Not Every Case of Temporal Arteritis Is Giant Cell Arteritis. Microscopic Polyangiitis Involving the Temporal Artery

To the Editor:

Microscopic polyangiitis (MPA) is a small vessel vasculitis associated with antineutrophil cystoplasmatic antibodies (ANCAs). The presentation can be diverse, but involvement of the temporal artery is rare.

We report the case of a 65-year-old patient who presented with a clinical picture compatible with giant cell arteritis (GCA). Pathological analysis of the temporal artery biopsy showed transmural inflammation and zones of fibrinoid necrosis. Further investigation revealed renal involvement and perinuclear ANCA positivity. The diagnosis of MPA was made, and the patient was treated accordingly.

This case illustrates the need to search for an alternative vasculitis in patients presenting with atypical temporal biopsy findings or when not all of the clinical findings fit the diagnosis of GCA.

Microscopic polyangiitis is a rare disease characterized by inflammation of the wall of small blood vessels. Its reported incidence is estimated at ±10 cases per million,[1] and males are more frequently affected. Antineutrophil cystoplasmatic antibodies are present in more than 90% of cases, mainly with myeloperoxidase specificity. The course of MPA can be aggressive, typically when kidneys or lungs are involved. Even with an adequate treatment, reported 5-year survival is still estimated to be approximately only 55%.[1]

Despite its classification as a small vessel vasculitis, the disease can be associated with larger vessel involvement and can thus mimic other vasculitides.[2,3] We report the case of a patient with an initial clinical presentation suggestive of temporal arteritis/GCA, but finally diagnosed with MPA.

CASE REPORT

A 65-year-old patient was referred to our hospital with an unexplained inflammatory syndrome. Her medical history was significant for a kyphoplasty for an osteoporotic vertebral fracture (8 years ago) and an ischemic cerebrovascular accident with dysphasia and right hemicorporal paresis (2 years ago), without obvious cause and with complete neurological recovery. She now sought medical attention for a sudden paresis of her right arm since 1 month. Neurological examination at presentation confirmed a loss of strength of the right arm; further clinical examination was unremarkable. Laboratory tests showed leukocytosis (22,000/μL), an elevated C-reactive protein level (206 mg/L; reference value, ≤5 mg/L), and an erythrocyte sedimentation rate of 81 mm/h (reference range, 1–5 mm/h). A chest radiography showed an infiltrate in the right lower lobe, but no clinical or biochemical improvement was seen after start of empirical antibiotic therapy (amoxicillin-clavulanic acid for 7 days). Abdominal ultrasound was normal. Electromyography showed diffuse muscle involvement in all 4 limbs, but no signs of polyneuropathy. Creatinine kinase was within normal limits. Brain magnetic resonance imaging revealed multiple periventricular and subcortical white matter lesions of older age.

More profound history taking revealed the presence of jaw claudication and localized temporal headache, with tenderness on palpation. A temporal artery biopsy was therefore performed. Anatomopathological examination showed transmural infiltration, with mononuclear and neutrophilic cells, and focal zones of fibrinoid necrosis, compatible with a necrotizing vasculitis (Fig. 1). A ^{18}F-fluorodeoxyglucose positron emission tomography with combined computed tomography scan showed only symmetrical increased fluorodeoxyglucose avidity of the inguinal and axillary lymph nodes and no signs of large vessel vasculitis.

Urinalysis showed a 24-hour proteinuria of 0.54 g per 24 hours without hematuria, and a serum creatinine of 1.05 mg/dL; antinuclear antibodies, rheumatoid factor, and anti–cyclic citrullinated peptide were negative. Perinuclear ANCAs were positive, with strong myeloperoxidase specificity (80 U/mL). On subsequent renal biopsy, a focal necrotizing pauci-immune glomerulonephritis was identified (Fig. 2).

The diagnosis of MPA with renal, muscular, and temporal artery involvement was made. The patient received induction treatment with high doses of corticosteroids and intravenous pulses of cyclophosphamide, with full recovery.

DISCUSSION

Involvement of both large and medium vessels has been described in patients with small vessel vasculitis. Nevertheless, involvement of the temporal artery remains a rare finding in ANCA-associated vasculitis (AAV). To our knowledge, only a few cases of temporal artery involvement in MPA have been described.[4–9] Because the AAVs, including MPA, require a different therapeutic approach and have a worse prognosis than GCA,[10,11] a correct diagnosis is indispensable to guide adequate therapy.

At presentation, our patient with biopsy-proven vasculitis fulfilled the American College of Rheumatology criteria for GCA (age >50 years, localized headache, tenderness of the temporal artery, erythrocyte sedimentation rate >50 mm/h).[12]

To base the diagnosis on these criteria alone, however, would have been incautious. Headache and jaw claudication are 2 cardinal symptoms reported in the majority of patients with cranial GCA[13] and seem to be more frequent in patients with transmural inflammation when compared with patients with vasa vasorum or periadventitial vasculitis. However, also in small vessel vasculitis with temporal artery involvement, cranial symptoms seem to be present with high frequency. Three series have described the clinical features of systemic

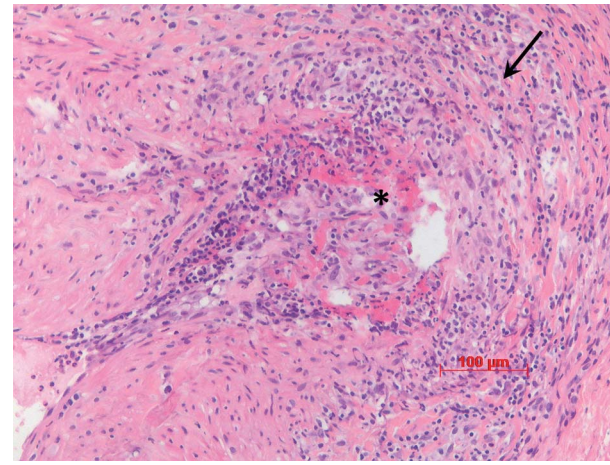

FIGURE 1. Temporal artery biopsy. Transmural mixed inflammatory infiltrate including neutrophilic polymorphs (arrow), with focal disruption of the lamina elastica interna and areas of fibrinoid necrosis (asterisk) (hematoxylin-eosin stain, original magnification ×200).

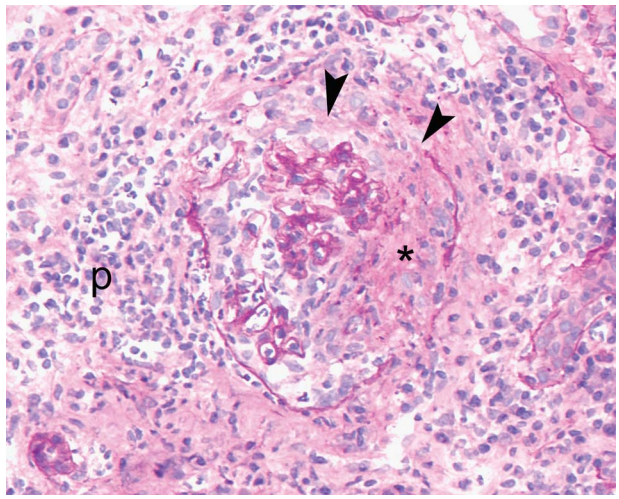

FIGURE 2. Kidney biopsy. Focal necrotizing glomerulonephritis. Periodic acid–Schiff stain on frozen tissue, original magnification ×200. *Crescent. Arrowheads point to the severe inflammation that also caused rupture of the parietal layer of Bowman capsule. P indicates periglomerular inflammation, mainly lymphocytic.

necrotizing vasculitis with involvement of the temporal artery. Of the 27 patients with systemic necrotizing vasculitis and temporal artery involvement (including 3 patients with MPA) in the series by Genereau et al.,[3] 22 (81%) presented with cephalic symptoms, on top of the systemic symptoms present in all patients. Hamidou et al.[5] studied 7 patients (including 3 MPA patients), of whom 6 (85%) had either headache or jaw claudication or both. In the series of Cavazza et al.,[6] including 3 patients with AAV, the frequency of cranial manifestations seemed somewhat lower (53%), but none of the AAV patients had transmural inflammation, which may account for the difference. Thus, based on the available literature, it seems impossible to differentiate between small vessel vasculitis and GCA by clinical evaluation of the cranial symptoms only, and supplemental information from serology and pathology seems indispensable.

Also, evaluation of the histopathologic findings should be done carefully. The typical findings on temporal artery biopsy in GCA include a transmural mononuclear cell infiltrate that may form granulomas, with the presence of multinucleated giant cells and fragmentation of the internal elastic lamina. However, vessel inflammation in GCA can also be restricted to the vasa vasorum or the periadventitial small vessels, whereas the presence of multinucleated giant cells is seen in approximately only 50% of cases and is not required for diagnosis.[6,14] In our patient, the transmural infiltrate and disruption of the internal elastic lamina were features suggestive of GCA. Fibrinoid necrosis, however, is a very uncommon finding in GCA, and also the presence of polymorphonuclear cells is rare and made us consider other types of vasculitis in our patient.[3,15]

Thus, although the presence of headache, jaw claudication, or constitutional symptoms, such as fever, fatigue, and weight loss, does not allow to differentiate between GCA and AAV, other features such as kidney and muscle involvement (in our case) or lung infiltrates or hemoptysis, ear-nose-throat symptoms, or polyneuropathy should raise the suspicion of AAV.[10,11] Fibrinoid necrosis should alert the pathologist that ANCA vasculitis might be involved.

CONCLUSIONS

The clinical presentation in this case could have been misleading. Both atypical temporal biopsy findings or incongruent symptoms in a patient with a clinical picture of temporal arteritis/GCA should prompt both the examining pathologist and the clinician to search for the presence of an alternative vasculitis, which should be treated accordingly.

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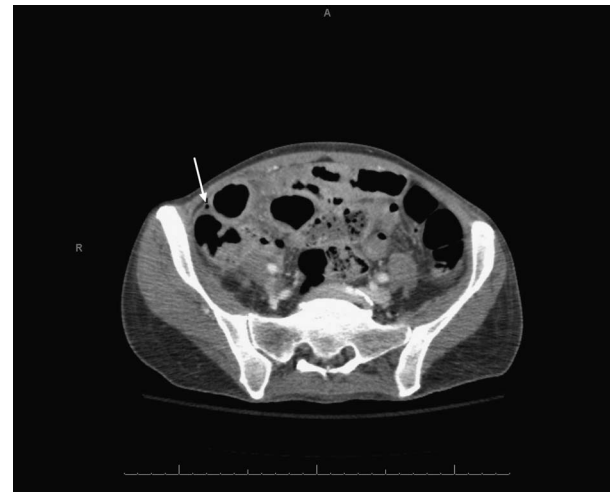

FIGURE 2. CT Abdomen showing small foci of air about inflamed loop.

Appendiceal Perforation in Eosinophilic Granulomatosis With Polyangiitis (Churg–Strauss)

To the Editor:

Eosinophilic granulomatosis with polyangiitis (EGPA), formerly known as Churg–Strauss syndrome, is a multisystem disorder that involves small and medium vessels. It is characterized by chronic rhinosinusitis, asthma, and prominent peripheral blood eosinophilia.[1–7] The most commonly involved organ is the lung, followed by the skin; however, any organ system can be affected including the cardiovascular, gastrointestinal, renal, and central and peripheral nervous systems.[7,8]

Gastrointestinal symptoms of EGPA are common and include abdominal pain (59% of patients), diarrhea (33%), gastrointestinal bleeding (18%), and colitis; however, perforation of small intestine is rare with only 61 cases having been documented in the literature.[8,9] Here, we report a case of EGPA with small bowel perforation involving the appendix following treatment with rituximab, and discuss the relevant literature. While bowel perforation has been reported in patients with EGPA, involvement of appendix has not been documented.

CASE SUMMARY

A 56-year-old male patient with steroid-dependent asthma and chronic allergic rhinosinusitis presented with mono-neuritis of the bilateral upper extremities and abdominal pain. Outpatient immunologic work-up with anti-nuclear antibody (ANA), anti-neutrophil cytoplasmic antibody (ANCA), and infections were negative. Computerized tomography (CT) abdomen showed gastric mural thickening suggestive of gastritis and multifocal nodular consolidation in lungs. CT chest revealed diffuse small airway disease with bronchial wall thickening, peribronchial ill-defined groundglass opacities and tree in bud nodules (Fig. 1). He was started on moxifloxacin for community-acquired pneumonia and underwent bronchoalveolar lavage which showed eosinophilia of 35% with no organism growth in culture.

Esophagogastroduodenoscopy revealed shallow ulcers in gastric fundus with no evidence of vasculitis in pathology report. Repeat immunologic work-up showed positive c-ANCA with a high titer of 1:256, elevated myeloperoxidase (MPO) antibody of 111 AU/mL, and C-reactive protein of 7.28 mg/dL. ANA, p-ANCA, and anti-proteinase 3 antibody (PR3) remained negative. Complete blood count revealed an absolute eosinophil count of 15.24/μL. Based on his clinical presentation and immunologic serologies, a diagnosis of EGPA was made. Treatment with pulse dose steroids along with rituximab 375 mg/m^2 weekly was initiated. He received four of four doses of rituximab leading to improvement in his pulmonary and neurologic symptoms. Unfortunately, 10 days following completion of the fourth dose of rituximab, he presented to the emergency department with severe abdominal pain associated with guarding and rigidity. A CT of the abdomen revealed markedly thickened hyperemic inflamed segment of small bowel in the right lower quadrant and small foci of air about inflamed loop consistent with severe enteritis and bowel perforation (Figs. 2 and 3). An emergent laparotomy was performed and revealed purulent peritonitis with ruptured appendix. Surgical pathology showed eosinophilic appendicitis

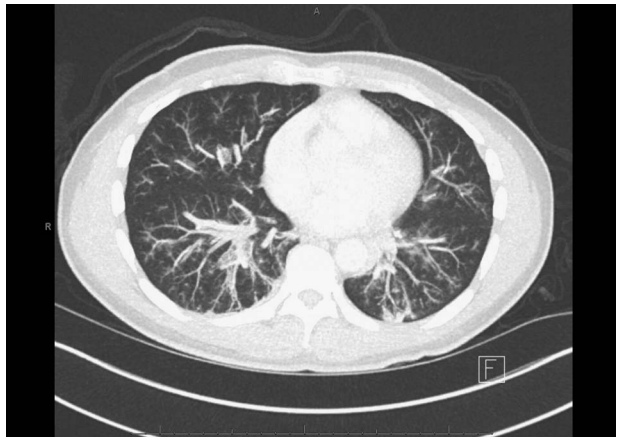

FIGURE 1. CT Chest showing groundglass opacities and tree in bud nodules.