Giant cell arteritis: a not-so-straightforward diagnosis in routine practice

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Abstract

We discuss the case of a 70-year-old female who presented acutely with temporal headache and vision disturbance. She was commenced on high dose glucocorticosteroids and a subsequent temporal artery biopsy revealed granulomatous inflammation affecting all layers of the temporal artery, confirming the suspected diagnosis of giant cell arteritis (GCA). At present, there are four validated histological patterns for the diagnosis of GCA. Nonetheless, the diagnosis of GCA remains challenging in subtle cases which do not show the "classic" histological features. There is currently a lack of agreement among experienced pathologists regarding the diagnostic features and classification of inflammation observed in TAB sections in the diagnosis of GCA. Recent research has attempted to standardize the minimum reporting criteria for the diagnosis of GCA however international controversy remains, justifying further work in this field.

Keywords Consensus; giant cell arteritis; temporal artery biopsy

Case report

A 70-year-old female presented to the emergency department with a 10-hour history of acute-onset left sided temporal headache and unilateral visual disturbance. She had a known history of ischaemic heart disease only. Clinical examination revealed extreme tenderness to palpation along the left temporal aspect of the forehead and investigations showed show mildly raised C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). A diagnosis of suspected giant cell arteritis (GCA) was made and the patient was commenced on immediate high dose glucocorticoid therapy. An elective temporal artery biopsy (TAB) was performed one week later. The biopsy was reported as showing granulomatous inflammation affecting all layers of the temporal artery, confirming the diagnosis of GCA.

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Discussion

GCA is a serious form of vasculitis typically affecting the temporal arteries, hence the alternative name of "temporal arteritis". Untreated, it can lead to serious ischaemic complications, most notably irreversible blindness.[1] It typically affects older individuals who classically present with headache, jaw claudication, temporal artery tenderness or fever.[2] A definitive diagnosis of GCA on clinical grounds can be challenging however, due to the often non-specific and varied clinical presentation hence the temporal artery biopsy (TAB) remains the gold standard test for the diagnosis of GCA.[1]

Recent research has shown that there is disconcordance between histopathologists in the assessment and reporting of TABs for the diagnosis of GCA.[3] Some of the reasons for this include, but not limited to: (1) variation in the interpretation of certain microscopic features, (2) variability in inflammation within consecutive sections of the same artery and the uneven density of inflammatory cells within the vessel wall and (3) a current lack of standardized reporting criteria.[3] The implications of this uncertainty are potential misdiagnosis of GCA causing unnecessary exposure to glucocorticosteroids and their side effects, denied access to biologics therapy for those that are eligible, and a delay in alternative diagnosis.

In an attempt to standardize reporting of TABs for the diagnosis GCA, Hernandez-Rodriguez et al. have described a validated classification system that categorises GCA based on its histological pattern.[4] The four patterns described are determined by the location of inflammatory cells within the temporal artery wall and are: (1) panarteritic pattern – inflammatory cells seen in all layers, (2) concentric bilayer pattern – inflammatory cells present in the adventitia and tunica intima only, (3) adventitial pattern – inflammatory cells within the adventitia only and (4) adventitial invasive pattern – inflammatory cells predominantly in the adventitia with focal infiltration into the tunica media.[4] Figure 1 illustrates an example of histology from a "normal" TAB; Figures 2–5 demonstrate the four patterns of inflammation which together comprize the proposed "dynamic model" of inflammation whereby inflammatory cells reach the vessel via the adventitial layer and invade in an "outside-in" manner

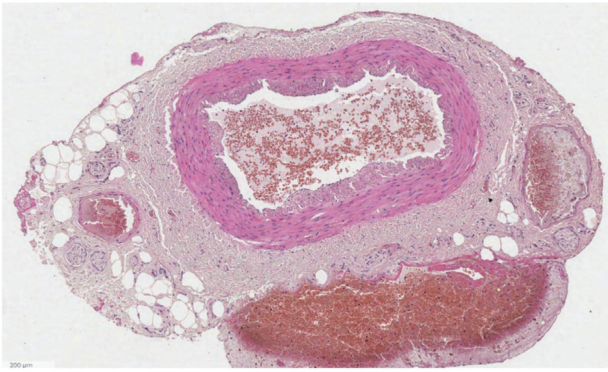

Figure 1 Normal temporal artery biopsy comprising three distinct layers: tunica intima, tunica media and adventitia. The internal elastic lamina (wavy line) distinguishes the boundary between the tunica intima and media. The blood vessels within the adventitia are also known as the vasa vasorum.

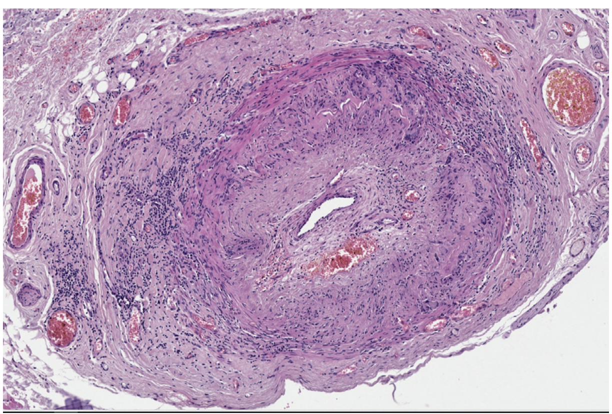

Figure 2 Panarteritic pattern GCA. This is considered when the inflammatory cells are seen distributed in all layers of the arterial wall.

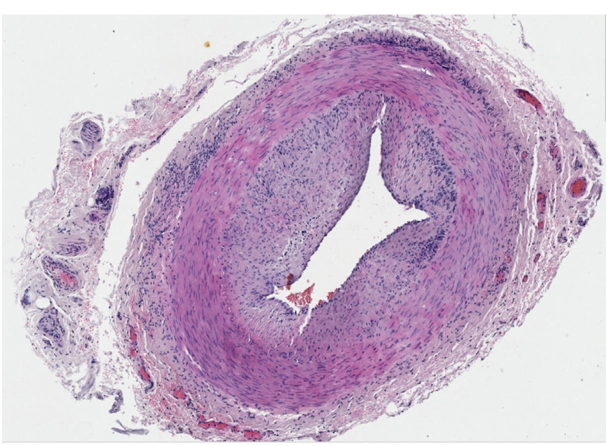

Figure 3 Concentric bilayer pattern GCA. Inflammatory cells are present in the adventitia and the tunica intima only, sparing the tunica media.

through the vessel wall. Despite this system, the spectrum of changes within a TAB can be great and there can be significant variability in consecutive sections, with skip lesions (areas of uninvolved artery) frequently present.

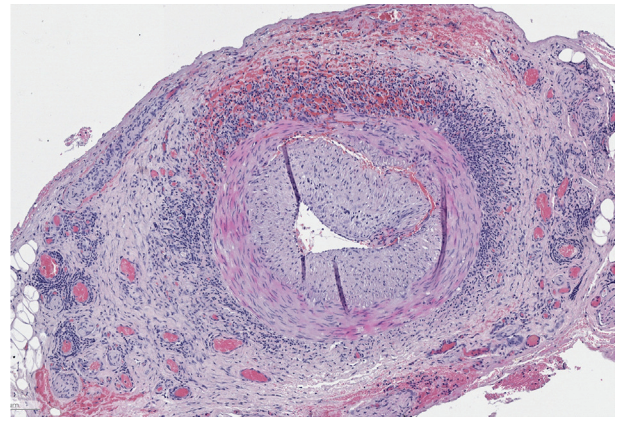

Figure 4 Adventitial invasive pattern GCA. Inflammatory cells are present predominantly in the adventitia with focal extension into the tunica media.

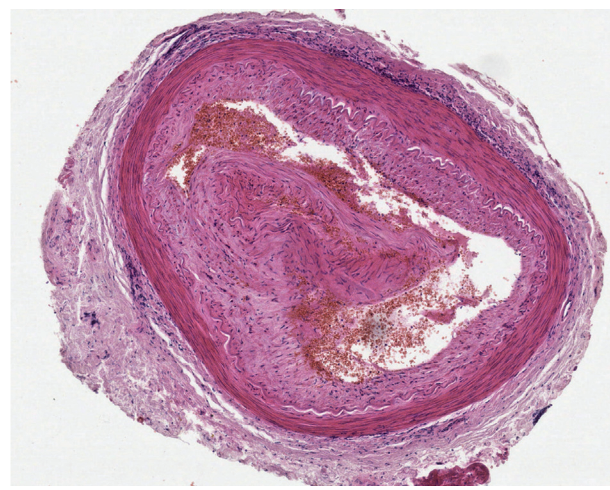

Figure 5 Adventitial pattern GCA. Inflammatory cells are present in the adventitia only.

Researchers, both local and international, have tried to address the issue of lack of standardized reporting criteria for the diagnosis of GCA. Our research group, Atlas of Histopathology Education for Advancing Diagnostics in GCA (AHEADgca), undertook a modified Delphi study with a group of geographically dispersed expert pathologists within the UK.[5] Through this work, we highlighted key areas of consensus which could form part of a standardized minimum reporting dataset, as well as drawing attention to where evidence is limited and/or lacking and requires further study. The core microscopic features which the participants felt would be useful to capture in a standardized reporting proforma are summarized in Table 1. Whilst this list is not exhaustive, it offers a systematic approach to capturing the varied histological manifestations of GCA during its evolution and ensures consistent reporting practices.

Similarily, Nair et al. have undertaken consensus work in this area within North America and Europe and they propose guidelines for the "processing, interpretation and reporting of TAB specimens" with reference to the existing literature.[6] Comparison of these studies highlights the diversity of opinion in this field but both groups advocate for standardization of

The proposed core microscopic features of a reporting template for the reporting of TABs in the diagnosis of GCA

Core microscopic items	Features
Inflammation	Types of cells present and the pattern of inflammation
Tunica media assessment	Intact or evidence of destruction
Tunica intima assessment	Any evidence of hyperplasia, fibrosis, oedema and/or occlusion (if yes, then grade of occlusion)
Other (non-core items)	Evidence of neoangiogenesis Isolated lymphocytic infiltration around vasa vasorum or distant blood vessels

Table 1

terminology, especially around use of terms such as "healed arteritis" and "treated arteritis" which lack a clear definition and hence can be misinterpreted.

Conclusion

GCA is a serious form of vasculitis which can cause irreversible complications if left untreated. At present, there is a lack of standardized reporting criteria and unresolved controversies amongst researchers internationally. Whilst some progress has been made, this remains an area of unmet need and clearer guidelines are required to ensure consensus when reporting of TABs for the diagnosis of GCA. ◆

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Practice points

- GCA is a serious form of vasculitis typically affecting the temporal arteries in older individuals. If not treated promptly, it can lead to serious irreversible ischaemic complications
- Four validated histological patterns of GCA have been described; panarteritic pattern, concentric pattern, adventitial pattern and adventitial invasive pattern
- If in doubt, additional levels on H&E sections can be useful in aiding the diagnosis of GCA
- There are ongoing controversies amongst researchers internationally and further studies are required to reach consensus

Self-assessment multiple-choice questions

1. What is the most common complication of untreated GCA?

a. Death
b. Hypertension
c. Cardiac arrythmias
d. Irreversible blindness
e. Subdural haemorrhage

Answer: d

2. Which layer of the temporal artery contains the vasa vasorum?

a. Tunica intima
b. Adventitia
c. Tunica media
d. Endothelium
e. Internal elastic lamina

Answer: b

3. Which of these are not one of the categories of giant cell arteritis as described by Hernandez et al.?

a. Granulomatous
b. Panarteritic
c. Adventitial
d. Concentric
e. Adventitial invasive

Answer: a