

Acute digital ischemia: A rare presentation of antisynthetase syndrome

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Abstract

Antisynthetase syndrome (ASS) is recognized as a subgroup of idiopathic inflammatory myopathies (IIMs). It is associated with autoantibodies directed against aminoacyl-transfer ribonucleic acid (tRNA) synthetase enzymes. We report the first case of anti-PL-7/anti-SSA 52kD ASS presenting as acute digital ischemia, an association not described previously. Occlusive vasculopathy is a rare but serious manifestation that can be seen at presentation in patients with ASS and may herald the onset of severe interstitial lung disease (ILD). Comprehensive evaluation should be performed to confirm the presence of subclinical myositis. Extensive myositis-specific antibody testing is strongly recommended even if initial screening autoimmune serologies are unrevealing.

Keywords: Antisynthetase syndrome, angiogram, ischemia, threonine-trna ligase/immunology

Introduction

Antisynthetase syndrome (ASS) is recognized as a subgroup of idiopathic inflammatory myopathies (IIMs) and is associated with autoantibodies directed against aminoacyl-transfer ribonucleic acid (tRNA) synthetase enzymes. Here we report a case of anti-PL-7/anti-SSA 52kD ASS presenting as acute digital ischemia, an association not described previously.

Case Presentation

A 61-year-old Caucasian female presented with acute-onset multi-digit ischemia. Her medical history was notable for hypertension, depression, and vitiligo treated with atenolol, venlafaxine, and topical clobetasol, respectively. She was employed as a bank teller and denied alcohol consumption, illicit drug use, trauma, or environmental exposures. She stopped smoking 7 years previously. Her family history was negative for autoimmune or hypercoagulable disorders.

Finger pain began acutely in her right 2nd-4th distal interphalangeal (DIP) joints 3 weeks prior to presentation without features associated with historical or current Raynaud's phenomena. She subsequently developed a dry cough without improvement despite a 7-day course of antibiotics. Noninvasive computed tomography (CT) angiogram of her upper extremities showed normal caliber axillary, brachial, radial, and ulnar arteries bilaterally. Pain and digital discoloration progressed, leading to referral and further evaluation.

Dry gangrenous skin changes were present on examination distal to DIP joints of the right 2nd-4th digits as well as left 2nd and 4th digits (Figure 1a, b). Acral coolness and sluggish capillary refill were noted. A faint, blanchable, non-palpable, macular rash was distributed along the left upper thigh, chest, and bilateral proximal arms. Proximal muscle strength was intact and symmetric to manual confrontation strength-testing. Other findings were unremarkable, except for bibasilar crackles.

Laboratory tests revealed a normal complete blood count, complement level, creatinine level, inflammatory marker level, and thyroid hormone level. Muscle enzyme levels were increased [lactate dehydrogenase (LDH) 32 U/L (range: 122-222), creatine kinase 459 U/L (range: 38-176), aldolase 26.1 U/L (range: <7.7U/L), alanine aminotransferase (ALT) 71 U/L (range: 7-45), and aspartate aminotransferase (AST) 85 U/L (range: 8-43)]. Findings of comprehensive hypercoagulability tests were negative. In addition, cryoglobulins, cold-agglutinins, and antiphospholipids were negative. Microbiology workup, including mycoplasma pneumoniae, was unrevealing.

Conventional angiography (Figure 1c, d) revealed bilateral fixed occlusive vasculopathy of the digital arteries. Ground-glass opacities consistent with ILD were seen in bilateral lower lobes. Extensive imaging studies did



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Figure 1. a-d. Dorsal (a) and palmar (b) images of the right hand demonstrating ischemic changes of digits 2-4. Conventional angiography, right hand, palmar view (c) showing patent radial and ulnar arteries to level of wrist bilaterally, fixed occlusions of the digital arteries at the level of the proximal interphalangeal joint on the radial side digit 2, radial and ulnar side digits 3 and 4, and ulnar side digit 5. Conventional angiography, left hand, palmar view (d) demonstrating fixed occlusions of digital arteries radial and ulnar side digits 2 and 4, ulnar side digits 3 and 5.

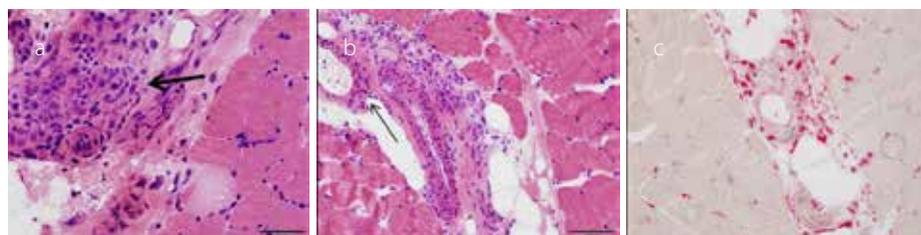


Figure 2. a-c. Muscle biopsy with H&E staining showing diffuse mononuclear cells in the perimysium (a, thick arrow) and perivascular inflammatory exudate in perivascular sites (b, thin arrow), consistent with inflammatory myositis. Muscle biopsy with acid-phosphatase staining (c) showing histiocytes and other inflammatory cells at endomysial and perimysial sites. Photos courtesy of Andrew G. Engel M.D., Mayo Clinic.

not identify any evidence of infection, atherosclerosis, vegetation, central thrombus, or occult malignancy. Electromyography showed normal nerve conduction with mild proximal myopathy but without features suggestive of inflammation. Lower extremity MRI, however, revealed patchy increased T2 signal in bilateral proximal adductors and distal vastus lateralis muscles.

Initial autoimmune serologies were only notable for weakly positive antinuclear antigen (ANA 1:80) with a speckled pattern. The extended myositis-specific and myositis-associated antibody panel revealed a strongly positive antithreonyl-tRNA synthetase [anti-PL-7] (>80

U/mL; range: <20 U/mL) and anti-SSA 52 kD (>80 U/mL; range: <20 U/mL) as well as a weakly positive anti-Ku (32 U/mL; range: <20 U/mL).

Skin biopsy was non-diagnostic, but muscle biopsy from the right vastus lateralis demonstrated a perivascular and perimysial inflammatory exudate consistent with IIM (Figure 2). ASS was diagnosed on the basis of the presence of anti-aminoacyl-tRNA synthetase antibodies, IIM in accordance with Bohan & Peter criteria, and interstitial lung disease (ILD) (1, 2).

The patient's clinical course was further complicated by progressive ILD, which significant-

ly improved with pulse dose methylprednisolone. She transitioned to high-dose oral prednisone plus adjunct oral mycophenolate mofetil. Four weeks later, pulmonary opacities resolved and muscle enzymes normalized. The initial digital ischemic areas demarcated, and no further territories were involved.

Discussion

Antisynthetase syndrome affects approximately 30% of patients with IIM (3). Diagnosis is based on the presence of anti-aminoacyl-tRNA synthetase antibodies and 2 or more of the following: inflammatory arthritis, IIM, or ILD. Fever, mechanic's hands, and Raynaud's phenomena may also be present but are less prevalent (4). While screening antibodies (ANA and extractable nuclear antigens [ENA]) are frequently positive in ASS, the absence of these autoantibodies does not rule out the presence of ASS. Therefore, if a high index of suspicion exists for ASS, further evaluation with myositis-specific antibody testing is needed even if antibodies for ANA or extractable nuclear antigens are negative (4). Anti-Jo-1 is the most frequent autoantibody associated with ASS, whereas anti-PL-7 accounts for only 5%-10% of cases (4, 5). Anti-SSA 52kD antibodies are found in 5%-15% of patients with IIM and are strongly associated with anti-Jo-1 or other anti-aminoacyl-tRNA antibodies (6). Anti-Ku is reported in 2%-23% of patients with IIM, with higher rates being observed in polymyositis-scleroderma overlap syndromes (6-8).

Significant clinical heterogeneity exists in case of ASS. Patients with anti-PL-7 antibodies may demonstrate mild subclinical myositis that is highly treatment responsive. On the other hand, anti-PL-7, anti-Ku, and anti-SSA-52kD have been independently associated with a higher frequency and greater severity of ILD (4, 9, 10). While the presence of anti-Ku raises the possibility of a polymyositis-scleroderma overlap, the acute onset, lack of preceding Raynaud's or cutaneous features of scleroderma, and weak positive anti-Ku titer makes this less likely. Digital ischemia from cutaneous vasculitis can occur in Sjögren's-myositis overlaps; however, such cases commonly result from immune complex cryoglobulin precipitate, which was not observed in our case. Two prior reports have described similar presentations of acute digital ischemia in patients with myositis or ASS (11, 12). However, both cases were associated with a positive anti-Jo-1 antibody, which was negative in our case.

The pathogenesis of this rare presentation is unknown but is speculated to be secondary to microcirculatory arteritis (11). At present,

there are no consensus guidelines for the management of digital ischemia in the setting of fixed occlusive vasculopathy. Beyond immunosuppressive therapy targeting features of active myositis or ASS, the efficacy of adjunct anticoagulants, antiplatelets, vasodilatory agents, or sequential pneumatic compression is unknown and requires further investigation.

Occlusive vasculopathy is a rare but serious manifestation that can be seen at presentation in patients with ASS and may herald the onset of severe ILD. If subclinical myositis is suspected, comprehensive evaluation should be performed for confirmation. Extensive myositis-specific antibody testing is strongly recommended even if initial screening autoimmune serologies are unrevealing.

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