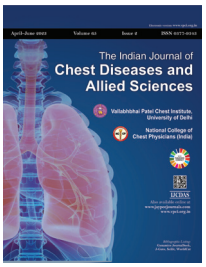
CASE REPORT

Organizing Pneumonia with Bilateral Pleural Effusions as the First Manifestation of Antisynthetase Syndrome: A Case Report



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Abstract

Antisynthetase syndrome (ASS) is a rare immune-mediated disorder characterized by interstitial lung disease (ILD) and polymyositis (PM)/dermatomyositis (DM) in association with antiaminoacyl-transfer-RNA antibodies most commonly anti-JO-1 antibodies. We present a case of a 67-year-old man who had uncontrolled type 2 diabetes and complained of coughing, dyspnea, and fever. The primary health center (PHC) physician diagnosed him with bilateral pneumonia based on a chest X-ray. After receiving multiple antibiotics over the course of a month, the patient was referred to us with nonresolving pneumonia. The patient later developed proximal muscle weakness and features of "mechanic's hand" and strongly positive for anti-JO-1 and anti-RO52 antibodies with high creatinine phosphokinase (CPK) levels and features of organizing pneumonia (OP) with bilateral pleural effusions which led to diagnosis of ASS. The patient was started on oral prednisolone and then switched to mycophenolate mofetil, which resulted in a significant difference in both clinical and radiological results. Furthermore, ASS presenting as OP with bilateral pleural effusion is a rare finding, especially as the first manifestation. This report highlights the significance of having an autoimmune workup, comprehensive medical evaluation, and long-term follow-up on patients to screen them for pneumonia and other ILDs.

Keywords: Anti-JO-1 antibodies, Anti-RO52 antibodies, Antisynthetase syndrome, Bilateral pleural effusions, Case report, Mycophenolate mofetil, Organizing pneumonia.

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Abbreviations used in this Article

ASS = Antisynthetase syndrome; BOOP = Bronchiolitis obliterans with organizing pneumonia; CPK = Creatinine phosphokinase; DAD = Diffuse alveolar damage; DM = Dermatomyositis; HRCT = High-resolution computed tomography; ILD = Interstitial lung disease; NSIP = Nonspecific interstitial pneumonia; OP = Organizing pneumonia; PHC = Primary health center; PM = Polymyositis; RA = rheumatoid arthritis; RT-PCR = Reverse transcription polymerase chain reaction; UIP = Usual interstitial pneumonia.

Aim

Patients presenting with organizing pneumonia (OP) and other ILDs should undergo autoimmune tests, a thorough medical examination, and long-term follow-up to ensure an accurate diagnosis of antisynthetase syndrome (ASS).

Background

Skeletal muscle and skin are particularly affected by ASS, a rare immune-mediated and systemic inflammatory illness. Antiaminoacyl-transfer-RNA antibodies, most often anti-JO-1 antibodies, characterize polymyositis (PM) and dermatomyositis (DM). Also, PM–DM, ILD, "mechanic hand," fever, and Raynaud's phenomenon are just a few of the many clinical symptoms of ASS.[1,2] Women are disproportionately affected, but adults overall suffer from this illness. The reason why is unclear.[2] Anti-JO-1 is the most prevalent of the antisynthetase antibodies and is present in about 80% of people with ASS, the others being PL-7, PL-12, OJ, and EJ.[3,4] Antisynthase syndrome is characterized by ILD and can develop even in the absence of myositis (myopathic ILD). The most common symptom of ASS is myositis, but the condition can also manifest with interstitial lung disease (ILD) and joint involvement. They also have an impact on the heart, lungs, and esophagus. Pulmonary involvement is common and may be a major cause of morbidity.[5] The development of PM/DM and the onset of ILD associated with ASS may occur simultaneously or at a later time. Interstitial lung disease can manifest in a variety of ways. Some of these ways include OP, diffuse alveolar damage (DAD), generalized ILD, and nonspecific ILD. The condition known as pleural effusion occurs seldom. Patients with a history of bronchiolitis obliterans with organizing pneumonia (BOOP) are unusually documented to appear initially with organizing pneumonia. We present a case of ASS that was misdiagnosed and treated as pneumonia at a primary care facility before being sent to us for further assessment.

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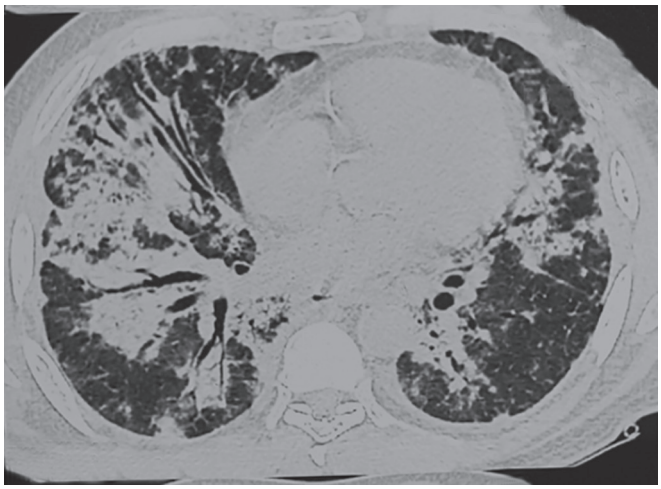


Fig. 1: The HRCT chest showing bilateral patchy opacities with air bronchograms suggestive of organizing pneumonia

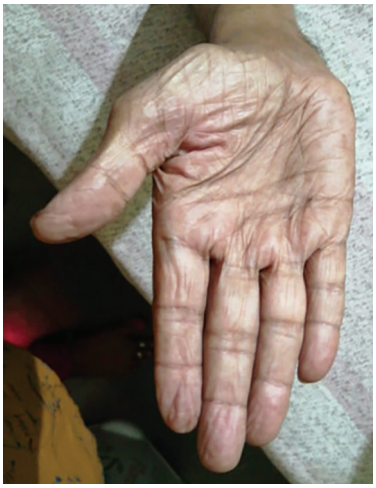


Fig. 2: Dermatological signs suggestive of "mechanic's hand" with thickened and cracked skin on the palmar surface of hands

Case Description

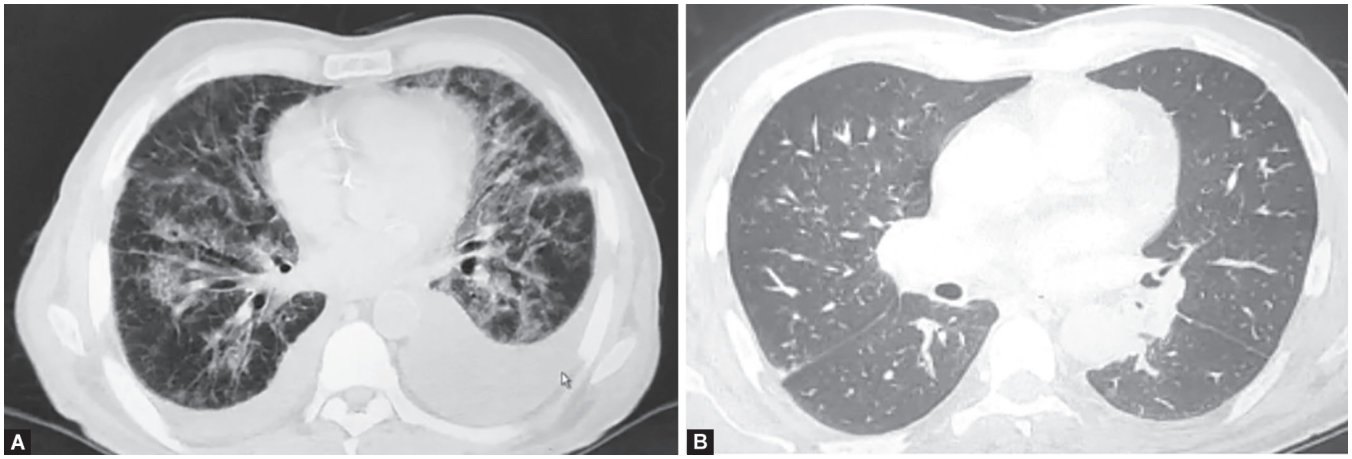
A 67-year-old man visited PHC complaining of diabetes mellitus type 2, respiratory distress, fatigue, and general illness. He was initially diagnosed with bilateral pneumonia using a chest scan, given a course of various medications over the course of a month, and then referred to us with difficult-to-treat pneumonia. On presentation patient's SpO_2 was 96% with tachycardia and normal blood pressure. The evaluation of his respiratory system indicated bilateral fine end-inspiratory crackles. High-resolution computed tomography (HRCT) of the chest revealed bilateral multifocal patchy consolidations, especially in lower zones, with minor bilateral pleural effusions (Fig. 1). The COVID-19 reverse transcription polymerase chain reaction (RT-PCR) was negative. Reports on bronchoalveolar lavage were not conclusive. Exudative lymphocytic pleural effusion was discovered following thoracentesis. The patient was given oral corticosteroids after a preliminary diagnosis of organizer pneumonia. There was no evidence of muscular pain, weakness, joint issues, or palm and finger thickening throughout this presentation. After being out of contact for 6 months due to the COVID-19 pandemic, presented with progressive exertional dyspnea, cough, loss of weight and appetite, proximal muscle weakness, palmar skin changes, and was wheelchair-bound for 2 months. Dermatological features were suggestive of "mechanic's hand" (Fig. 2) with thickened and cracked palmar skin. In addition, he complained of severe gastric reflux disease symptoms. Except for proximal muscular weakness, both the upper and lower extremities were neurologically normal upon evaluation. He had poorly controlled type 2 diabetes, with a glycated hemoglobin level of 10.9%. Two-dimensional echocardiography revealed tachycardia with normal-sized chambers and good left and right ventricular function. Creatinine phosphokinase (CPK) levels were 942 U/L, erythrocyte sedimentation rate (ESR) was 40 mm/first hour, and thyroid stimulating test (TSH) was 4.78 mIU/L. A repeat HRCT chest revealed the same findings as the initial scan with increased bilateral pleural effusions. The patient's clinical and radiographic features suggested that a diagnosis of PM/DM-ILD/ASS should be seriously evaluated. Diagnostic criteria for ASS were established by Connors et al.[5] etc. and Solomon et al.;[1] a significant positive ANA and myositis profile for anti-JO-1 and anti-RO52 antibodies with high CPK levels led to a diagnosis of ASS. In this example, the diagnostic criteria were met without the need for an invasive surgery like a lung biopsy, which carries the risk of consequences. Clinical and radiological responses improved dramatically after the patient was started on oral prednisolone and then switched to mycophenolate mofetil (Fig. 3).

All individuals with idiopathic pulmonary fibrosis (ILD) without a known cause should be tested for antisynthetase antibodies. Antisynthetase syndrome was first formally defined in 2010 by Connors et al.[5] Mechanic's hand, Raynaud's phenomenon, myositis, inflammatory bowel disease, arthritis, and/or fever for no apparent reason are all required for a diagnosis of ASS (Table 1). More stringent criteria were provided by Solomon et al., which call for the presence of either two major requirements or one major requirement and two minor needs in addition to the presence of aminoacyl-tRNA synthetase autoantibodies.[1]

The diagnostic criteria are given by Connors et al. and Solomon et al. allow the ASS to be recognized as a unique entity, which may be beneficial in both clinical and research contexts. Nonspecific interstitial pneumonia (NSIP), diffuse alveolar damage (DAD), usual interstitial pneumonia (UIP), and OP are all patterns shown on histology. The incidence of these histological characteristics differs between studies, with NSIP being the most common pattern.[1,5] Although OP is frequently observed in rheumatoid arthritis (RA), presenting after the beginning of arthritis, it is uncommon in PM–DM, manifesting prior to the development of myositis as in this patient. However, PM complicated by organized pneumonia has a better prognosis than UIP or DAD.[6]

However, we caution that the absence of an antisynthetase antibody does not rule out the presence of antisynthetase syndrome because autoantibody levels fluctuate with disease activity, centers, and laboratories vary in which autoantibodies they routinely test, and there may be undiscovered autoantibodies not yet available for laboratory detection.[6] If an antisynthetase antibody is not present, it is not feasible to make a formal diagnosis of ASS and in those patients, histology gives a clue to the diagnosis. However, these patients may benefit from pharmacologic therapy, as is indicated for patients with a formal diagnosis of ASS.[6,7]

Raynaud's phenomenon, severe gastric reflux illness, and nonerosive arthritis are all conditions that frequently coexist in patients with ASS. Furthermore, ILD is the most common presenting symptom of ASS and a major cause of complications and death.



Figs 3A and B: The HRCT chest suggestive of improved opacities showing; (A) Ground glass opacity (GGO) with bilateral mild-to-moderate pleural effusions (right > left) showing; (B) Decreased opacities and pleural effusions compared to previous HRCT chest after starting on steroids and mycophenolate mofetil

Table 1: Proposed diagnostic criteria for ASS

Connors et al.[5]	*Solomon et al.*[1]
Required: Presence of an antiaminoacyl tRNA synthetase antibody	Required: Presence of antiaminoacyl tRNA synthetase antibody
In addition, one or more of the following clinical features:	In addition, two major or one major and two minor following criteria:
• Raynaud's phenomenon • Arthritis • ILD • Fever (not attributable to another cause) • Mechanic's hands (thickened and cracked skin on hands, particularly at fingertips)	*Major:* 1. Interstitial lung disease (not attributable to another cause) 2. PM or DM by Bohan and Peter criteria *Minor:* 1. Arthritis 2. Raynaud's phenomenon 3. Mechanic's hands

tRNA, transfer RNA

In patients with ASS, myositis may not manifest until much later in the course of the disease, if at all. The hyperkeratosis and scaling that characterize mechanic's hands should be looked for in the hands of patients with interstitial lung disease to urge further testing for antisynthetase antibodies and muscle enzymes.[7,8]

Over 50% of those with ASS experience some form of joint pain, from mild arthralgia to debilitating erosive arthritis. "Mechanic's hands" affects 30% of patients, while Raynaud's phenomenon affects 40% of patients.[9]

Our patient was diagnosed with ASS based on the presence of a positive anti-JO-1 antibody, which accompanied the patient's other symptoms of fever, mechanical hand, PM, and ILD. Our patient did not have "mechanic hands" or proximal muscle weakness at the time of diagnosis, but these symptoms developed later.

The patient's condition has stabilized on a tapering schedule of steroids and mycophenolate mofetil after a favorable response to steroid therapy.

Conclusion

It is unusual for ASS to manifest first as OP with bilateral pleural effusion. Patient screening for chronic or OP and other ILDs should include an autoimmune workup, comprehensive clinical evaluation, and long-term follow-up, as demonstrated by this case. Even in diseases with a dismal prognosis, patient outcomes and survival can be improved with the early introduction of steroids and immunosuppressive medicines.

Clinical Significance

Interstitial lung disease (ILD), PM/DM, and antiaminoacyl-transfer-RNA antibodies (mainly Anti-JO-1) are all hallmarks of antisynthase syndrome (ASS), a rare immune-mediated disease. Differentiating AS from other inflammatory myopathies needs a thorough clinical, serologic, and radiologic assessment of AS-ILD because of its widespread pulmonary involvement and rapid progression. Glucocorticoids are the backbone of treatment, although often other immunosuppressive medicines are needed to get the condition under control. Patients' responses to treatment may be affected by their antibody profile, making prompt diagnosis and symptom detection crucial. The combination of the patient's symptoms (fever, mechanics hands, PM, ILD, and positive anti-JO-1 antibodies) led us to conclude that our patient was suffering from ASS. The patient did not present with "mechanical hand" or proximal muscle weakness at the time of diagnosis but developed these symptoms subsequently.

The patient's condition is stable while on a tapering schedule for steroids and mycophenolate mofetil.

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