

Vasculitis Presenting with Lower
Extremity MyalgiaOhad Oren^{1*}, Giris Jacob², Michal Oren³, Valerie Aloush⁴ and Jacob N. Ablin⁴¹Internal Medicine, Pennsylvania Hospital, University of Pennsylvania, Philadelphia, Pennsylvania, USA²Department of Internal Medicine F, Tel Aviv Sourasky Medical Center, Tel Aviv University, Tel Aviv, Israel³Tel Aviv Sourasky Medical Center, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel⁴Department of Internal Medicine F and the Institute of Rheumatology, Tel Aviv Sourasky Medical Center, Tel Aviv University, Tel Aviv, Israel

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Abstract

Giant Cell Arteritis (GCA) is the most common form of vasculitis in the adult population. It classically presents with new-onset headache in a patient older than 50 years, and reflects predominantly-intracranial vessel pathology. We describe a 67-year old man who presented with subacute myalgia of the lower extremities and constitutional symptoms, and was later found to have an extra-cephalic presentation of GCA. Magnetic Resonance Imaging of the lower extremities demonstrated diffusely enhanced signal intensity in the distribution of the quadriceps muscle, initially leading us to suspect an inflammatory myopathy. Muscle biopsy under radiographic guidance, however, was normal. Confronted with a middle-aged gentleman with non-specific symptoms and elevated laboratory markers of systemic inflammation, we performed a biopsy of the temporal artery and nailed the atypical, 'silent' form of GCA. The patient responded favorably to treatment with prednisone.

Introduction

GCA is an inflammatory vasculopathy involving medium and large vessels. Among the most commonly affected vessels are the temporal artery ("temporal arteritis") and the extra-cranial branches of the carotid artery. However, GCA may also affect the aorta and its major branches, and thus should not be thought of solely as a cranial vasculitis. The diagnosis of GCA may be challenging due to its protean manifestation and the overlap with various rheumatological disorders (ie. *Polymyalgia rheumatica*). The importance of timely recognition and early treatment cannot be overemphasized. GCA represents an emergent neuro-ophthalmologic condition and temporal artery biopsy with immediate steroid administration should be seriously considered, in order to decrease the likelihood of irreversible loss of vision.

Case Presentation

A 67-year-old man presented to the emergency department with a 3-week history of myalgia in both lower extremities accompanied by anorexia, weight loss and low-grade fevers. He reported no joint pain or swelling, skin changes, headache, vision impairment, nausea, vomiting, bowel habit alteration, fatigue, or mood changes. The patient described squeezing pain in both lower extremities, particularly in his thighs, that started abruptly 3 weeks prior to his presentation. His discomfort was symmetric, constant and severe and was alleviated by application of heat. He recounted some difficulty arising from a sitting position and reaching above the head (neither was due to pain). The patient had not observed any redness or swelling around the involved area and denied shoulder or hip pain or history of recent trauma. He had lost 22 pounds (10 kg) in the preceding month. He recalled two occasions on which he had recorded temperature up to 37.9°C in the three-week period leading to his admission.

The patient's medical history was notable for hypertension, hyperlipidemia, diabetes mellitus and duodenal ulcer. His medications included sitagliptin, insulin glargine, insulin glulisine, folic acid and omeprazole. He had no known drug allergies. His family history was notable for rheumatoid arthritis in his mother and coronary heart disease and hypertension in his father. The patient previously worked as an engineer, was married and had two healthy children. He had no recent history of travel outside the country. He had a 30 pack-year smoking history and refrained from consuming alcoholic beverages.

On exam, mild atrophy of the quadriceps muscles was noted bilaterally with grade 3/5 muscle strength on hip flexion. Other parts of the examination were unremarkable, including joint range of motion and deep tendon reflexes. Laboratory studies showed hemoglobin level of 10.3 gram/liter with an MCV of 84.2 fl, platelet count 366,000 per/millimeter, and white-cell count 12,400 per millimeter, with 81.5% neutrophils. Erythrocyte Sedimentation Rate (ESR) was 58 mm/hour, and C-reactive Protein (CRP) was 23.8 mg/dl. Albumin level was 3.0 gram/dl and ferritin was 833 ng/ml.

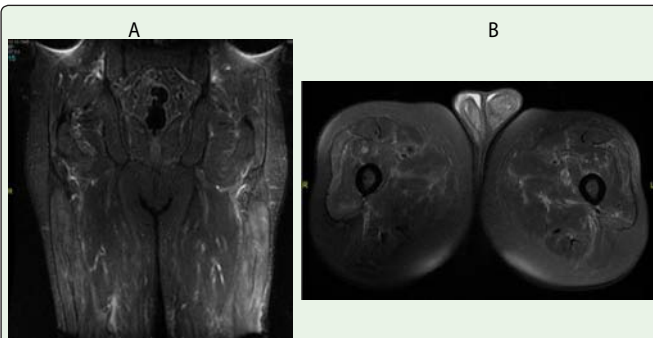


Figure 1: STIR images of MRI of the thighs, with coronal (a) and axial (b) sections showing increased signal intensity of both quadriceps muscles.

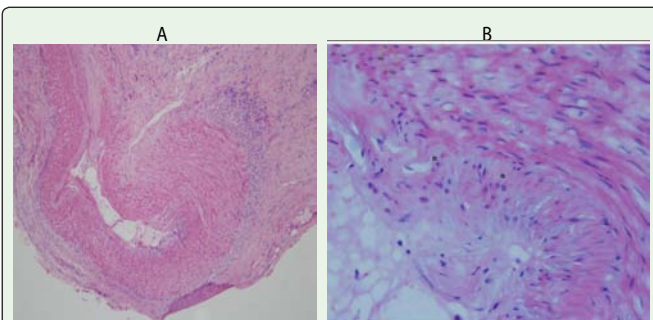


Figure 2: Biopsy of the left temporal artery depicted (A) lymphocytic infiltration of the adventitial layer on low-power light microscopy, and (B) fragmentation and distortion of the internal elastic lamina (seen between the two asterisks) on higher power.

Upper endoscopy revealed a healed scar in the duodenal bulb. Colonoscopy demonstrated a 5-mm pedunculated polyp in the sigmoid colon, a biopsy of which was consistent with tubular adenoma with low-grade dysplasia. CT scan of the chest, abdomen, and pelvis was unremarkable except for a sclerotic focus in the left femoral neck suggestive of enostosis (Bone Island). A peripheral blood film showed mild ovalocytosis and polychromasia with normal representation of precursors.

MRI of the thigh area (figure 1) showed irregular high signal intensity in the quadriceps muscle bilaterally, slightly more on left side.

An MRI-guided biopsy of the quadriceps muscle on the right was subsequently done, but showed no evidence of inflammation or necrosis. No findings suggestive of vasculitis were detected either.

A 1.5 centimeter segment of the left temporal artery was excised. Low-power light microscopy revealed marked adventitial infiltrate composed predominantly of lymphocytes with no granulomas or multinucleated giant cells (figure 2, A). Magnification showed disruption of the internal elastic membrane, a finding that was reinforced by staining with elastin (figure 2, B).

The patient's constitutional signs and symptoms were attributed to GCA. The patient was treated with 40 mg of daily prednisone for one month, gradually tapering his steroids down to 30 and 20 mg, 1 and 2 months later, respectively. His symptoms rapidly improved and he achieved complete resolution of his myalgia within 2 weeks; no additional febrile episodes were observed. Within 6 weeks, his

hemoglobin climbed to 12.7 mg/dl, albumin increased to 3.6 g/dl, and ESR decreased to 6 mm/hour. The patient continues to do well 6 months following discharge.

Discussion

The riddles posed by our patient's clinical presentation were multiple: his symptoms had not been classical for the medium/large-vessel vasculitis with which he was eventually diagnosed; the findings on examination were indeterminate for either pure muscular or vascular abnormality; and the muscle imaging result was starkly discordant with the histological pattern. To reconcile these gaps, an appreciation of the evolving role of imaging studies in the diagnosis of vasculitic disorders is needed.

Although imaging is not necessary for the diagnosis of GCA, recent studies have revealed intriguing evidence regarding the distribution of large-vessel involvement [1]. Through the use of Ultrasonography (US) and Positron Emission Tomography (PET), extracranial vasculitis has been shown to involve both the upper and lower extremity vasculature [2]. Most GCA patients who harbor vasculitic changes in their extremity vessels do not report limb weakness. However, a sizable minority do experience significant morbidity from extension of their arteritis into non-typical vascular territories, as shown by imaging studies, and could potentially benefit from glucocorticoid therapy [3].

Understanding the etiology of the patient's lower extremity weakness is of considerable interest. Neuromuscular involvement is a rare but well-described complication in patients with GCA. Possible manifestations include cranial neuropathy, cervical radiculopathy and mononeuritis multiple [4,5]. The pathogenesis of the mentioned neurological entities, in patients with GCA, is endoneural ischemia secondary to vasculitis. The discussed patient, experiencing symmetric and proximal lower extremity weakness (and pain) had muscle vasculitis as the most likely mechanism underlying his symptoms. Muscle vasculitis in GCA is an infrequent but interesting phenomenon that has been previously described [6]. A precise understanding of the biology of small vessel vasculitis in GCA remains to be established. Another conundrum regards the normal CPK level in a patient with muscle vasculitis. The explanation for that might be that only small vessels were involved and so did not result in gross muscle injury. An alternative rationale may be that only nerve-supplying arterioles were affected by vasculitis, impacting muscle tissue in an indirect fashion.

Our patient did not manifest the classic features of GCA. His symptoms were nonspecific, and ranged from myalgia and weight loss to low-grade fever and extremity weakness. Faced with an apparent impasse, posed by the results of our diagnostic endeavors, we chose to go back and take the road not taken - departing from the seemingly localized nature of the presentation and taking a more holistic approach towards a case of systemic inflammation in an elderly patient. Careful integration of the patient's extracranial symptoms with the initially-ambiguous imaging and histological data allowed us to head in the right direction and eventually reach a definitive diagnosis.

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