14. DIGITAL ISCHEMIA AND INTERSTITIAL LUNG DISEASE IN ANTISYNTHETASE SYNDROME WITH PL-12 ANTIBODY

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Introduction: Antisynthetase syndrome (ASS) is a rare idiopathic inflammatory myopathy with nearly 89% showing interstitial lung disease (ILD). The hallmark of ASS is the presence of serum autoantibodies directed against aminoacyl-tRNA synthetases that include Jo-1 (most commonly detected), PL-7, PL-12, OJ, EJ, KS, Wa, YRS and Zo. However, in a small subpopulation without evidence of myositis, the diagnosis may be critically delayed, hindering management of this rapidly progressive disease. We report an interesting case of anti-PL-12/anti-SSA 52kD ASS presenting as acute digital ischemia, an association rarely described previously. In cases with ILD, the severity of lung condition generally determines the prognosis.

Case description: A 77-year-old Caucasian female presented with sudden onset of painful, blue discolouration in her bilateral fingertips two weeks after mild lower respiratory tract infection and occasional pyrexia. She was a non-smoker, otherwise independent lady who had background history of ischemic heart disease, diverticulosis and hypertension. Her physical examination revealed dusky blue digits and dry ulceration. She had extensive investigations that showed raised CRP (61mg/L), eGFR 39ml/min/1.73m², weak positive rheumatoid factor and cold agglutinins, equivocal Lupus anticoagulant, negative ANCA, clear urinalysis, bilateral chronic inflammatory change on chest xray and thromboi of digital arteries on Doppler ultrasound of hands. She was initially treated for infection due to ongoing temperatures and had multiple scans with no definite source. An inflammatory aetiology was then thought likely due to lack of response to antibiotics and steroid therapy was commenced with settling of fevers and inflammatory markers. Autoimmune screens initially were negative but became more prominent over time with a positive Ro antibody and ultimately a positive Anti PL12 antibody, keeping with anti-synthetase syndrome.

She subsequently developed florid interstitial lung disease, further ischemia and ultimately necrosis of her fingertips. Due to the onset of lung disease she was treated with IV steroids, Cyclophosphamide and Prostaglandins with some initial benefit. She received 3 cycles of cyclophosphamide and managed to come off supplemental oxygen. However, she had issues with recurrent chest infections due to immunosuppressive therapy which resulted in delays in her cyclophosphamide pulses and need for antibiotics. She later developed clostridium-difficile gastroenteritis and subsequent ileus of her bowel which was managed conservatively and found it difficult to overcome. As time went on, the progress that she had made with her hands started to deteriorate again. There were also further issues with intestinal obstruction, and sadly ultimately passed away with aspiration pneumonia.

Discussion: ASS is recognized as a rare autoimmune inflammatory myopathy of unknown etiology, 2–3 times more prevalent in women than in men. The clinical manifestations include myositis, polyarthritis, ILD, mechanic’s hands, and Raynaud phenomenon. The hallmark of ASS is the presence of serum autoantibodies directed against aminoacyl-tRNA synthetases that include Jo-1, PL-7, PL-12, OJ, EJ, KS, Wa, YRS and Zo. Anti-Jo1 is the most commonly detected antibody. These autoantibodies may arise after viral infections, or patients may have a genetic predisposition.

Our case was interesting as the autoimmune profile was positive for Anti-Ro/SSA and anti-PL-12. Anti-Ro/SSA and anti-La/SSB are traditionally associated with Sjögren’s disease and Sjögren’s-related ILD, however, anti-Ro/SSA has been independently associated with ASS and more severe and fibrotic ILD. It has been described that patients with anti-PL-12-ASS are most often clinically diagnosed with amyopathic dermatomyositis or ILD alone and there is higher prevalence and increased severity of ILD than PM/DM. Moreover, the prevalence of muscle symptoms (weakness and myalgia) is significantly lower in patients with anti-PL7/PL12 as compared to those with anti-Jo1 and less associated with malignancy as compared to DM. Interestingly, anti-PL-12 is also associated with higher rates of Raynaud phenomenon.

Our case also reports that not all patients with antisynthetase antibodies or even those classified as ASS have all manifestations of this syndrome. Diagnostic criteria refer to presence of anti-synthetase antibody plus two major criteria or one major criterion and two minor criteria (Connors et all.2010). When the lungs are affected, the severity and extent of lung damage generally determines the prognosis because respiratory failure is the leading cause of death. Clinical presentation guides towards therapeutic management that mostly includes corticosteroids, immunosuppressive medications, and/or physical therapy.

Key learning points: Digital ischemia could be a rare presentation of ASS. Clinical features of antisynthetase syndrome (ASS) include interstitial lung disease, ‘mechanic’ hands, myositis, polyarthritis and Raynaud’s phenomenon. Extensive myositis specific antibody testing is strongly recommended even if screening autoimmune serologies are unrevealing. Anti-PL-12 ASS has significantly lower prevalence of muscle symptoms (weakness and myalgia) and more association with Raynaud’s phenomenon as compared to those with anti-Jo1. It is imperative to recognize lesser-known manifestations of ASS in the absence of clinical myositis as delay in diagnosis and treatment worsens the prognosis.

Conflicts of interest: The authors have declared no conflicts of interest.