Classically Presenting GCA with an Unusual Evolution: a Case Report

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Abstract

Giant cell arteritis (GCA) is a primary vasculitis of large and medium-sized arteries. It is the most common vasculitis affecting the elderly. GCA involves the cranial branches of the carotid arteries and classically presents with cranial symptoms such as headache or jaw claudication. Aortitis can occur, and cases of mesenteric ischemia have been reported. Diagnosis can be challenging, and subclinical mesenteric ischemia in GCA may be more prevalent than previously recognized.

Resume

L'artérite temporale est une vasculite primaire des artères de gros et de moyen calibre. Il s'agit de la vasculite la plus courante chez les personnes âgées. Elle touche les ramifications crâniennes des carotides, et la forme classique se manifeste par des symptômes crâniens comme la céphalée ou la claudication intermittente de la mâchoire. Une aortite peut survenir, et des cas d'ischémie mésentérique ont été rapportés. Le diagnostic peut être difficile à poser, et l'ischémie mésentérique infraclinique dans les cas d'artérite temporale est peut-être plus fréquente que ce que l'on croyait auparavant. Ce cas met en évidence la nature systémique et l'évolution clinique potentiellement imprévisible de l'artérite temporale. Nous décrivons les caractéristiques histopathologiques de l'atteinte mésentérique et résumons l'état actuel de la documentation scientifique sur le sujet en mettant l'accent sur des stratégies de prise en charge.

Case presentation

A 70-year-old woman went to the emergency room complaining of a new-onset pan-cranial headache and a sensation of periorbital fullness with a blurred vision of the right eye. History taking revealed increased fatigability with scalp sensitivity, jaw claudication, nausea, and mild epigastric pain. Initial workup revealed augmented erythrocyte sedimentation rate and C-reactive protein. The patient was started empirically on oral prednisone with a presumptive diagnosis of GCA, which was subsequently confirmed by temporal artery biopsy. Unfortunately, the patient discontinued taking prednisone because of significant nausea and was prescribed on intravenous (IV) methylprednisolone.

An abdominal computed tomography angiogram excluded any infiltration or stenosis of the primary vascular trunk of the abdominal aorta. However, a significant thickening of the wall of the descending thoracic aorta was observed. Despite IV methylprednisone (1 mg/kg), the abdominal pain continued to worsen. A simple abdominal radiograph detected free air, and a CT scan confirmed bowel perforation. Emergent laparotomy identified and resected 100 cm of ischemic appearing small intestine. Histologic slides of the intestinal resection showed multifocal mucosal ischemia, with transmural lymphohistiocytic infiltration, which included rare multinucleated giant cells. Despite requiring a second surgery for anastomotic leak, the patient tolerated weaning of corticosteroids and was discharged with a daily dose of prednisone and followed as an outpatient.

Conclusion

This case highlights the systemic nature of GCA and the potential for an unpredictable clinical course and life threatening complications despite early clinical diagnosis and treatment. A high index of clinical suspicion of involvement of non-cranial arteries by GCA and prompt treatment are key to favourable clinical outcomes in this disease.

Introduction

Giant cell arteritis (GCA), also known as temporal arteritis, involves the cranial branches of the carotid arteries, especially the temporal artery. Symptoms at presentation usually include headache, jaw claudication, and ophthalmologic disturbances. This systemic vasculitis can affect medium to large vessels including the aorta and its major branches. Mesenteric involvement in GCA is a rare occurrence, especially severe mesenteric ischemia.

In this article, we report the case of a patient with classic GCA who didn't improve with the recommended prednisone treatment and subsequently developed extensive mesenteric ischemia that required surgical resection. We also summarize the state of the literature on this disease with a focus on management strategies.

Case Presentation

A 70-year-old woman, with a history of high blood pressure, went to the emergency room for a pan-cranial headache. Earlier the same day, she had an episode of lightheadedness followed by a fall and head trauma during a training session at the gymnasium, without loss of consciousness, convulsions, or post-ictal period. Upon arrival, the patient had a 5/10 pulsatile pan-cranial headache with neck pain, without focal neurological symptoms, which were relieved by treatment with acetaminophen. The patient reported a sensation of periorbital fullness with a blurred vision of the right eye, fluctuating over a couple of weeks. She also complained of fatigue, nausea, and epigastric pain that had been progressing for a few days.

Initial assessment revealed tachycardia (110 bpm) with normal blood pressure (131/83 mmHg), without tachypnea or fever, or orthostatic hypotension. The remaining physical examinations including neurologic exam, visual fields, and acuity, were unremarkable. Initial workup revealed a leukocytosis of 15.8 with significant neutrophilia (13.75), thrombocytosis (619), and normal hemoglobin (119). Serum electrolytes and liver function tests were in normal range. A cranial computed tomography (CT) scan was performed, which revealed a mild leukoencephalopathy without focal lesions. Electrocardiogram was in sinus rhythm.

An ophthalmology consultation reported narrow, closable angles and evolving cataracts without convincing evidence of temporal arteritis. However, clinical suspicion of the latter remained, as further workup revealed an elevated ESR of 90

Figure 1. Cross-sectional view of the circumferential thickening of the aortic wall, as seen in the thorax CT angiography.

mm/h and a C-reactive protein (CRP) at 361.5 mg/L. Consultation by internal medicine noted scalp sensitivity and a history of mandibular pain when chewing. The neurological examination and temporal artery pulse remained normal. With a presumptive diagnosis of GCA, a temporal biopsy was ordered. The patient was initiated on prednisone (60 mg orally per day) and was discharged with a follow-up three days later.

At the follow-up, the patient reported that she was unable to start prednisone because of nausea. She was immediately admitted for intravenous (IV) corticosteroid therapy for 48 hours and was initiated on methylprednisolone 40 mg IV q6h from prednisone. Because of persistent abdominal pain, an abdominal computed tomography angiogram was ordered and excluded any infiltration or stenosis of the primary vascular trunk of the abdominal aorta. However, aortitis remained in the differentials as a significant thickening (3 mm) of the wall of the descending thoracic aorta was observed (Figure 1).

Pathology of the temporal artery was consistent with a diagnosis of active arteritis with luminal thrombosis. However, no giant cells were observed (Figure 2).

Figure 2. Histologic images (hematoxylin and eosin stain) of the biopsied temporal artery, showing intense transmural lymphohistiocytic inflammation and luminal stenosis.

Figure 3. Histologic images of intense transmural lymphohistiocytic inflammation and luminal stenosis of the mesenteric arteries (a). Representative section of the small ischemic bowel, showing complete loss of the intestinal epithelium and villi in the area fed by affected arteries (between dotted lines) (b).

The patient showed a slight initial improvement in her general well-being on corticosteroids yet continued to complain of abdominal pain. In the days that followed, nausea persisted with frequent bilious vomiting and no bowel movement. Plain abdominal radiographs were compatible with subocclusive phenomena and no sign of constipation. Repeat laboratory tests demonstrated a reduction in CRP from 361.5 to 156.0 mg/L, and normal lactate reassured the treating team of any significant ischemic event.

Abdominal pain and distension continued to worsen, and by day 10 of hospitalization, a simple abdominal radiograph demonstrated free air. An emergent CT scan was compatible with a bowel perforation with severely collapsed ileal loops. However, the site of the perforation could not be determined radiologically. So, an emergent laparotomy was performed, and a continuous 100 cm section of the ischemic appearing small intestine was identified and resected, with a nodular appearance and numerous apparent microperforations.

On histologic examination there was extensive mesenteric arteritis with occasional giant cells, associated with multifocal mucosal ischemia (Figures 3 and 4).

A complete vasculitis panel showed no significant titers of antineutrophil cytoplasm antibodies, rheumatoid factors, and anti-nuclear antibodies. After the surgical resection, the patient received 500 mg/day of methylprednisolone in addition to aggressive rehydration and vasopressor support. Unfortunately, an anastomotic leak occurred 2 weeks later, requiring a temporary ileostomy while on prednisone 60 mg orally per

day tapering doses. After a few weeks, the patient successfully went through reanastomosis and is currently at home on weaning prednisone doses.

Discussion

GCA is a primary vasculitis of large and medium-sized arteries, with an incidence of approximately five per 100,000 people ≥ 50 years old. The incidence increases with age, and it's three times more common in women than men.¹

GCA commonly involves the cranial ramifications of the carotid arteries, such as the temporal arteries, but can also involve the aorta. While the most feared complication of GCA

Figure 4. Rare intramural multinucleated giant cells (arrow) identified within the inflamed mesenteric arteries.

(permanent blindness) is irreversible, involvement of the mesenteric arteries can be life-threatening. The mesenteric involvement by GCA is rare, but it is associated with mortality rates reaching 70%.²

In a meta-analysis of 17 studies, the most frequent causes of death in GCA were cardiovascular disease (39%), cerebrovascular disease (14%), infection (13%), and malignancy (12%). However, no difference in the long-term mortality in GCA was observed at the populational level. Deaths attributed to gastrointestinal (GI) problems comprised 4% in this review. Increased mortality in GCA because of GI (ulcer/hemorrhagic) bleeding was also reported.³

While mesenteric ischemia can be the presenting manifestation of GCA, it also can develop during ongoing treatment. From a series of 28 histologically proven mesenteric-GCA cases, 12 were diagnosed before the appearance of GI symptoms. Mesenteric ischemia occurred either soon after initiation of steroid therapy ($n = 6$; mean time to onset after starting steroid, 12 ± 11 days) or with a low-dose steroid regimen ($n = 6$; dosages, 0–10 mg/day).⁴

From case reports, it was noted that the clinical manifestations of GCA-associated mesenteric ischemia and biological markers (CRP), are very nonspecific. Previous studies reported that the mesenteric vasculature has an extensive network of collateral vessels that are vital for ensuring visceral perfusion. During the occlusion of a major vessel, these collateral vessels can dilate and maintain perfusion of the entire adjacent territory.² This might explain why the serum lactate levels remained normal in this case of mesenteric ischemia with extensive abdominal wall necrosis. Furthermore, the patient in this study presented only a few abdominal symptoms until the development of an acute abdominal event, suggesting the increased prevalence of subtle or subclinical mesenteric ischemia in patients with GCA than previously recognized.

As mesenteric involvement is rare, one must explore the differential diagnosis when faced with this unusual presentation, including polyarteritis nodosa (PAN) and the ANCA-associated vasculitides. In this case, we considered the latter unlikely given the ANCA negativity, lack of eosinophilia, and lack of typical histopathologic findings. Although PAN typically affects small- and medium-sized arteries and arterioles, there are reported cases of the temporal arteries affected by PAN. No reference standard test to diagnose PAN is available, and as such, the PAN diagnosis often rests on the appropriate clinical context and the classic histopathology findings of segmental transmural inflammation of muscular arteries with fibrinoid necrosis.⁵ In contrast to PAN,

GCA typically lacks fibrinoid necrosis and contains scattered multinucleated giant cells.

Takayasu arteritis is extremely rare in North America but remains in the differential diagnosis. It can be difficult to distinguish from GCA, and the diagnosis relies heavily on the demographics of the presenting patient, as it predominantly afflicts young women of Asian or Middle Eastern descent.⁷ The histopathologic features of Takayasu arteritis overlap with GCA. The inflammatory infiltrate is more severe in the adventitia and outer half of the media, whereas the opposite is true for GCA.

Of particular note is the well documented yet poorly known fact that giant cells are not required for a histologic diagnosis of GCA. Indeed, multi-nucleated giant cells can be absent in up to 50% of patients with GCA.⁶ Therefore, in the appropriate clinical context, as seen in this case, the diagnosis of GCA should not be put into question if there is histologic evidence of arteritis in the absence of giant cells.

Minimal data exist concerning the medical treatment of mesenteric ischemia in GCA. According to the recommendations of EULAR 2018, a reasonable dose would be prednisone 40 to 60 mg/day or equivalent. For a fleeting amaurosis or acute vision loss, methylprednisolone 0.25 to 1 g/day for 3 days should be considered.⁸

Adjunctive therapy should be used in selected patients with GCA (refractory or relapsing disease, an increased risk for glucocorticoid-related adverse effects or complications) using tocilizumab, a humanized monoclonal antibody against IL-6 receptors. However, it has been associated with an increased incidence of GI perforation and hence was avoided in our situation.⁹

Other lines of treatment are controversial, such as antiplatelets, and few guidelines currently recommend their use. Statins failed to demonstrate any benefit in GCA.¹⁰ Methotrexate may be used as an alternative but was not tested in our patient.⁸

In summary, this case illustrates the systemic nature and potentially unpredictable clinical course of GCA despite early recognition and treatment of the disease. Mesenteric involvement by GCA may well be underrecognized, which underlines the importance of having a low threshold for vascular imaging in the context of bowel symptomatology. Given the potentially grave consequences of this disease, aggressive initial treatment (intravenous methylprednisolone) should be considered not only in cases with significant visual impairment but also when there is a high index of suspicion of mesenteric ischemia.

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