Case Report

Non-Resolving Pneumonia Masquerading Antisynthetase Syndrome

Aditya Aggarwal, Vinod Joshi and Shubhra Jain

Institute of Respiratory Diseases, SMS Medical College, Jaipur (Rajasthan), India

This article is available on www.vpci.org.in

ARTICLE INFO

Received: April 17, 2020

Accepted after revision: February 2, 2021

Indian J Chest Dis Allied Sci 2021;63:101-104

KEY WORDS

High resolution computed tomography, Creatine kinase, Video assisted thoracoscopic surgery, Non-specific interstitial pneumonia, Antisynthetase syndrome.

ABBRIVATIONS USED IN THIS ARTICLE

HRCT = High Resolution Computed Tomography

CK = Creatine kinase

ILD = Interstitial Lung Disease

mMRC = modified Medical Research Council

CBNAAT = Cartridge Based Nucleic Acid Amplification Test

CTD = Connective Tissue Disorder

CCP = Cyclic Citrullinated Peptide

VATS = Video-Assisted Thoracic Surgery

EULAR = European League Against Rheumatism

ACR = American College of Rheumatology

Abstract

We report the case of a 35-year-old, non-smoker female who presented with arthralgia, dyspnoea, chest pain, fever and cough. Chest radiograph (postero-anterior view) showed ill-defined opacities in bilateral lower lung zones. High resolution computed tomography (HRCT) of chest revealed bilateral lower lobe consolidation with air bronchogram and interstitial septal thickening with ground-glass opacity. Diagnosis of polymyositis was confirmed by high titre of Jo-1 antibody and serum creatine kinase (CK) (1216 U/L). Video-assisted thoracoscopic lung biopsy showed evidence of non-specific interstitial pneumonia.

Introduction

Antisynthetase syndrome is a clinical condition characterised by polymyositis/dermatomyositis associated with antisynthetase antibodies, arthritis, Raynaud's phenomenon, mechanic's hands, and interstitial lung disease (ILD). Pulmonary complications in polymyositis has been reported in up to 40% of cases with the prevalence of ILD ranging from 5% to 30%. Arthralgia and respiratory symptoms occur simultaneously in less number of cases.

Case Report

A 35-year-old, non-smoker, female presented with dyspnoea mMRC (modified Medical Research Council) grade 2, high grade fever, chest pain, productive cough since 10 days with no improvement on antibiotics. On further clinical evaluation, she had bilateral proximal interphalangeal joints arthralgia, bilateral proximal muscle weakness and dyspnoea since six months. Patient had no other chronic diseases, such as hypertension or diabetes and no history of alcohol abuse. She had no past history of anti-tuberculosis treatment. She did not give any history of exposure of home/work-place and history of any drug intake.

Corresponding author: Dr Shubhra Jain, Assistant Professor, Institute of Respiratory Diseases, SMS Medical College, Jaipur (Rajasthan); India; E-mail: shubhrajainap@gmail.com

On general physical examination, Grade 3 clubbing was present and roughening and cracking at tip of the skin and sides of the fingers was present (Figure 1). On auscultation crepitations were present in bilateral infra-clavicular and infra-axillary areas.

Complete blood count, liver and renal function tests were within normal limits. C-reactive protein was high (7mg/L). Serology human immunodeficiency virus was non reactive. *Mycobacterium tuberculosis* was not detected by CBNAAT (Cartridge-based nucleic acid amplification test). Chest radiograph (postero-anterior view) showed bilateral heterogeneous opacities in the lower zones. High-resolution computed tomograph of chest showed bilateral lower lobe patchy infiltrations with ground-glass opacities (Figure 2).

In view of non-specific interstitial pneumonia pattern, patient was screened for connective tissue disorder (CTD). Anti-nuclear antibody test was positive (1:80 titre with cytoplasmic and speckled pattern). Rheumatoid factor was positive (307 IU/mL). Anti-cyclic citrullinated peptide (anti-CCP) was negative. Serum creatine kinase was 1216U/L. CTD profile showed positive Jo-1 antibody. Video-assisted thoracic surgery (VATS) lung biopsy showed small alveolar spaces separated by uniformly thickened alveolar wall with lymphoplasmacytic infiltration along with mild fibrosis (Figure 3). On the basis of clinical, radiological, and histological assessment, a diagnosis of antisynthetase syndrome was made.

Figure 1. Clinical photograph of the finger of the patient showing roughening and cracking at tip of the skin and sides of the fingers (Mechanic's Hand).

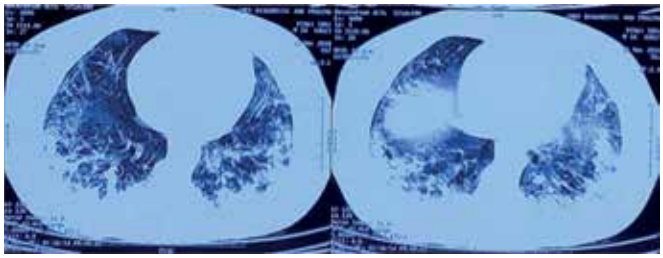

Figure 2. High resolution computed tomography of the chest showing bilateral lower lobe consolidation with air bronchogram and interstitial septal thickening with ground glass-opacities.

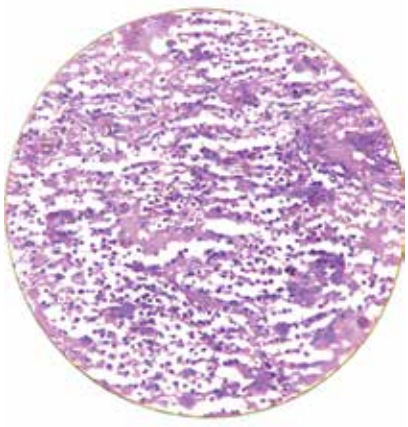

Figure 3. Photomicrograph showing small alveolar spaces separated by uniformly thickened alveolar wall with lymphoplasmacytic infiltration along with mild fibrosis typical of non-specific interstitial pneumonia pattern.

Discussion

Antisynthetase syndrome is a clinically heterogenous small subset of DM-PM which are idiopathic inflammatory myopathies. It consists of a constellation of the following symptoms: myositis, arthropathy, fever, Raynaud's phenomenon, Mechanic's hands, and ILD, along with the presence of serum autoantibodies against aminoacyl-tRNA synthetases, most commonly the anti-Jo-1 antibody. Other relevant antibodies include anti-PL-7 and anti-PL-12. In a patient who presents with both myositis and ILD, an anti-Jo-1 antibody is a very sensitive and specific test for antisynthetase syndrome.[1]

For the diagnosis of antisynthetase syndrome as per Solomon *et al*[2], in addition to the presence of an aminoacyl-tRNA synthetase autoantibody, there must be two major or one major and two minor criteria. Major criteria includes: ILD (not attributable to another cause), polymyositis or dermatomyositis as per Bohan and Peter criteria. Minor criteria includes: arthritis, Raynaud's phenomenon, Mechanic's hands. As per European League Against Rheumatism (EULAR)/ American College of Rheumatology (ACR) criteria for classifying idioputhic inflammatory myopathies, variables like age of onset, muscle weakness, skin manifestations, laboratory measurements, muscle biopsy can be used and classify patients as having "definite," "probable," and "possible" disease based on two different scoring systems depending on whether a muscle biopsy has been performed.[3]

The clinical presentation of antisynthetase syndrome is variable and the precise phenotype is dependent upon the specific autoantibodies present.[1] For instance, anti-Pl-7 is correlated with more severe ILD and

myositis is almost always present in those with anti-Ro/SSA.[4] Myositis is present in 78% to 91% of patients with anti-Jo-1 positive antisynthetase syndrome and it usually presents after many years of the onset of the disease.[1,5] The myositis may present as an isolated elevation of creatine kinase or with clinical symptoms of proximal muscle weakness and pain. Electromyogram studies, magnetic resonance imaging of the muscle, and muscle biopsies can all aid in the diagnosis and in monitoring the disease progression; however, these are not necessary to make a diagnosis. The findings on muscle biopsy in antisynthetase syndrome are similar to those seen in other idiopathic inflammatory myopathies; however, with some unique features including fragmentation of perimysium connective tissue, perimysium inflammation, and perifascicular atrophy.[5] Arthralgia is present in approximately 75% of patients, and tends to be asymmetric, non-deforming, non-erosive arthritis, which can present similarly to rheumatoid arthritis.[6,7] This is the primary presenting symptom in approximately 27% of patients.[6]

Interstitial lung disease has been shown to be present in 69% to 90% of anti-Jo-1 positive patients and is commonly an initial presenting symptom, prior to the onset of a myopathy.[7,8] The ILD associated with antisynthetase syndrome can be severe and is the major cause of morbidity and mortality. It typically presents as exertional dyspnoea, often with a non-productive cough.[8] High-resolution CT scans can be useful in the diagnosis of ILD and most commonly show a diffuse, patchy, ground-glass opacities and basal consolidations, whereas honey-combing and bronchiectasis are seen infrequently.[9] A lung biopsy is also useful in the diagnosis and characterisation of ILD in antisynthetase syndrome, with common findings including non-specific interstitial pneumonia, usual interstitial pneumonia, cryptogenic organising pneumonitis or bronchiolitis obliterans organising pneumonia and diffuse alveolar damage. Spirometry often shows decreased forced vital capacity and reduced diffusion capacity, and upright and supine spirometry may reveal evidence of respiratory muscle weakness. When comparing antisynthetase syndrome to non-antisynthetase syndrome idiopathic inflammatory myopathies, those with antisynthetase syndrome are more likely to show ILD as the initial presenting symptom, corticosteroid responsive and recurrences of the ILD.[8] Studies have shown that anti-Jo-1 positive disease tends to have worse pulmonary outcomes, compared to other antisynthetase syndrome antibodies including anti-PL-12, and the combination of anti-Jo-1 and anti-Ro (anti-SSA) antibodies tends to be associated with more severe respiratory illness.[10] Other cardio-pulmonary manifestations include pulmonary hypertension, cardiomyopathy, myocarditis, pericardial effusions, and pleural effusions.

Antisynthetase syndrome is associated with high morbidity, therefore, prompt diagnosis and treatment is important. The recommended first-line treatment involves corticosteroids at a dose of 1mg/kg/day, tapered after 6–8 weeks. Treatment can also involve steroid sparing immunomodulatory agents, such as cyclophosphamide, azathioprine, mycophenolatemofetil, cyclosporine, tacrolimus, rituximab, and intravenous immunoglobulin. One case report of refractory antisynthetase syndrome after a trial with a number of immunosuppressive treatments showed remission with four months of treatment with mycophenolatemofetil at a dose of 2g/day, which was well-tolerated.[11] Relapse is another important factor to monitor for those patients who are tapered or discontinued off immunotherapy. Predictors of poor prognosis include older age of onset, malignancy, and negative immunologic tests. Management should also include a malignancy screen as there exists an association between various malignancies and antisynthetase syndrome. Appropriate clinical precautions applicable to patients on long-term immunosuppressants, such as vaccination, *Pneumocystis jiroveci carinii* pneumonia prophylaxis and management of adverse effects (*e.g.*, osteoporosis prevention with glucocorticoids) also recommended for these patients.[12]

In conclusion, antisynthetase syndrome can present with isolated respiratory symptoms, such as cough and shortness of breath with associated, delayed or absent muscle symptoms. Clinician should remain alert to potential extra-pulmonary symptoms of connective tissue disease, which will help in an earlier diagnosis and appropriate treatment to improve outcomes in such patients.

References

1. Katzap E, Barilla-LaBarca M, Marder G. Antisynthetase syndrome. *Curr Rheumatol Rep* 2011;13:175–81.
2. Solomon J, Swigris JJ, Brown KK. Myositis-related interstitial lung disease and antisynthetase syndrome. *Jornal Brasileiro de Pneumologia* 2011;37:100–09.
3. Lundberg IE, Tjärnlund A, Bottai M, Werth VP, Pilkington C, de Visser M, *et al.* European League Against Rheumatism/American College of Rheumatology. Classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. *Arthritis Rheumatol* 2017;69:2271–82.
4. Dugar M, Cox S, Limaye V, Blumbergs P, Roberts-Thomson PJ. Clinical heterogeneity and prognostic features of South Australian patients with antisynthetase autoantibodies. *Int Med* J 2011:674–9.

5. Schmidt WA, Wetzel W, Friedländer R, Lange R, Sörensen HF, Lichey HJ, *et al.* Clinical and serological aspects of patients with anti-Jo-1 antibodies: an evolving spectrum of disease manifestations. *Clin Rheumatol* 2000;19:371–7.
6. Lefevre G, Meyer A, Launay D, Machelart I, DeBandt M, Michaud J, *et al.* Seronegative polyarthritis revealing antisynthetase syndrome: a multicentre study of 40 patients. *Rheumatology* (Oxford). 2014; Epub.
7. Lega JC, Fabien N, Reynaud Q, Durieu I, Durupt S, Dutertre M, *et al*. The clinical phenotype associated with myositis-specific and associated auto-antibodies: a meta-analysis revisiting the so-called antisynthetase syndrome. *Autoimmun Rev* 2014;13:883–91.
8. Richards TJ, Eggebeen A, Gibson K, Yousem S, Fuhrman C, Gochuico BR, *et al*. Characterization and peripheral blood biomarker assessment of anti-Jo-1 antibody positive interstitial lung disease. *Arthritis Rheum* 2009;60:2183–92.
9. Ingegnoli F, Lubatti C, Ingegnoli A, Boracchi P, Zeni S, Meroni PL. Interstitial lung disease outcomes by high-resolution computed tomography (HRCT) in Anti-Jo1 antibody-positive polymyositis patients: a single centre study and review of the literature. *Autoimmun Rev* 2012;11:335–40.
10. Schnabel A, Hellmich B, Gross W, Gang L. Interstitial lung disease in polymyositis and dermatomyositis. *Curr Rheumatol Rep* 2005;7:99–105.
11. Sharma K, Orbai AM, Desai D, Cingolani OH, Halushka MK, Christopher-Stine L, *et al.* 2005; Antisynthetase syndrome-associated myocarditis. *J Card Fail* 2014;Epub.
12. Public Health Agency of Canada. *PHAC: Canadian Immunization Guide.* Section 3 - Vaccination of specific populations (acquired/secondary immunodeficiency). *Available from URL:* http://www.phac-aspc.gc.ca/publicat/ciggci/p03-07-eng.php#a4. Accessed on…….