

## Exceptional Case

# A cardiorenal-pulmonary-cutaneous-muscle syndrome

Sebastian Schöpp<sup>1</sup>, Saban Elitok<sup>1</sup>, Markus Bieringer<sup>1</sup>, Wolfgang Schneider<sup>2</sup> and Friedrich C. Luft<sup>2</sup>

<sup>1</sup>Franz-Volhard Clinic, HELIOS Klinikum-Berlin, Berlin, Germany and <sup>2</sup>Charité Medical Faculty, Experimental and Clinical Research Center, Berlin, Germany

Correspondence and offprint requests to: Friedrich C. Luft; E-mail: luft@charite.de

### Abstract

Anti-synthetase syndrome is a relatively recently described auto-immune disease characterized by auto-antibodies to enzymes that acetylate transfer RNA (tRNA). Interstitial pulmonary disease and inflammatory myopathy are regular findings. Our patient also exhibited a lupus-like glomerulonephritis. An important clue was the presence of ‘mechanics’ hands. Nephrologists need to be aware of this syndrome.

**Keywords:** anti-synthetase syndrome; interstitial lung disease; lupus nephritis; mechanics hands

### The case

A 50-year-old plumber presented with worsening shortness of breath, muscle pain and progressive weakness to the point that he could no longer walk without assistance. Six months earlier he had been treated at another hospital for pneumonia that did not really resolve with treatment. Acute respiratory distress syndrome had developed necessitating intensive care. Muscle weakness was noted at that time and elevated muscle enzymes were reported but no specific diagnosis was made. He was discharged to a rehabilitation facility. On physical examination, it was found that he had wasted appearance, breathing rate of 22 per min with an oxygen saturation of 92% while breathing ambient air, heart rate 100 bpm, blood pressure 100/50 mmHg, and a temperature of 37.8°C. He had rales and percussion dullness bilaterally, no peripheral oedema, no murmurs or abdominal masses. Both thighs were tender to the touch and his palmar skin was thickened bilaterally.

The haemoglobin was 14 g/dL, white blood cell count 18.3 Gpt/L, while the serum electrolytes and creatinine levels were normal. His urinalysis showed proteinuria 2+ with ‘nephritic’ urinary sediment. Striking were creatine kinase 3545 U/L, creatine kinase MB 143 U/L, troponin 610 ng/L, lactate dehydrogenase 782 U/L and C-reactive protein 79 mg/L. A chest roentgenogram showed infiltrates and pleural effusions bilaterally with hilar adenopathy. Computed tomography (CT) confirmed these findings (Figure 1). Subpleural reticular opacities, bullous formation and traction bronchiolectasis were suggestive of a fibrotic interstitial process. Although the patient had no chest pain and a non-specific electrocardiogram, coronary angiography was done, but revealed only diffuse, peripheral disease.

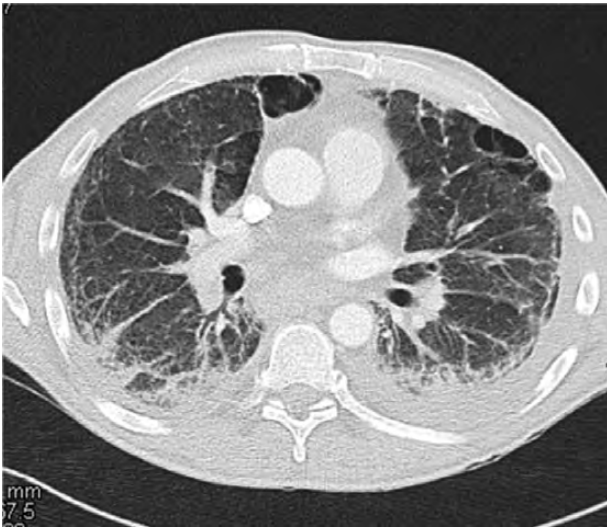
Nonspecific anti-nuclear antibodies were 1:640 U/L, anti-neutrophil cytoplasmic antibodies were negative,

complement fractions were borderline normal, no cryoglobulins were found, the serum creatinine level was 78 µmol/L, and 1.5 g proteins were excreted in the urine in 24 h. Magnetic resonance imaging of both thighs was done (Figure 2) and this gave a picture consistent with myositis. A renal biopsy was done (Figure 3) that showed focal proliferative changes and basement membrane thickening most reminiscent of lupus nephritis, World Health Organization classification III. Prednisone and cyclophosphamide were administered, which resulted in clinical improvement. What does this patient have and how can the diagnosis be established?

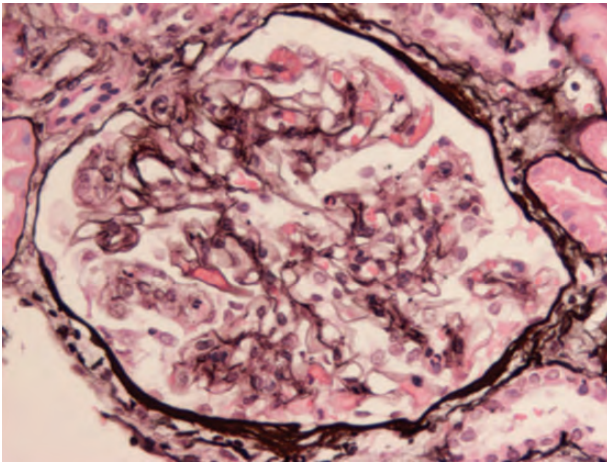
Anti-synthetase syndrome was defined about 20 years ago [1]. The condition is characterized by anti-synthetase auto-antibodies and commonly interstitial lung disease, inflammatory myopathy, polyarthritis, fever and ‘mechanics hands’, which our patient had [2]. To date, eight anti-synthetase auto-antibodies have been identified, all of which are directed against enzymes that acetylate transfer RNA (tRNA) [3]. The one first described and most commonly found is anti-Jo-1 (directed against histidyl-tRNA synthetase). Although they are less common, the seven other auto-antibodies in this group (anti-PL-12, anti-PL-7, anti-EJ, anti-OJ, anti-KS, anti-YRS and anti-Zo) confer a similar clinical phenotype [2].

Our patient had glomerulonephritis and a renal picture reminiscent of lupus erythematosus. Positive ANA antibodies are found in about half of the patients, but clinical renal disease is not that common [4]. The patient recently described by Christopher-Stine *et al.* had normal renal function and only trace proteinuria [2]. Our patient had antibodies directed against PL-7, a threonyl tRNA synthetase.

From our patient, we learned that the anti-synthetase antibody syndrome is a protean chronic autoimmune condition in which interstitial lung disease and inflammatory myopathy are prominent findings. We

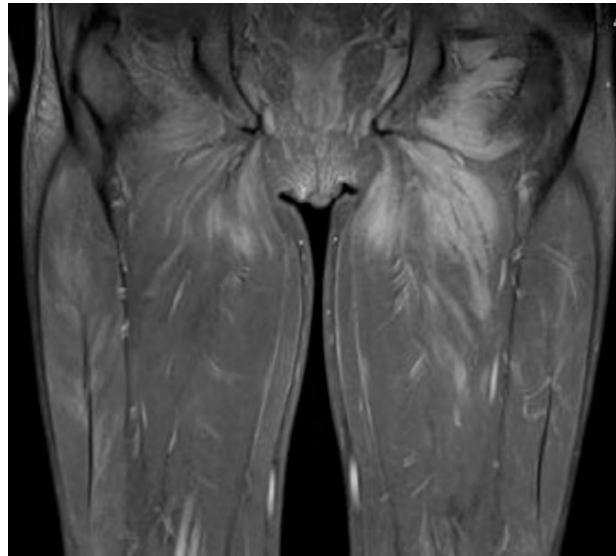


**Fig. 1.** Selected axial CT image shows bilateral effusions with reticular and ground-glass opacities and bullous formations.



**Fig. 2.** Single glomerulus with focal proliferation, basement membrane thickening and hyaline deposits.

advise that clinicians always carefully inspect the patient's hands, including palms and fingertips. Antinuclear antibodies are common in anti-synthetase antibody syndrome, while severe renal involvement is not. Our



**Fig. 3.** Magnetic resonance imaging of both thighs consistent with myositis.

patient will hopefully not be an exception to that rule. However, glomerulonephritis may occur.

*Conflict of interest statement.* None declared.

## References

1. Marguerie C, Bunn CC, Beynon HL et al. Polymyositis, pulmonary fibrosis and autoantibodies to aminoacyl-tRNA synthetase enzymes. *Q J Med* 1990; 77: 1019–1038
2. Christopher-Stine L, Robinson DR, Wu CC et al. A 21-year-old man with fevers, arthralgias, and pulmonary infiltrates. *N Engl J Med* 2012; 367: 2134–2146
3. Mimori T, Imura Y, Nakashima R et al. Autoantibodies in idiopathic inflammatory myopathy: an update on clinical and pathophysiological significance. *Curr Opin Rheumatol* 2007; 19: 523–529
4. Dugar M, Cox S, Limaye V et al. Clinical heterogeneity and prognostic features of South Australian patients with anti-synthetase autoantibodies. *Intern Med J* 2011; 41: 674–679

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