

# Unusual Presentation of Polyarteritis Nodosa

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**ABSTRACT.** We describe an unusual presentation of a localized form of polyarteritis nodosa (PAN) manifested by acute onset of severe calf pain. Biopsies of the gastrocnemius muscle and fascia revealed an acute necrotizing arteritis with fasciitis. The lumens of affected vessels were occluded by thrombi. PAN localized to calf muscles is extremely rare. To our knowledge this is the first report of evidence of fascial involvement believed to contribute to the severity of the clinical features of PAN. The occurrence of multiple intraluminal thrombi in conjunction with anticardiolipin antibodies suggested the possibility of a coexisting coagulopathy, and they were also likely contributors to the severity of the pain. (J Rheumatol 2001;28:871-3)

*Key Indexing Terms:*

VASCULITIS

LOCALIZED

FASCIITIS

THROMBI

ANTIPHOSPHOLIPID ANTIBODIES

Polyarteritis nodosa (PAN) is a multisystemic disease characterized by involvement of medium size and small muscular arteries throughout the body. In its classical form, it presents as a multisystem illness although there have been some reports of disease localized to one or 2 organ systems, most commonly the skin<sup>1,2</sup>. Very rarely, PAN has been reported to be localized to calf muscles with, to our knowledge, a total of only 9 cases reported to date. We describe a case of PAN that presented with acute severe calf pain that was secondary to vasculitis involving the gastrocnemius muscle and its fascia. In addition, affected vessels were occluded with thrombi. This presentation differed from those reported in the literature in a number of ways.

## CASE REPORT

A 54-year-old black man presented to the emergency department with a 3 day history of acute onset of calf pain. He initially developed pain in his right calf, which was followed by involvement of the left calf about 24 hours later. Within 48 hours the pain had become so severe that he was unable to walk. On the day of admission, the pain was so severe that he was unable to bear weight or sit with his legs in a dependent position. The pain was minimally responsive to narcotics. He denied any other symptoms and, in particular, denied any respiratory, gastrointestinal, neurological, mucocutaneous, or constitutional symptoms. His history was significant for a right total knee replacement following a gunshot wound, a left hip fracture following a motor vehicle accident, and a 15 year history of diabetes

mellitus. He had a history of alcohol abuse but denied any consumption of alcohol in the 8 years preceding admission. He had a 35 pack-day-year history of smoking. He denied any illicit drug use or high risk sexual behavior. Family history was significant for a sister having systemic lupus erythematosus (SLE) and another sister dying from a stroke at the age of 51.

Examination revealed a well developed male who was in significant distress when he attempted to bear weight. His blood pressure was 133/77 and temperature was 99.6°F. There was a flexion deformity of his right knee of roughly 20°. He had scars from his previous arthroplasty but no other cutaneous lesions were noted apart from three 0.5 mm depigmented macular scarred lesions over his right knee, which he stated were secondary to repetitive trauma as part of his printing job. His calf muscles were exquisitely tender to palpation. There was no evidence of warmth, swelling, or color change. Peripheral pulses were present and within normal limits. There was decreased strength in both lower legs secondary to pain. Sensation to light touch was intact bilaterally. Reflexes were present and equal bilaterally. The rest of the examination, including neurologic examination of the upper extremities and testicular examination, was within normal limits.

Investigations revealed hemoglobin 16.8 g/dl, white blood cells (WBC) 19,100/ $\mu$ l with 97% polysegmented neutrophils, 2% monocytes, and 1% lymphocytes, platelets 285,000/ $\mu$ l, erythrocyte sedimentation rate (ESR) 86 mm/h, C-reactive protein (CRP) 21.6, normal complement levels, creatinine, CPK, and LDH. Antinuclear antibody (ANA) was positive at 1:160 (speckled pattern), but extractable nuclear antigen (ENA) profile, including antibodies to Smith, SSA, and SSB, was negative. Antineutrophil cytoplasmic antibody (ANCA) was negative. Hepatitis B and C serologies, cryoglobulins, and stool guiac testing were negative. Alkaline phosphatase was mildly elevated at 301 but transaminases were within normal limits. Urinalysis was significant for protein 30 mg, but without red cells or casts. Repeat urinalysis was negative for protein. Anticardiolipin antibody findings were: IgM 10, IgG 15, IgA 5 (normal 0-10 for each subclass). Ankle/brachial indices, lower extremity Doppler studies, and chest radiography were within normal limits. Electromyographic study of the left lower extremity revealed findings of muscle membrane irritability at the left tibialis anterior and left medial gastrocnemius muscle, with occasional fasciculations suggestive of a perimuscular mild inflammatory process. No evidence of a myopathic or myositic process was noted. Biopsies of the right gastrocnemius muscle and of its fascia were performed; sections of

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both tissues revealed acute necrotizing arteritis with transmural mononuclear infiltrates staining positive for CD45 (CLA). Focal segmental fibrinoid necrosis and intraluminal and intramural fibrin deposits were noted (Figure 1). There was an acute inflammatory process that extended into the adjacent muscle and the adipose/fibrous tissue of the fascia with associated perineural inflammation (Figure 2); no evidence of myonecrosis was seen. The lumens of affected vessels were occluded by thrombi (Figures 1 and 2).

A diagnosis of PAN isolated to muscles with coexistent involvement of the fascia was made. He was given prednisone 1 mg/kg/day and noted marked improvement in his symptoms within 24 hours. At that point, he was able to ambulate with a cane and did not require the use of any narcotic medications. Within the following few weeks, there was total resolution of his calf pain with a decrease in his WBC to 11.5, ESR to 11, and CRP to 1. Anticardiolipin antibodies also returned to within normal limits. He was followed as an outpatient for a period of about 3.5 months, during which time his prednisone was tapered to 20 mg qd without recurrence of his symptoms or increase in ESR or CRP. He was lost to followup.

## DISCUSSION

We describe a case of polyarteritis nodosa with involvement localized to the calf muscles in association with severe fascial involvement. Extensive review of the literature revealed 9 case reports of PAN presenting with leg pain, with disease confined primarily to the calf muscles<sup>3-8</sup>. Our case differs in a number of respects from the previous reports.

Reports of muscle biopsies from all previous cases showed evidence of vasculitis, with some also reporting disruption of adjacent muscle fibers. Similarly to previous reports, the biopsy from our patient showed evidence of an inflammatory process consisting of lymphocyte infiltration extending into the adjacent muscle and adipose/fibrous tissue, in addition to the necrotizing arteritis. Unlike

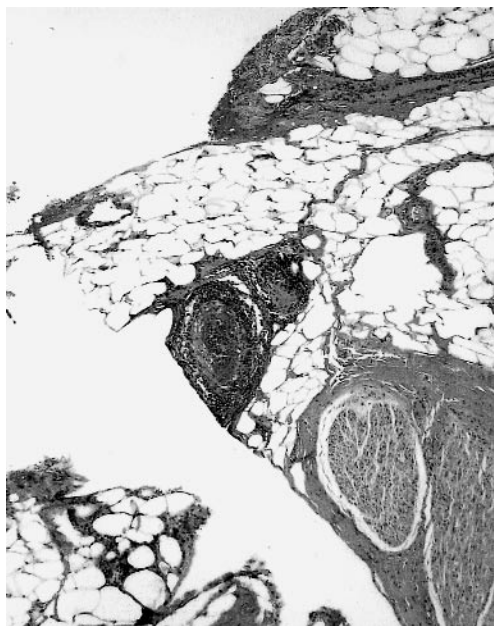


Figure 1. Fasciitis with occlusive vasculitis of perineural vessels (magnification 100 $\times$ ).

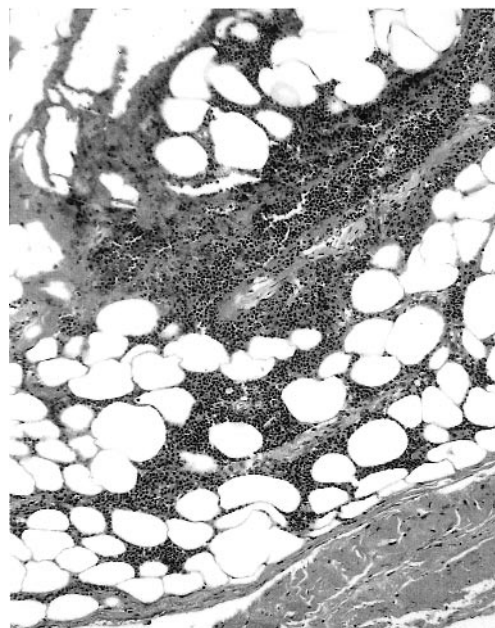


Figure 2. Foci of round cell infiltrates in perineural fibroadipose tissue (magnification 350 $\times$ ).

previous reports, there was evidence of acute necrotizing arteritis involving the fascia in addition to marked fasciitis. The coexistence of the fasciitis may account for the severity of the symptoms experienced by the patient. To our knowledge there have been no previous reports of fascial involvement occurring as part of PAN.

The presentation also differed from previous reports in the acuteness of onset and severity of symptoms. Our patient presented with a 3 day history of severe debilitating pain that limited his ability to stand or sit. In contrast, previous case reports have described pain, stiffness, and swelling in calf muscles that vary from 2 to 6 months, indicating a more subacute onset. We did not detect calf swelling in our case, presumably because the pain primarily resulted from acute ischemia secondary to occlusive vasculitis. Although previous case reports described disease localized to muscles, at least 3 of the cases had constitutional symptoms with marked fevers, one had associated indurated areas over the calf, and a fifth had a preceding history of intermittent symptoms suggestive of a connective tissue disease. In contrast, our patient's only symptom was that of severe calf pain. He had a positive ANA but lacked other diagnostic criteria for SLE, and ENA profile was negative; hence, the ANA was thought to be nonspecific.

Antiphospholipid antibodies (aPL) and the antiphospholipid syndrome have been reported in patients with vasculitis, including PAN<sup>9</sup>. Of interest is a report of a child presenting PAN limited to the musculoskeletal system and skin with circulating aPL and perinuclear ANCA<sup>10</sup>. There has been speculation whether aPL exist as a nonspecific epiphenomenon due to the microvascular disturbance that

occurs as part of vasculitis, or are related to the underlying pathogenesis of the disease. It has been suggested that the endothelial cell disruption that occurs as part of vasculitis may reveal the presence of immunologically cryptic antigens that in turn stimulate the production of these antibodies. Our patient had anticardiolipin antibodies, although of a low titer, and histopathologic examination of his muscle biopsy revealed occlusion of affected vessels by thrombi. It is likely that the thrombi exacerbated the ischemia resulting from the associated vasculitis, and thus contributed to the more acute and severe pain seen in our case compared with previous reports. Although speculative, the aPL may have been thrombogenic and hence involved in the pathogenesis of the disease. The anticardiolipin antibodies in our patient returned to normal levels following treatment with high dose prednisone.

In summary, we describe an unusual presentation of a localized form of polyarteritis nodosa manifested by acute onset of severe calf pain requiring hospitalization. To our knowledge this is the first case of a patient in whom there was documented evidence of fascial involvement that likely contributed to the severity of the clinical features. The severity of his presentation may also be explained by the occurrence of multiple intraluminal thrombi that in the presence of anticardiolipin antibodies suggest a coexisting coagulopathy. Although this is an extremely rare presentation of PAN, we feel it should be included in a differential diagnosis of patients presenting with acute calf pain, particularly when

other causes, such as deep venous thrombosis and thromboembolic disease, have been excluded. In addition, the marked response to prednisone suggests that, in localized forms of PAN, this therapy is likely to be sufficient. Lastly, the finding of thrombi in conjunction with anticardiolipin antibodies suggests these antibodies may be involved in the disease process.

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