in 111 cases where the intra-operative findings were compared with the histological findings and showed a 100% negative predictive value for biopsy negative specimens (22).

Complications secondary to temporal artery biopsy are not common. There have been reports of skin necrosis after temporal artery biopsy due possibly to arteritis changes in smaller collateral arteries. Facial nerve injury can occur due to inadvertently not picking a safe zone and injuring the main branches of the facial nerve. Clinically this leads to weakness of muscles of facial expression and frontalis muscle weakness. Four cases of facial nerve injury were identified in one study. This can result in a permanent eyebrow droop on one side. It has been advocated that biopsy be orientated at the more parietal than frontal region to avoid injury to the frontal branch of the facial nerve (23, 24, 25).

Histological assessment of the specimen

The specimen is sent to the laboratory in a sterile pot with formalin. The dimensions of the specimen are measured especially the length. The specimen is bisected or trisected (3 mm each length) and then 'embedded'. The specimen is dehydrated, cleared, and infiltrated with the embedding material. They are ready for external embedding. The tissue sample is placed into moulds along with liquid embedding material (such as agar, gelatine, or wax) which is then hardened. Longer specimens need to have more sections taken. Three levels each from the individual trisected specimen are examined after staining with Haematoxylin and Eosin.

Haematoxylin stains the nuclei blue and Eosin stains the cytoplasm, red blood cells and collagen fibres. The remaining part of specimen is stained with Elastic Van Giessen (EVG) staining. This stain is useful in demonstrating atrophy of elastic tissue. Specific immuno-histochemical stains are carried out in some institutes but the typical findings of giant cells and inflammatory cells (as below) help in earlier diagnosis (26).

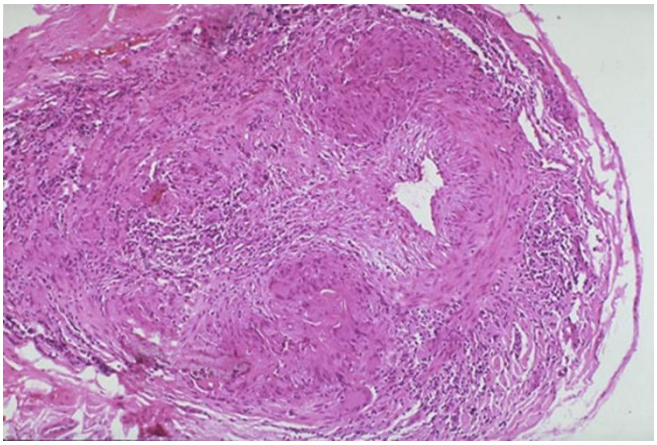

Figure 2. Focal granulomatous inflammation and sometimes giant cells are visible. Courtesy library.med.utah.edu

Patients and Methods

Study Design

This is a retrospective case series study of individuals that underwent temporal artery biopsy in a district general hospital Darent Valley Hospital in Kent. There is great interest in the sequence of events that eventually lead to a TAB. Here are reviewed the events and outcomes of individuals that had a temporal artery biopsy. To achieve an adequate number of cases, the audit covered a number of years from 2009 to the current year.

Case Retrieval

All data of individuals undergoing a temporal artery biopsy were retrieved from our theatre link of operation records on our intranet called 'Theatreman'. Case notes identified by first identifying specific codes for 'temporal artery biopsy' from the Information Technology department and then were compared with operating theatre data and histological data. The case-notes were electronic through our Electronic Health Records (EHR).

Biopsy results were extracted from the Darent Valley Hospital online Histopathology system. Seventy-six patients had a temporal artery biopsy from 2009 to 2018. All biopsies carried out were direct referrals form the emergency department and clinics. We documented all correspondence from the general practitioner and specialists. Each individual was evaluated using the American College of Rheumatology (ACR) criteria. The American College of Rheumatology criteria were used to diagnose GCA. Scoring criteria included age, headache, scalp tenderness, ESR and TAB results. The biopsy confirmed the diagnosis despite many individuals scoring three or four based on clinical suspicion and ESR. The biopsy criteria were the presence of inflammation and microscopic presence of chronic inflammatory cells in the muscle. There also is disruption of the internal elastic lamina with or without the presence of giant cells (27, 28).

The history of glucocorticoids administration was assessed throughout the period of the individual's illness. Operation notes identified the date of the procedure and grade of surgeon. The time elapsed from surgical referral to biopsy were recorded in days. This data was then transferred on to an excel sheet held on a computer.

Data Collection

A standard audit questionnaire helped in retrieving data. A single surgeon collected all the data from the case notes and later transferred all the data on to a Microsoft excel spreadsheet. The basic epidemiological data collected was age at biopsy, gender and mode of referral.

Presenting symptoms were unilateral or bilateral headache, visual symptoms and jaw claudication. Signs recorded were ESR, ophthalmologic examination signs and scalp tenderness. Positive findings on scalp examination were tenderness by palpating the

artery, thickening and pulsation/no pulsation. We observed the duration in days from the surgical referral to biopsy and the date of commencement of corticosteroids. We recorded age above 50 years and ESR above 50 mm/sec as positive criteria according to the ACR. The histology results documented were for all TABs whether positive or negative and the specimen length of the temporal artery. The grade of the operating surgeon was either a surgical consultant or registrar. We gave particular attention to the visual signs /symptoms like amaurosis fugax or blindness, the findings of fundoscopy and the ophthalmologist opinion.

We documented the start date of steroid therapy and previous administration of steroids. The change in dose of steroids was not possible to evaluate throughout the patient's history.

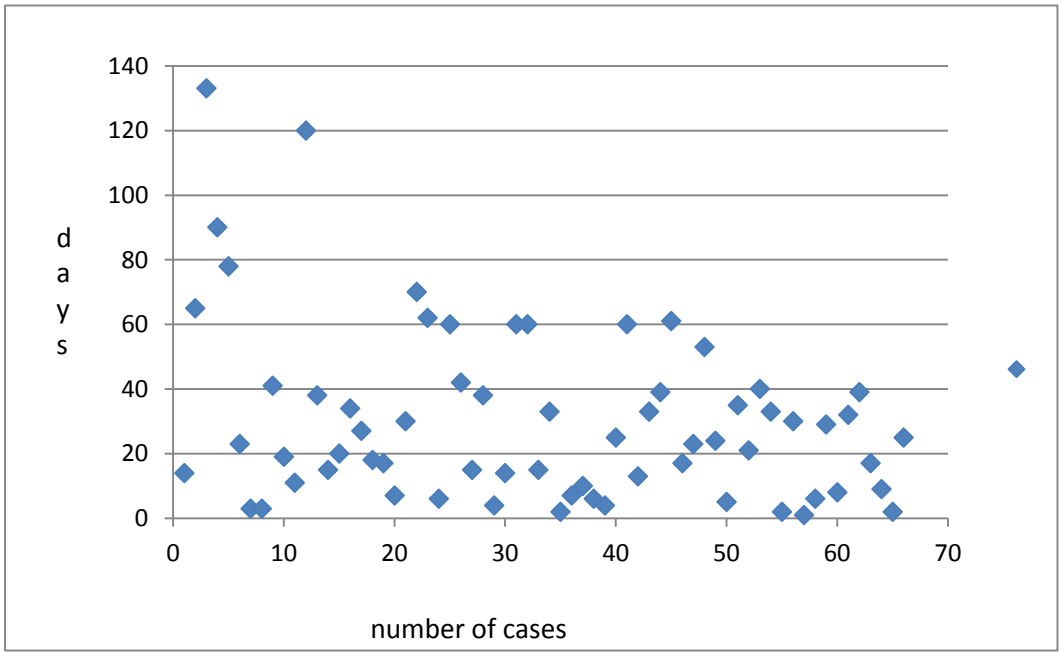

Figure 3. Length of delay from diagnosis to biopsy date

Results

There were 76 individuals in the series. Only 10 temporal artery biopsy results were positive on histology for temporal arteritis. Six patient's notes were not retrievable. The presenting signs and symptoms were as per Table 1.

Table 1. The presenting signs and symptoms of the patients with temporal arteritis

Age > 50 years	*64/70*
ESR > 50mm	*19/70*
Temporal tenderness	*49/70*
Temporal headaches	*58/70*
Jaw claudication	*12*
ACR scores	
ACR score 1	*6*
ACR score 2	*16*
ACR score 3	*32*
ACR score 4	*11*
ACR score 5	*2*
Time till surgery	
1 week	*17*
2 weeks	*8*
>2 weeks	*55*
Biopsy length	
1 cm or above	*30*
<1cm	*36*
No artery/inadequate sample	*4*
Biopsy findings	
Positive biopsy	*10*
Negative biopsy	*60 (6 inadequate specimens, vein, too small)*

Description of patients

The mean age was 67.9. The youngest age to have a TAB was only 38 and oldest was 87 years old. There were 48 women out of 70 cases (68% of the total).

The mean Erythrocyte Sedimentation Rate (ESR) calculated was 34.9 from 66 documented individuals that had an ESR done. The minimum ESR documented was zero and maximum was 110. There were four patients with no record of an ESR.

Headaches were the most common symptoms as observed in our study. The pain is typically sudden and localised to one side of the scalp. However, it can occur in the parietal, occipital and frontal regions as well. The headache is new and different from any other type of headaches. Twelve patients never had headaches out of the 70 but still had a biopsy done. Nine individuals with headaches had bilateral involvement.

Forty-nine of the 70 individuals had a tender scalp on examination as an emergency or in clinic review. Some cases had documentation of thickness or non-pulsatile artery.

Nine individuals had pain in the muscles of mastication while eating and chewing characteristic of jaw claudication.

The visual findings were amaurosis fugax, complete or partial visual loss or diplopia. Five patients had complete visual loss. We recorded

visual acuity testing and finding characteristic signs of Acute Anterior Ischemic Occlusive Optic Neuritis (AAION). Four other patients had visual impairment with characteristic findings of AAION but managed to receive GC therapy urgently to avoid loss of vision. Six individuals had vague symptoms like blurring of vision and diplopia. It is important to note that two individuals that had characteristic AAION did not have histologically positive biopsies.

Discussion

The management of GCA begins with the clinical diagnosis. A biopsy is occasionally required when there is no clear clinical diagnosis based on the ACR criteria. The treatment revolves around the immediate treatment, prolonging remission and the prevention of relapse. The aim of immediate treatment is to control the immediate systemic inflammatory response and to avoid complications like acute visual loss. There have been extensive studies on the optimal treatment modalities for the last 20 years. Glucocorticoid treatment remains the mainstay acute treatment for GCA despite the risk of adverse events.

The immediate side effects of steroids include glucocorticoid effects such as hyperglycaemia especially in patients with diabetes mellitus and mineralocorticoid effects such as fluid retention. Other side effects include mania, psychosis and depression, osteoporosis, Cushing's disease, obesity, new onset diabetes mellitus, peptic ulcers and depression on reduction or cessation of steroids. Less common effects are hepatic steatosis, avascular necrosis and weight gain. Prolonged administration of prednisolone may lead to adrenal suppression. Eventually, this may cause the body to temporarily lose the ability to manufacture natural corticosteroids especially cortisol, which results in dependence on prednisone. Prednisone is tapered if taken for more than seven days.

Individuals with PMR are commonly on low dose prednisolone for chronic systemic symptoms. Clinicians should be aware of the likelihood of needing higher doses of steroids to combat the effects of GCA. Meticulous evaluation based on the clinical signs and symptoms is compulsory to avoid injudicious use of high dose steroids in high-risk individuals.

Even in this era of evolving clinical practice where more and more individuals are performing duplex ultrasonography to confirm or rule out a clinical diagnosis of TA, a biopsy still carries importance. In our trust there is growing enthusiasm in performing DUL in clinic on individuals with a suspicion of GCA (29).

Previous studies have showed that between a quarter and one third of all patients having TAB yield a positive temporal artery biopsy. In our case series, the results showed that 12% of biopsy specimens came back positive (30). Of these positive biopsies, eight cases out of 10 were an ACR score of three and above and probably did not need a biopsy. If we look at the clinical criteria, most patients had an ACR score of 3-4 fulfilling the diagnosis of temporal arteritis on the first clinical encounter and at the most could have benefitted with DUL without the need for a biopsy. We can safely treat patients based on clinical presentation and laboratory ESR findings. This will avoid unnecessary use of steroids on individuals with low clinical suspicion of GCA.

We know that a biopsy will have a higher chance of being positive in the first two weeks than later. Twenty-five biopsies were performed within 2 weeks in our series. Narvaez et al in his study evaluated the effects of duration of steroid treatment on biopsy results. The highest positive results were achieved (78%) in the individuals that had a biopsy within 2 weeks of commencing steroids. It obviously suggests that there is a lesser chance of getting a positive biopsy result in patients having a biopsy after 4 weeks of steroid therapy (31).

There is considerable debate on the length of specimen needed to confirm GCA. GCA is a chronic granulomatous inflammation with skip lesions interspersed with normal artery sections. There was a general statement in all biopsy negative results: 'as GCA is a patchy disease, we

cannot exclude arteritis due to the existence of skip lesions in GCA.' Skip lesions were seen in 8.5% of specimens with active vasculitis in a previous study (32). The biopsy specimen is divided into 3-4 segments and each visualised under the microscope individually. Various studies have shown that the median specimen lengths for positive biopsies were ranging between 5mm and 12 mm but the established benchmark has been 1 cm and above (33). In another study a length of 20 mm or longer had a 2.8 times more likelihood of having GCA compared to those less than 20 mm in length (34). In our series, 30 specimens were at least 1cm long prior to fixation. Forty specimens were shorter than 1cm or were not adequate samples.

There is a degree of contraction of the biopsy specimen before fixation with formalin. It can extend to 12% of contraction for GCA positive specimens and 22% for GCA negative specimens. The length of the specimen is calculated by measuring the in-vivo with the ex-vivo size before fixing. If this is true then a specimen of 10mm would contract by more than 2mm if negative for GCA (35).

Complicated cranial GCA carries a high risk of visual loss and cerebrovascular accidents. The provision for ophthalmological review and imaging of the head needs to be readily available. In evolving visual changes, the recommendation is to administer intravenous GC for the first 2-3 days in hospital and then change to oral treatment to prevent the catastrophe of visual loss (26, 36).

High dose GC treatment must continue until the individual's inflammatory phase is well controlled. Tapering regimes of GC therapy are proposed in the British, European and French consensus guidelines (26, 37, 38).

Numerous studies on various biological and non-biological agents show prolonged remission and reduction of recurrent relapses. Methotrexate has been shown to reduce the dose of GC required in patients with recurrent disease and in those which cannot take high dose GCs (7, 39). Recently Tocilizumab has been recommended in relapsing GCA in the British National Institute of Clinical Excellence guidelines (40).

Table 2. Proposed pathway for the management of Temporal Arteritis (Cont)

Diagnosis:

Clinical

- Age >50
- Abrupt onset headache (usually unilateral in the temporal area)
- Scalp pain or difficulty in combing hair
- Visual symptoms (blurring loss/diplopia)
- Jaw/tongue claudication
- Systemic symptoms of fever, weight loss, loss of
- appetite, depression and tiredness
- Symptoms of polymyalgia rheumatica
- Limb claudication

Poor Prognostic Symptoms:

- Features predictive of ischaemic neuro-ophthalmic complications
- Jaw claudication
- Visual symptoms (amaurosis fugax, and diplopia).

Examination:

- Abnormal superficial temporal artery: may be tender, thickened with reduced/absent pulsation
- Scalp tenderness
- Transient or permanent visual loss (partial or complete) in 20% patients
- Visual field defect

- Relative afferent papillary defect on swinging flashlight test
  - Anterior ischaemic optic neuritis (Pale, swollen optic disc with haemorrhages)
- Central retinal artery occlusion
  - Upper cranial nerve palsies.
  - Features of large vessel GCA: Asymmetry of pulses and blood pressure and bruits (usually of the upper limb)

Duplex Ultrasound(DUL)

- clinic review with characteristic 'halo' sign

Laboratory Investigations:

- Markers of a raised inflammatory response
- ESR and CRP, anaemia, thrombocytosis, raised alkaline phosphatase, raised α1 and α2 globulins.
- However, Temporal arteritis can occur in the face of normal inflammatory markers, if the clinical picture is typical

TAB

- confirmation of clinical diagnosis

MRI/FDG PET/CT

- suspected proximal disease

Differential Diagnosis:

- Herpes zoster, migraine, cluster headache, acute angle glaucoma, TMJ pain, cervical spondylosis, malignancy

Management of GCA:

- Acute

Complicated GCA (cranial symptoms and signs)

- Visual ischemia

Hospital admission with Intravenous high dose GC 3 days

High dose oral GC

- Visual loss

Oral 60 mg prednisolone to protect contralateral eye

- Uncomplicated GCA

Prednisolone 60mg

Tapering dose of GC

Low dose GC +/- Methotrexate/tocilizumab for recurrent relapse or GC tapering

Steroid Withdrawal:

- Consider steroid reduction only in the absence of clinical symptoms, signs and lab abnormalities suggestive of active disease.
- This should be balanced against the need to use the lowest effective dose, patient wishes and steroid side effects.
- Suggested tapering regimen:

40-60mgs prednisolone continued until symptoms and laboratory abnormalities resolve (at least 3 to 4 weeks)

Then dose reduction by 10mg every 2 weeks to 20mg,

Then by 2.5mg every 2-4 weeks to 10 mg,

Then by 1mg every 1-2 months provided there is no relapse.

Table 3. Proposed pathway for the management of Temporal Arteritis (Cont)

After Care:

- Rheumatology specialist review
- Screening for cardio-vascular disease, hypertension and hyperlipidaemia
- Bone protection and proton pump inhibition if indicated.
- Systemic symptoms, limb claudication or persistently high-inflammatory markers despite adequate glucocorticosteroid therapy. →PET and MRI
- TA Patients screening for abdominal aortic aneurysms (repeat every 2 years whenever indicated).

Monitoring of Therapy:

- Clinical assessment + inflammatory markers
  (Evidence of relapse, disease-related complications and glucocorticosteroid-related complications)
- Jaw and tongue claudication.
- Visual symptoms.
- Vascular claudication of limbs, bruits and asymmetrical pulses.
- Polymyalgia symptoms.
- Osteoporotic risk factors and fractures.
- Perform the following investigations:
  At each visit: full blood count, ESR/CRP, urea and electrolytes, glucose.
  Every 2 years: chest radiograph to monitor for aortic aneurysm (echocardiography, PET and MRI may also be appropriate).
  Bone mineral density may be required.

Management of Relapse:

- Return of symptoms of GCA, ischaemic complications, unexplained fever or polymyalgia symptoms.
- Return of headache → higher dose of glucocorticosteroids.
- Jaw claudication requires 60 mg prednisolone.
- Eye symptoms need the use of either 60 mg prednisolone or IV methylprednisolone.
- Assessment of large vessel involvement.

For recurrent relapse:

- Early introduction of methortrexate or alternative immunosuppressant
- In recurrent relapse or failure to wean glucocorticosteroid dose. These immunosuppressive agents should be started at the third relapse.
- Tocilizumab has been approved for Temporal Arteritis

Ophthalmological considerations

- Aspirin, Ophthalmology review for ischemic symptoms/signs
- Bone protection / PPI → Omeprazole, Alendronic Acid,
- Calcium and vitamin D

Conclusion

Temporal artery biopsy is useful for the diagnosis of cranial GCA. The various imaging modalities especially duplex ultrasonography are an important adjunct to the clinical diagnosis. The treatment should not be delayed if there is good clinical suspicion or with risk of visual loss.

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Competing interests. None to declare

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