

Role of temporal artery resection in Horton's arteritis (Review)

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Abstract. Horton's arteritis is found in the literature under various names, such as temporal arteritis, Horton's disease senile arteritis, granulomatous arteritis or giant cell arteritis (GCA). The pathogenic mechanism is the result of an inflammatory cascade triggered by a still unknown factor that causes dendritic cells in vessels to recruit T cells and macrophages, which form granulomatous infiltrates. The clinical picture consists of a daily headache with temporal localization, with moderate to severe intensity, unilateral or bilateral, with a history of months, years. Other changes may include pain in the cheek or tongue during chewing (claudication), weight loss, generalized fatigue, low-grade fever, and frequent pain in the limbs, in the context of coexisting rheumatic polymyalgia. Visual symptoms represent a special category, involving blurred vision, scotomas, and even sudden blindness. Histopathological examination of the temporal artery biopsy reveals focal thickening of the intima, with interruption of the lamina propria, with transmural inflammatory infiltrates, sometimes with multinucleated giant cells. In this article, we aim to review the role of temporal artery resection in the diagnosis of Horton's arteritis, but we also discuss the hypothesis of a potential therapeutic benefit of this procedure. However, there are also clinical situations in which there has been a considerable improvement in clinical symptoms and especially in vision deficit, with the improvement of the visual field after surgery performed for biopsy. It is difficult to estimate the influence of temporal artery resection alone, given that most

patients also have concomitant cortisone treatment. However, in some cases, the rapid improvement of symptoms immediately after surgery, with the improvement of visual acuity and visual field, along with the disappearance of the headaches, can create the premises for future studies on a therapeutic contribution of temporal artery resection in GCA.

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1. Introduction

Horton's arteritis is found in the literature under various names, such as temporal arteritis, Horton's disease senile arteritis, granulomatous arteritis or giant cell arteritis (GCA). The term GCA refers to the type of inflammatory cells present in the wall of the affected vessel, and the term of 'temporal arteritis' refers to the frequent involvement of the temporal artery. GCA is a vasculitis that affects large vessels. Vasculitis is defined by the inflammation of the vascular wall (arteries, veins, and capillaries) with consecutive vascular thrombosis, causing ischemia and necrosis in the related tissue territories. The cause is unknown, with changes in the immune response, such as autoimmunity, trigger infections, and genetic susceptibility. Smoking is a negative prognostic factor. The classification of vasculitis is made according to several criteria with clinical implications: The type of vessel affected, etiology, and location. Takayasu arteritis, Horton temporal arteritis, rheumatic polymyalgia are described as large vessel vasculitis. Horton's arteritis is often associated with rheumatic polymyalgia (50% of cases); in essence, it seems that they are different manifestations of the same disease (1,2).

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The underlying mechanism is the inflammation of the vasa vasorum in the wall of the large arteries. The most affected are the arteries in the head and neck, but large thoracic arteries can also be affected. GCA can affect the aorta and cause an aneurysm or dissection. Up to 67% of the patients with GCA may experience an inflammation of the aorta that can lead over time to an aneurysm or a dissection of this large artery. Varicella-zoster virus antigens have been identified in 74% of the temporal artery biopsies that have identified giant cells, suggesting that this type of viral infection can trigger the inflammatory cascade (3,4).

GCA affects 1 in 15,000 individuals over the age of 50 years. Although this type of arteritis most commonly affects patients over the age of 50, it is much more common over the age of 70 and it predominantly affects women (5,6).

In this article, we aim to review the role of temporal artery resection in the diagnosis of Horton's arteritis, but we also discuss the hypothesis of a potential therapeutic benefit of this procedure.

2. Pathogenesis of Horton's arteritis

The pathogenic mechanism of Horton's arteritis is the result of an inflammatory cascade triggered by a still unknown factor that causes dendritic cells in vessels to recruit T cells and macrophages that form granulomatous infiltrates. The activation of T helper 17 (Th17) lymphocytes causes the release of IL-6, IL-17, IL-21 and IL-23 interleukins. The activation of Th17 lymphocytes leads to their continuous activation in positive feedback via IL-6. This vicious circle can be disrupted by glucocorticoids and, more recently, by IL-6 inhibitors (7-10).

3. Clinical picture of temporal GCA

The clinical picture in temporal GCA consists of a daily, intermittent or continuous headache with temporal localization, with moderate to severe intensity, as a burn or as a pulsation, unilateral or bilateral with a history of months, years. Other charges may include pain in the cheek or tongue during chewing (claudication), weight loss, generalized fatigue, low-grade fever, and frequent pain in the limbs in the context of coexisting rheumatic polymyalgia (11,12).

Visual symptoms represent a special category of symptoms, involving blurred vision, scotomas, and even sudden blindness. This symptomatology is explained by the progression of GCA-type vascular lesions in the ophthalmic artery. Sometimes, the impaired vision is the reason for the first presentation to the doctor. The eye can be involved in 76% of cases, by involving the ophthalmic artery that causes anterior ischemic optic neuropathy. Other ophthalmological symptoms in GCA may be diplopia, acute tinnitus (13,14).

The physical examination reveals thickened temporal arteries, sensitive to palpation, with absent or low pulse. The palpation of the temporalis muscle does not reveal trigger points for the painful crisis, and the consistency of the muscle is normal. However, the temporalis muscle may be sensitive to palpation. Vascular murmurs in the subclavian and axillary arteries may be auscultated. A complete or incomplete inflammatory biological syndrome may be present, but ESR



Figure 1. Intraoperative aspects during sampling of a right temporal artery biopsy in a patient with clinical symptoms suggestive of giant cell arteritis.

is constantly increased over 50-60 mm/1 h, as is C-reactive protein (CRP). We also observe thrombocytosis, but also hepatic cytolysis syndrome and other cutaneous manifestations are noted (15-17).

4. Positive diagnosis in GCA

If the clinical suspicion of temporal arteritis is raised, a temporal artery biopsy is required for confirmation (Fig. 1). Arterial inflammation is most commonly segmental, so in our experience, it is necessary to excise a segment approximately 5 cm long in the artery, in order to avoid a false-negative result (Fig. 2). Histopathological examination reveals jumping microscopic lesions, with variations in histological aspects, and focal thickening of the intima can be observed, with interruption of the lamina propria, with transmural inflammatory infiltrates, sometimes with giant multinucleated cells-representative, but not mandatory (Figs. 3 and 4) or with panvasculitis at the vasa vasorum level, the latter with mixed inflammatory infiltrates, including lymphoplasmocytic cells and neutrophils (Fig. 5). However, a negative result does not exclude the diagnosis. Given that the vascular wall is infiltrated into plaques, the biopsy may be taken from arterial segments, where the lesions are missing. Unilateral biopsy of a 1.5-3 cm long segment has a sensitivity of 85-90%, the excision of a temporal artery segment of at least 1 cm being mandatory. Temporal artery biopsy may confirm a clinical diagnosis or is a diagnostic criterion (18-20).

Color Doppler ultrasound is a non-invasive diagnostic method with the potential to replace biopsy by identifying the halo sign. Brain magnetic resonance imaging (MRI) examination is mandatory to rule out a brain pathology that causes symptoms such as headache or sudden visual loss (Fig. 6) (21,22).

The differential diagnosis includes other causes of headache with common clinical features such as cluster headache, migraine, carotid artery pain secondary to spontaneous carotid artery dissection or after endarterectomy, ischemic stroke. Idiopathic carotidodynia is also described, a self-limiting inflammation of the carotid sheath or adventitia possibly virally induced. Other differential diagnoses, such as

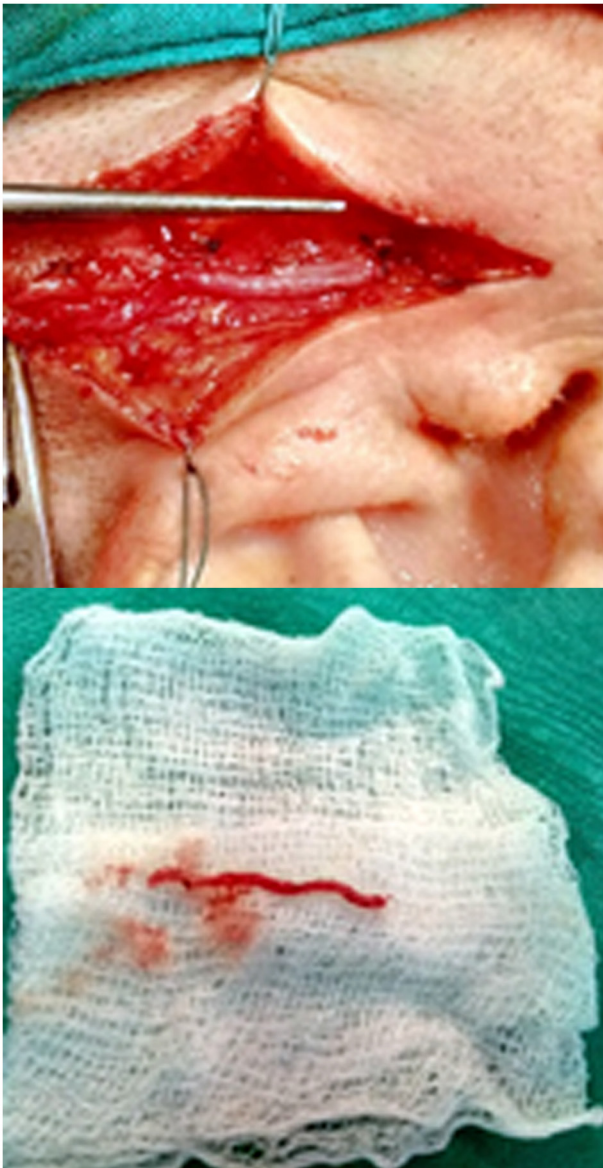


Figure 2. Intraoperative appearance with skeletonization of a 5-cm long segment with obvious inflammatory lesions in the arterial wall.

chronic inflammatory diseases, include Takayasu's arteritis and primary amyloidosis (23-25).

5. Principles of treatment in Horton's arteritis

Treatment for Horton's arteritis should be initiated early after diagnosis in order to avoid sudden blindness, a complication found in 30% of the untreated patients, due to the involvement of the ophthalmic artery. Considering this particular aspect, GCA is considered a medical emergency (26-28).

Prednisone or prednisolone is the treatment of choice and should be given in high daily doses of 60 mg. It should be started from clinical suspicion, even before confirmation by biopsy, although initiation of steroid treatment may change the histopathological appearance. Pain is dramatically reduced in a few days. Once the pain subsides and the ESR value is corrected, prednisone can be reduced in a few weeks to a dose of 5-10 mg with continuous monitoring of ESR for 12-18 months.

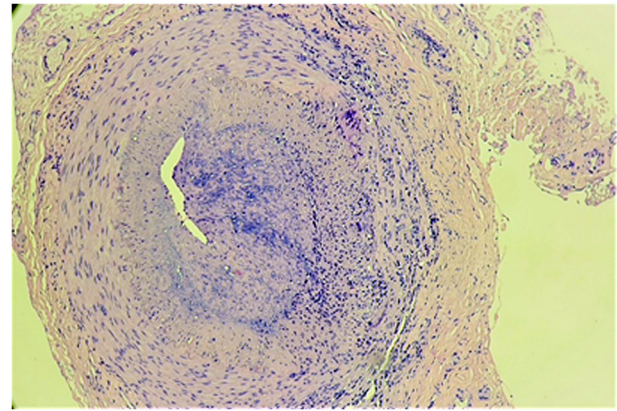


Figure 3. The temporal artery at the level of which a focal thickening of the intima is observed, with the narrowing of the vascular lumen, inflammatory infiltrated with the giant multinucleated cell. Hematoxylin and eosin staining, magnification, x40.

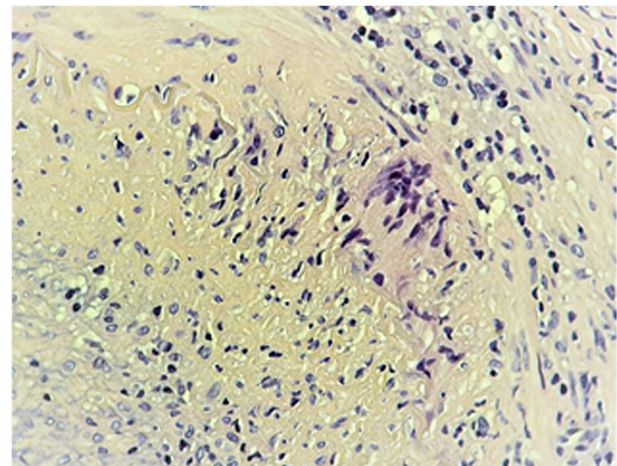


Figure 4. Multinuclear giant cell, detail. Hematoxylin and eosin staining, magnification, x40.

The administration of IV corticosteroids becomes necessary for the acute occurrence of acute visual loss (29-31).

In addition, tocilizumab and other immunological modifiers seem a promising therapeutic option in refractory cases or patients developing long term complications of corticoid treatment (32,33).

6. Resection of the temporal artery in Horton's arteritis

In general, patients with clinical suspicion of GCA should have a temporal artery biopsy to confirm the diagnosis, especially if corticosteroid therapy is to be instituted. The decision to start corticosteroid therapy without a biopsy seems easy, but difficulties may occur a few months after treatment, when the side effects of corticosteroids become prominent, and it is difficult to reduce the dose. In addition, performing the biopsy after the initiation of cortisone therapy can influence the lesions in the vascular wall, as previously mentioned (34).

A small number of patients with GCA (perhaps 8-10%) have clinically obvious inflammation of the large vessels; therefore, it is easy to choose the site of the vascular biopsy. The biopsy

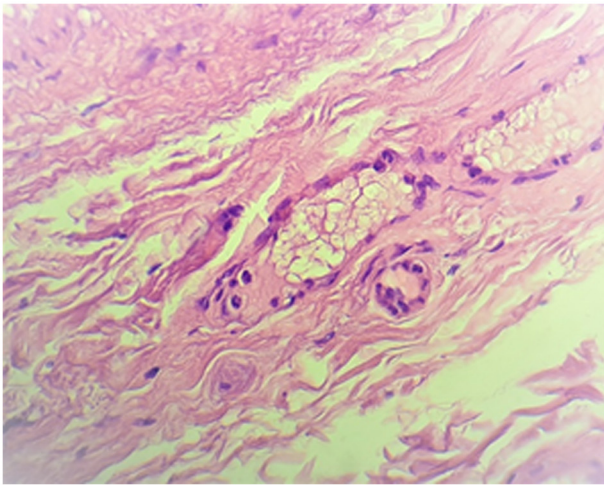


Figure 5. Aspects of mixed inflammatory infiltrate, with perivascular neutrophil polymorphonuclear cells, with focal panvasculitis. Hematoxylin and eosin staining, magnification, x40.

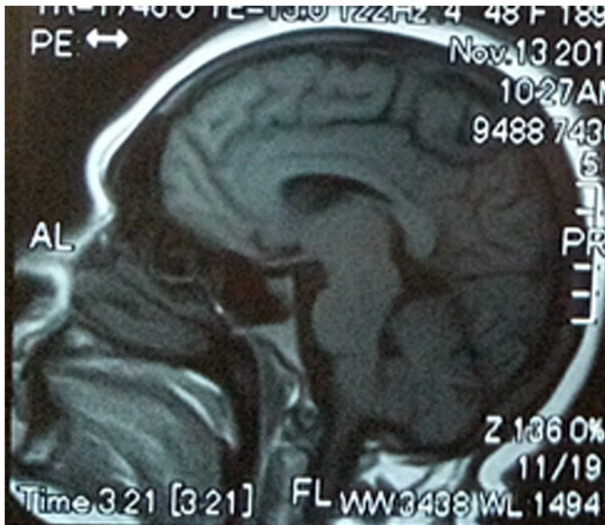


Figure 6. Brain magnetic resonance imaging performed in a patient with a clinical suggestion of Horton's arteritis and visual disturbances on the right eye that did not detect specific brain pathology corresponding to the clinical picture.

should be conducted on the most symptomatic side first. In most cases, a single biopsy is required. When the temporal artery involved has classic physical features of inflammation with sensitivity, swelling, and erythema above, a small part of the abnormal segment should be sufficient to confirm the diagnosis, but this favorable situation is quite rare. In patients with less pronounced abnormalities, a larger sample, such as 4 to 6 cm, should be obtained and examined microscopically at several levels with the extemporaneous histological examination if possible, for and subsequently with the use of paraffin-embedded sections (Fig. 7). In order to diagnose as many cases as possible, a specimen from the second temporal artery should be taken in the same session if the frozen sections of the first specimen are normal (35,36).

Undoubtedly, temporal artery resection has diagnostic benefits in Horton's arteritis. However, there are also some particular clinical situations in which we could see an

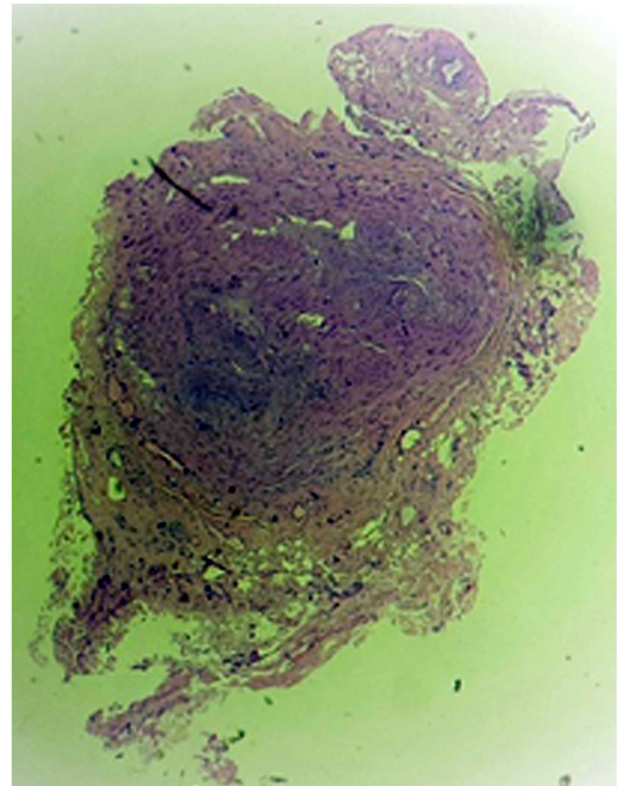


Figure 7. Section of the temporal artery without inflammatory aspects, with thickening of the vascular wall and narrowing of the lumen, in a patient with suggestive clinical symptomatology.

improvement in clinical symptoms, especially in vision deficit, with the improvement of the visual field after surgery performed for biopsy. In particular, we observed a considerable improvement of the visual field in the right eye 24 h after performing the right temporal artery biopsy in a 57-year-old female patient with a clinical picture of GCA with severe vision impairment in the right eye, only partially improved after corticosteroids; intraocular pressure was normal in both eyes at the time of visual field determination. It is difficult to estimate the impact of temporal artery resection alone, considering most patients also have concomitant cortisone treatment, but the rapid improvement of symptoms immediately after surgery with the improvement of visual acuity and visual field, along with the disappearance of headache, can create the premises for future studies on the therapeutic contribution of temporal artery resection in GCA. The clinical results of the resection are more obvious if the intervention is performed quickly after the appearance of ocular symptoms, before the appearance of irreversible lesions on the optic nerve by distal lesions on the vasa nervorum.

7. Conclusions

The segmental excision of the temporal artery has definite diagnostic benefits as a confirmatory element of a suggestive clinical picture or a diagnostic element in Horton's arteritis; nonetheless, there are also clinical data that may argue for a therapeutic contribution of this intervention. Thus, segmental arterial resection sometimes results in the disappearance

of temporal pain and, in some cases, even the improvement of vision, if practiced quickly after the onset of visual disturbances. Future studies are needed in order to support this clinical hypothesis. Even in cases where temporal artery resection is followed by an improvement in the clinical picture, cortisone treatment remains mandatory, given the systemic autoimmune pathogenesis.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

DV, MD and MPC contributed substantially to the conception and design of the review, the acquisition, analysis, and interpretation of the literature findings, and were involved in the drafting of the manuscript. BB, OP and AC contributed substantially to the acquisition, analysis and interpretation of the literature findings and were involved in the drafting of the manuscript. ISE and MGG contributed substantially to the acquisition of the literature findings and were involved in the critical revisions of the manuscript for important intellectual content. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All the authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Patient informed consent for publication of the data/images associated with the review was obtained. The authors followed the international regulations in accordance with the Declaration of Helsinki and all identifying information was removed.

Competing interests

The authors declare that they have no competing interests.

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