

# Synovitis with pitting edema as the presenting manifestation of antisynthetase syndrome

**Introduction:** The Anti-Synthetases Syndrome (ASS) is an autoimmune disease associating inflammatory myopathy, interstitial pneumonitis, polyarthritis, raynaud syndrome, characteristic cutaneous involvement ("hands of mechanics") and autoantibodies anti-aminoacyl transfer RNA synthetases including anti-JO-1. One can also observe general manifestations like fever or asthenia. We report the case of a patient who presented acute oedematous polyarthritis that revealed an anti-synthetase syndrome.

**Observation:** This is a 65-year-old patient with a history of hospitalization in pneumology for acute respiratory distress syndrome related to infectious hypoxemic pneumonitis, admitted in 2017 to the rheumatology department for exploration of acute polyarthritis, evolving for 1 month, affecting the elbows, knees, wrists, small joints of the hands and ankles associated with distal edema at the 4 members keeping the bucket. The patient was afebrile. On neurological examination, he had weak osteotendinous reflexes in the lower limbs without associated muscular deficit. The rest of the somatic examination was without notable abnormalities. In biology, he had a biological inflammatory syndrome (CRP 37.7 mg/l), lymphopenia at 1000 El/mm<sup>3</sup>, LDH at 2 times normal and CPK at 3 times the normal. In the immunoassay, antinuclear antibodies were positive at 1/800 as well as anti-ENA, anti-JO-1. The tumor markers were negative. X-rays of the affected joints were without abnormalities. Thoraco-abdominopelvic Computed Tomography (CT) showed ventilatory disturbances of both basal pyramids with bronchiectasis and low abundance left pleural effusion. The functional respiratory explorations had objectified a restrictive syndrome. Muscle biopsy revealed a discrete perivascular inflammatory infiltrate with no type of necrosis or regeneration. Faced with these elements, the diagnosis of ASS was retained and the patient was put on corticosteroids at the dose of 1 mg/kg/day with a clear clinical-biological improvement. The patient was lost to follow-up for 5 months, then he was referred to rheumatology in a febrile state associated with a muscular deficit of the 2 scapular and pelvic belts, following the abrupt cessation of his treatment on his own. He also had a biological inflammatory syndrome (CRP 166.5 mg/l) with myolysis (CPK at 4 times normal and LDH at 3 times normal). He received 3 boluses of methylprednisolone (1 gram/bolus) relayed by prednisolone at a dose of 1 mg/kg/day for one week. However, at a dose rate of 0.3 mg/kg/day, the patient relapsed and presented with fever and biological inflammatory syndrome; hence the decision to switch to cyclophosphamide as a monthly infusion at a dose of 0.7 mg/m<sup>2</sup> body surface area combined with corticosteroid therapy at a dose of 0.3 mg/kg/day. The patient received a total of 6 courses of cyclophosphamide with a poor response to treatment. It was recommended, therefore, to put him on rituximab and while waiting for this treatment he was put on azathioprine 100 mg/day.

**Conclusion:** Our clinical case highlights the importance of thinking about the ASS in polyarthritis, which is also associated with interstitial lung disease. Indeed, the rapid diagnosis of this syndrome allows a good management of the patient and avoids evolving into a severe form of the disease may be life-threatening especially by pulmonary fibrosis. Similarly, it is essential to better understand the pathophysiological mechanisms of the ASS in order to implement effective therapeutics.

**Keywords:** antisynthetase syndrome • autoimmune disease

## Introduction

Antisynthetase Syndrome (ASS) is a rare

autoimmune condition characterized by inflammatory myopathy, interstitial lung

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disease, joint involvement, raynaud's phenomenon, characteristic skin involvement ("mechanic's hands") associated with anti-aminoacyl transfer RNA synthetase autoantibodies notably anti-JO-1 [1]. General manifestations such as fever and asthenia may also be observed [2]. The diagnosis is based on a global approach that includes clinical, biological, radiological features as well as muscle biopsy findings [3]. Treatment of ASS is not well codified and may be challenging [2]. Thus, immunosuppressive therapies are often used to control pulmonary and muscle manifestations of the disease [3, 4].

To our knowledge, ASS may exceptionally manifest with pitting edema, unlike other autoimmune diseases [5]. We report a case of a patient who presented with synovitis with pitting edema revealing an antisynthetase syndrome.

### Observation

A 65-year-old man presented with a one-month history of a polyarthritis affecting the elbows, knees, wrists, small joints of the hands and ankles along with an edema of the lower limbs. The patient had no fever. Neurological examination showed weak osteotendinous reflexes in the lower limbs with no muscle weakness.

Laboratory tests revealed an elevated serum C-reactive protein (CRP) level (37.7 mg/l), a normocytic anemia, lymphopenia (1000 elements/10<sup>3</sup>) and increased Lactate Dehydrogenase (LDH) and Creatine Phosphokinase (CPK) levels at 3 times the upper limit of normal. On the Immunological assay, antinuclear antibodies were positive at 1/800 as well as anti ENA and anti JO-1. Tumour markers were negative.

X-ray of the affected joints were normal. The thoraco-abdomino-pelvic CT scan showed ventilatory disorders in the basal pyramids with bronchiectasis, a ground-glass appearance and a small amount of left pleural effusion.

Lung functional evaluation revealed a restrictive syndrome. On muscle biopsy, a discrete perivascular inflammatory infiltrate was found without any necrosis or regeneration. Based on these findings, the diagnosis of antisynthetase syndrome was retained and the patient received corticosteroids at the dose of 1mg/kg/day with a clear clinical and biological improvement. The patient had been lost to follow-up for 5 months, then he presented with a fever along with a muscular deficit affecting the scapular and pelvic girdles. In fact, the patient had decided to stop his treatment. Laboratory finding showed elevated inflammatory markers (CRP 166.5 mg/l), as well as an increased serum CPK and LDH

levels up to 4 times the normal limit. He received 3 boluses of methylprednisolone (1 gram/bolus) followed by prednisolone (1mg/kg/day) for a week. However, on tapering to a dose of 0.3 mg/kg/day, the patient relapsed and developed a fever and a biological inflammatory syndrome; hence the decision to switch to a monthly infusion of cyclophosphamide at a dose of 0.7 mg/m<sup>2</sup> body surface area in combination with corticosteroids at a dose of 0.3 mg/kg/day. The patient received a total of 6 courses of cyclophosphamide with a poor response to treatment. One week after the onset of treatment, the patient developed a generalised pruritic erythema rash which was diagnosed as an allergic reaction to cyclophosphamide according to pharmacovigilance investigation. The patient was treated with antihistaminic drugs. However, a hypopigmented rash with some scaling persisted for several weeks. Cyclophosphamide was therefore stopped and the patient was put on Azathioprine 100 mg per day with a good response to treatment.

### Discussion

Antisynthetase syndrome is an infrequent condition that belongs to the group of inflammatory myopathies [2]. Initial presentation of ASS with a distal edema is unusual [1]. Actually, edema is generally not associated with myositis, however it may be related to arthritis or scleroderma, in the group of overlapping myositis [1]. ASS can, in fact, manifest by a symmetrical distal polyarthritis very similar to rheumatoid arthritis and the muscular manifestations may occur late in the illness or even be subclinical [6], as shown in our case report. Lefevre et al [7] reported in their multicentre study 40 cases of seronegative polyarthritis revealing ASS with late and infrequent pulmonary and muscular involvement.

Joint involvement is observed more commonly in patients with serologically positive ASS (64% to 83%) [8]. A meta-analysis of 27 studies found that patients with anti-Jo1 antibodies were more likely to present with myositis, mechanic's hands and arthralgias compared to those with no anti-Jo1 antibodies [9]. Besides, ASS should be considered in patients who present with arthritis with some particularities such as negative or weakly positive anti-CCP antibodies [10], positive antinuclear antibodies [10], raynaud's phenomenon [10] or fissure damage of the fingers. Four joint disorders have been described in ASS: simple arthralgias, non-erosive and non-deforming polyarthritis of the small joints, deforming but non-erosive polyarthritis with subluxation of the thumb, and erosive symmetrical polyarthritis [8].



**Figure 1. Extensive lesions on the body that are depigmented and itchy.**

Lung involvement is the most common extramuscular manifestation [11] and patients with ASS have a worse prognosis compared with patients with polymyositis and dermatomyositis as the pulmonary damage remains the main determinant of survival [12].

Although inflammatory myopathies have been associated with malignancy [13], no cancer was detected in our patient.

Due to the lack of prospective data to guide treatment decisions, ASS management remains a challenge for practitioners. High-dose corticosteroid therapy (1mg/kg/day) seems to be effective in the first line of treatment [2, 8] and acts in particular on muscular, articular and general manifestations and certain forms of interstitial lung disease [8]. Immunosuppressive drugs have been tested and have proven to be effective, especially as they allow cortisone sparing. Cyclophosphamide,

especially in pulmonary forms, mycophenolate mofetil, methotrexate, azathioprine and intravenous immunoglobulin have been used with variable results [2]. Rituximab has been used as a second-line treatment for patients with interstitial lung disease resistant to conventional therapies with moderate results [2, 14].

### **Conclusion**

We conclude that synovitis with pitting edema can be a clinical manifestation of antisynthetase syndrome. Actually, we should consider the ASS when an atypical arthritis is associated with interstitial lung disease and muscle involvement. Indeed, the rapid diagnosis allows a good management of the illness and avoids the evolution towards a severe form especially by the fibrosing lung disease. It is also essential to better understand the pathophysiological mechanisms of ASS in order to implement effective therapies.

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