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Coronary arteritis: An entity to be considered in giant cell arteritis

Giant cell arteritis (GCA) is a potentially fatal medium- to large-vessel vasculitis with ocular and systemic involvement. The most common ocular manifestation is anterior arteritic ischemic optic neuropathy (AAION), which can be blinding and may affect 1 or both eyes. Systemically, aortitis is the most serious potential complication of GCA, as it can lead to aortic dissection and aortic aneurysms.[1]

Coronary arteritis has classically been associated with polyarteritis nodosa, Kawasaki disease, and Takayasu's arteritis, but it can also be seen in the antineutrophil cytoplasm antibody–associated vasculitides such as granulomatosis with polyangiitis and eosinophilic granulomatosis with polyangiitis. Only few reports have been documented, however, in relation to GCA. Most of these cases were determined in the context of fatal myocardial infarctions (MIs), in which autopsy revealed pathologic findings of coronary GCA.

The following appears to be one of the first cases of a patient with temporal artery biopsy-proven GCA with ocular manifestations, who subsequently developed an MI, with evidence of coronary arteritis on autopsy.

A 76-year-old female with an ocular history of glaucoma and pseudophakia OU presented to the eye clinic with a superior visual field defect in her right eye. She reported a history of GCA 2 years prior, for which she had been treated with prednisone. GCA review of systems at this visit was significant for right temporal pain, scalp tenderness, jaw pain, and 5-pound weight loss.

Medical history was significant for diabetes mellitus, hypertension, hypercholesterolemia, cholecystectomy, and a remote history of breast cancer treated with mastectomy and chemotherapy approximately 30 years prior. She was an ex-smoker with a 25 pack-year history.

Vision was 20/40-1 OD and 20/30-2 OS. Intraocular pressures (IOPs) were 7 and 14 mm Hg. She had a grade 4 relative afferent pupillary defect of the right eye. Posterior segment examination revealed florid disc edema of the right optic nerve. Erythrocyte sedimentation rate was 63 mm/hour, C-reactive protein was 14.2 mg/L, and platelets were 401 $\times$ 10^9/L.

She was started on 80mg of oral prednisone for presumed AAION secondary to GCA, and temporal artery biopsy confirmed the diagnosis. Three days after presentation, vision in the right eye markedly declined to hand motions. She was started on intravenous (IV) methylprednisolone 250 mg every 6 hours. Examinations over the next several days revealed a cherry red spot consistent with central retinal artery occlusion secondary to GCA. The right eye became hypotonous, with an IOP of 3 mm Hg.

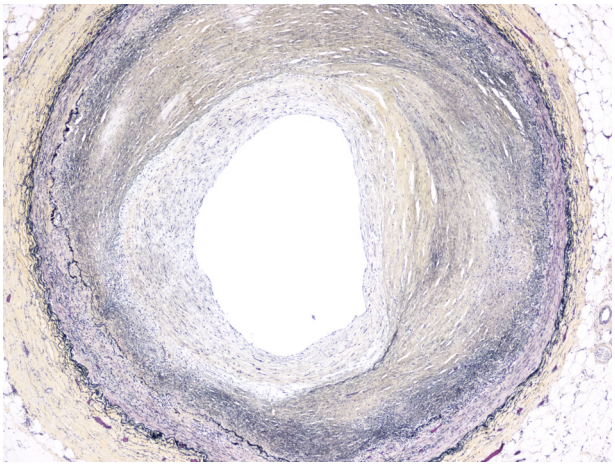

Fig. 1—4x magnification photo-micrograph of temporal artery. The internal elastic lamina is thinned, fragmented and absent over a 240 degree circumference. This is in keeping with the lymphocytic infiltration of the surrounding media and adventitia.

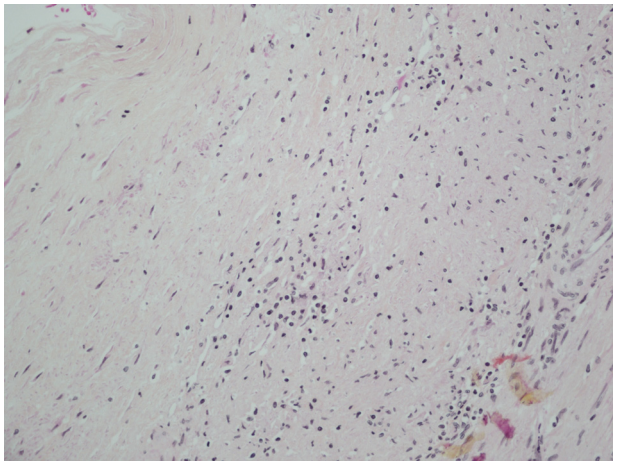

Fig. 2—10x mangification photo-micrograph of temporal artery. Lymphocytes can be appreciated, indicating chronic inflammatory infiltration.

The patient finished her course of IV methylprednisolone and was restarted on oral prednisone.

Three weeks after initial presentation, she was experiencing significant side effects from the steroids, including vomiting, diarrhea, and weakness. Her eye remained hypotonous, and she was now having right periorbital pain, which was attributed to likely ischemia of the ophthalmic artery.

The patient was admitted to hospital on the following day because increasing weakness, anorexia, and weight loss. The next morning, she died of cardiorespiratory arrest, shortly after developing epigastric pain and nausea. Her most recent electrocardiogram, performed 7 years earlier, revealed a septal infarct of undetermined age.

Postmortem autopsy revealed inflammatory infiltrate within the external elastic laminar and medial layers of the coronary arteries (Fig. 1). The internal elastic lamina was thinned and fragmented (Fig. 2). No giant cells were seen, but in the context of the positive temporal artery biopsy, the specimen was identified as evidence of unequivocal active arteritis.

In addition to aortitis, a general increased cardiovascular risk has been associated in patients with GCA.[1,2] A large population study of more than 3000 patients with GCA confirmed significantly increased risks for MI, peripheral vascular disease, and cerebrovascular accidents.[2]

A multitude of factors likely contributes to the increased cardiovascular mortality in patients with GCA. The presence of chronic inflammatory changes may compound pre-existing atherosclerosis, and steroid treatment itself may play a role.[1,2] It is postulated here that arteritis itself is an additional cause of cardiac pathology in patients with GCA.

Several cases of GCA-associated coronary arteritis have been reported in which the patients suffered vision loss. In 1 instance, the vision loss occurred 3 years before the coronary event.[3] Another case was more similar to the one presented here, in which the MI occurred only 3 days after vision loss.[4]

This case report supports the existing hypothesis that coronary arteritis is a true entity that can cause mortality in GCA. Although atherosclerotic disease is still likely the most common cause of MI in patients with GCA, it is possible that a significant number of GCA-related MIs are actually secondary to coronary arteritis but simply have not been identified because of lack of autopsy.

A large retrospective study spanning 6 decades recently evaluated the risk for acute coronary syndrome (ACS) in patients with GCA compared with a cohort of patients without GCA.[5] The results suggested that there was no overall increased risk for ACS in patients with GCA and furthermore showed that certain cardiovascular risk factors were actually less frequent in patients with GCA.[5] However, this study did not include cases of sudden death as part of its documented ACS events; as such, the analysis may have inadvertently excluded patients with GCA who did indeed suffer MIs, similar to the patient in the present case. Moreover, even if ACS incidence is similar between the 2 groups, it does not mitigate the fact that coronary arteritis is a real disease entity with associated morbidity and mortality.

Although there is robust evidence of an association between GCA and aortic aneurysms, the incidence of aortic aneurysms is so low that screening with aortic computed tomography scans is not currently recommended.[1] Furthermore, a recent Cochrane Review submitted that there was currently insufficient evidence to even suggest the use of aspirin to reduce cardiovascular morbidity in patients with GCA.[6] Thus, it is unlikely that screening protocols for the much less recognized entity of coronary arteritis in patients with GCA will be implemented imminently. However, clinical inquiry into signs and symptoms of aortic arch aneurysms, such as upper limb claudication and asymmetrical pulses, can be assessed easily in clinic. Similarly, symptoms of angina suggestive of possible coronary arteritis can simply be screened for in patients with GCA. As further studies seek to establish screening guidelines, it is important to consider coronary arteritis among other causes of GCA-related cardiovascular morbidity.

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A case of POEMS and chronic papilledema with preserved optic nerve function

A 44-year-old male developed bilateral symmetric lower limb weakness, numbness, and absent ankle jerk reflexes over the course of 2 months. A lumbar puncture (demonstrating protein of 101 mg/dL), electromyography, nerve conduction studies, and mild monoclonal gammopathy were consistent with the diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP). He was treated with intravenous immunoglobulins and azathioprine by a neurologist with resolution of his symptoms. A year after discontinuing treatment he developed visual scotomas and periodic headaches and was referred to our ophthalmology clinic.

On presentation, his visual acuity was 20/20 in each eye, there was no random amplified polymorphic DNA, and optic nerve heads were bilaterally swollen with disc hemorrhages. Body mass index was 21 kg/m^2. 24-2 Humphrey visual fields demonstrated minimally enlarged blind spots bilaterally (Fig. 1A). Magnetic resonance imaging and magnetic resonance venography of the brain were normal, and repeat lumbar puncture demonstrated opening pressure of 28 cm H_2O with increased cerebrospinal protein. An extensive autoimmune and infectious work-up was negative. There was no history of alcohol abuse.

The papilledema was felt to be in keeping with an uncommon presentation of CIDP.[1–5] The patient was treated with oral prednisone and diuretics with improvement of the headaches. The moderate chronic papilledema persisted for 4 years, but visual function (central acuity and visual fields) remained nearly normal and unchanged (Fig. 1B).

Four years later the patient developed acute ascites and was diagnosed with hepatomegaly and end-stage liver disease of unknown etiology. He also developed mild diabetes mellitus. Liver biopsy results were nonspecific, and cytology of ascitic fluid was negative for malignancy. A closer look at the patient's past investigations for CIDP revealed he had been remotely followed for a mild immunoglobulin A (IgA) lambda monoclonal gammopathy, enlarged axillary lymph nodes, and splenomegaly of unknown etiology. Monitoring and repeated testing for lymphoma and multiple myeloma, including repeat serum protein electrophoresis, had yielded similarly inconclusive results for 3 years leading up to his development of papilledema.

A few months after onset of liver failure, the patient developed a pathological hip fracture, severe portopulmonary hypertension, and renal and respiratory failure. He was admitted to a peripheral hospital, where he developed spontaneous bacterial peritonitis of unknown etiology and ultimately succumbed to his disease. No autopsy was performed.

At this point we re-examined an iliac crest biopsy performed 4 years earlier, which demonstrated normocellular bone marrow with 1 medium-sized focal infiltrate of plasma cells (CD138$^+$) with lambda light chain restriction. The focal involvement was $<10\%$; Congo Red staining was negative for amyloid. Lymphocytes were predominantly CD3$^+$, with some CD20$^+$. In the context of other systemic features (mild IgA lambda monoclonal gammopathy, enlarged axillary lymph nodes, splenomegaly, hypothyroidism, and diabetes), CIDP was rejected as an underlying diagnosis and the patient was diagnosed with POEMS (polyradiculoneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, and skin changes).

POEMS is a rare paraneoplastic syndrome arising from a monoclonal plasma cell neoplasm and often misdiagnosed as CIDP.[6] Papilledema can be a feature in both conditions. Mandatory diagnostic criteria in POEMS are polyneuropathy and monoclonal gammopathy (present in our patient from onset). Other major criteria are sclerotic bone lesions, elevated vascular endothelial growth factor (VEGF), and Castleman's disease (giant lymph node hyperplasia). Minor criteria include organomegaly, endocrinopathy, skin changes, papilledema, extravascular volume overload, and thrombocytosis. Our patient developed several of these criteria years after initial presentation.

Pathological diagnosis of POEMS can be difficult to make because of subtle bone marrow biopsy findings. One third of biopsies demonstrate no detectable clonal plasma