Nonspecific interstitial pneumonia revealing an antisynthetase syndrome

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Abstract

One of the most common interstitial lung diseases in antisynthetase syndrome is nonspecific interstitial pneumonia (NSIP). A 49-year-old woman presented with slow progression exertional dyspnea, myalgia, and arthralgia. The radiological findings indicated an NSIP pattern. Autoantibodies were found to be positive, but no lung biopsy was performed. Even though corticosteroid therapy significantly improved the patient's dyspnea, the patient developed mechanic's hands, the anti-synthetase antibody (PL12) became positive, and creatine phosphokinase (CPK) levels increased. As a result, the antisynthetase syndrome was established. The patient follow-up after three years revealed an improvement in symptoms under corticosteroid therapy.

Learning points

This case report is important because:

- It shows an incomplete presentation of a rare health condition
- Lung biopsies were not performed even after the progression of symptoms under corticosteroid therapy
- Even though the patient has bad prognosis factors, his condition improved under standard corticosteroid therapy with no need for immunosuppressive therapy.

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Introduction

Interstitial lung disease (ILD) is the most common extra muscular manifestation of the antisynthetase syndrome (ASS), which is a rare systemic autoimmune disease related to anti-aminoacyl transfer RNA synthetase antibodies. In addition to the classical triad made of ILD, myositis, and positivity to antisynthetase antibodies, other less specific symptoms such as polyarthritis, mechanic's hands, Raynaud's phenomenon, or symptom overlapping with Sjogren syndrome and systemic sclerosis, can be found. Heterogeneity in the observed phenotypes and the severity of the disease make difficult the diagnosis and the treatment of ASS. In all cases, pulmonary lesions are major determinants of morbidity and mortality. Non-specific interstitial pneumonia (NSIP) is one of the most identified patterns. The atypical and incomplete clinical presentation of ASS and the difficulty of radiological diagnosis of NSIP can lead to a challenging situation.

Case Report

A 49-year-old woman with a medical history of hypothyroidism treated by a hormonal substitution, presented to our pulmonology department with exertional dyspnea with a slow progression, myalgia, inflammatory arthritis and a dried mouth sensation, for three months. She was not a smoker and had no professional exposure to any toxic. Bilateral pulmonary crepitations were objectivated, with clubbing of the fingernails and curled fingers. Chest X-ray showed poorly bounded opacities especially at the base level with rail images (Figure 1). High resolution computed tomography scan (HRCT) showed extensive ground glass opacities (GGO), with mild reticulations, and traction bronchiectasis, with a

basal predominance of the abnormalities and a relative subpleural sparing. Peripheral parenchymal condensations were present too. NSIP was strongly radiologically advocated. An etiological approach was done. Drug toxicity was ruled out. Blood work showed no abnormalities neither in blood counts, nor liver and kidney functions. Bronchoscopy was normal. Lymphocyte excess was found in the Bronchoalveolar lavage (20%). Accessory salivary gland biopsy showed a grade 2 sialadenitis. Immunological investigations were negative, except for a positive antinuclear antibody (1/160) with a positive RO-52 antibody, thus nonspecific interstitial pneumonia with autoimmune features was diagnosed. The pulmonary functions test showed a mid-restrictive syndrome. Corticosteroid therapy was initiated (1 mg/kg/day) for four weeks. A progressive digression was scheduled. Despite the improvement of the dyspnea, the patient developed mechanic's hands. The antisynthetase syndrome was confirmed facing a radiological aspect of (NSIP), in a patient suffering from myalgia with an increased CPK level, arthritis, mechanic's hands, and a secondary positivity of anti-synthetase antibody (PL12). After three years, she is still under 5 mg of prednisone with a great improvement in her symptoms.

Discussion

The diagnosis of (NSIP) is not easy. But the real challenge is to determine even it is idiopathic or related to another condition. In all cases, the pathogenesis involves aggressions, inflammatory responses, and fibrosis. Autoantibodies against cytokeratin and vimentin are frequently identified in patients with NSIP [1-3], which makes an autoimmune etiology very relevant, even though the initial aggression remains unknown [4]. It is common to find NSIP in patients with autoimmune disorders such as dermatomyositis, and Sjogren's syndrome [5,6]. By the way, patients with NSIP must be closely monitored because autoimmune disorders can appear afterward. In our patient, NSIP was diagnosed prior to an ASS.

The complete form of ASS includes the triad of ILD, myositis, and arthritis which is only reported in 19.5% at disease onset according to Cavagna *et al*.'s study and the absence of any of these elements is considered as an incomplete form [7,8]. In our patient, at first, the diagnosis of NSIP was based on CT scan findings because of respiratory manifestations. Arthralgia and myalgia were present at disease onset. Secondarily, mechanic's hands argued in favor of ASS, but based on literature, it is not a frequent association [9]. Autoantibodies were initially identified but specific anti-synthetase antibody (PL12) showed up afterward.

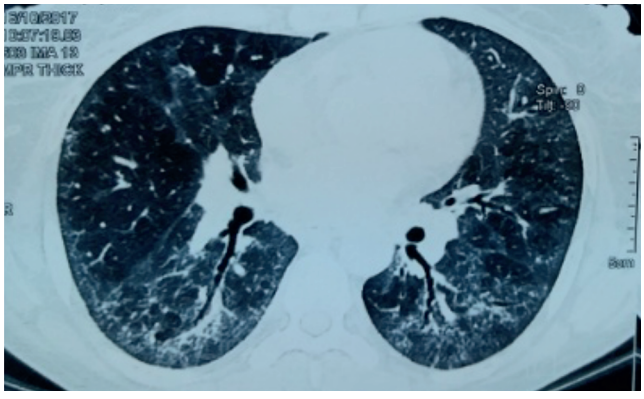

Figure 1. Ground glasses opacities with mild reticulations, and traction bronchiectasis, with a basal predominance of the abnormalities and a relative subpleural sparing.

ILD is the most frequent complication of the ASS in 69% to 100% of cases [8)]. It was noted to be the initial presentation in 15% to 30% of ASS patients in various studies and in our patient, too [10].

Among ILD, to establish the diagnosis of NSIP itself, there is a lack of approval among radiologists. HRCT aspect may be suggestive of NSIP but cannot reliably rule out its main differential diagnosis which is idiopathic pulmonary fibrosis and overlap NSIP-organized pneumonia which has a worse prognosis [11]. In some cases, we can find features that indicate the etiology of NSIP. In this clinical case, we discovered interstitial pneumonitis with elements of fibrosis, like bronchiectasis and reticulations but GGO was predominant. It would have been easier if the diagnosis of ASS was made prior to NSIP. Even though there is difficulty in making the diagnosis and the etiology of NSIP, there are no fair recommendations about the necessity of an anatomopathological study unless an idiopathic context is present. If NSIP is related to collagen and connective tissue disease, it becomes no longer compulsory [12]. That is why no biopsy was done on our patient.

In some cases, transbronchial cryobiopsy, or surgical lung biopsy, is needed especially in patients with no autoimmune features. A selection of biopsy targets with the surgeon and the radiologist must be done. Getting samples from different lobes may improve the relevance of the pathological reading [13]. Some series of surgical lung biopsies showed that an aspect of NSIP on the HRCT corresponds, histologically to usual interstitial pneumonia (UIP) in 40% of cases [14].

Antisynthetase syndrome associated with ILD has a bad prognosis, especially if the HRCT scan shows a pattern of usual interstitial pneumonia and the respiratory muscle is involved. ASS with NSIP pattern has a bad prognosis too, especially in the male gender, patients with a low DLCO, and positive autoantibodies anti-RO-52. Our patient has no bad prognosis factors except a positive anti-Ro-52 [9,15]. The evolution was favorable with a regression of symptoms under corticosteroid therapy. According to the latest literature, early treatment with corticosteroids, mycophenolatemofetil and rituximab improves the prognosis [16].

Conclusions

ASS is a rare autoimmune disease and represents a distinct entity within idiopathic inflammatory myopathies. ILD is the main determinant of morbidity and mortality. The role of lung biopsy remains controversial, especially in the NSIP pattern. An integrated clinical, radiological and pathological approach to ILD should be favored. There are no standardized treatment guidelines for ASS because of its rarity.

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