



Case Report

Antisynthetase syndrome and interstitial lung disease: A case report

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ARTICLE INFO

Keywords:

Antisynthetase syndrome
Non-specific interstitial pneumonia
Interstitial lung disease
Case report

ABSTRACT

Introduction: Myositis, Raynaud's phenomenon, fever, interstitial lung disease, mechanic's hands, and arthropathy are symptoms of Antisynthetase Syndrome (ASS), which is defined by the development of antibodies against t-ribonucleic acid (RNA) synthetase, particularly anti-Jo-1.

Case presentation: The case is about 29 years female with 1 month history of non-productive cough and dyspnea on exertion which was later diagnosed as ASS.

Discussion: The diagnosis of an inflammatory myopathy is based on clinical findings such as subacute development of symmetrical muscle weakness and signs such as laboratory investigations revealing skeletal muscle inflammation. Creatinine phosphokinase (CPK) is mainly used to demonstrate skeletal muscle involvement.

Conclusion: Interstitial lung disease is a frequent occurrence and is associated with a bad prognosis during the course of antisynthetase syndrome.

1. Introduction

Antisynthetase Syndrome (ASS) is a rare autoimmune disorder with prevalence of 1.5 cases per 100,000, characterized by Interstitial Lung Disease (ILD), non-erosive arthritis, inflammatory myositis, Raynaud's phenomenon, unexplained fever and/or mechanic's hands in the setting of antibodies against amino acyl-transfer ribonucleic acid (RNA) synthetases, with anti-Jo-1 antibody being the most common [1,2]. ASS has unclear pathogenesis; however, it is hypothesized that immune intolerance and immune self-reactivity have major implications [3,4]. ASS is considered a challenging and under-recognized clinical entity that requires a high index of suspicion as it can mimic other diseases such as infections [5]. Clinicians should be familiar with this entity. There is favorable response to steroids and immunosuppressants [5]. We describe here a case of 29-year lady with assemblage of clinical manifestations of antisynthetase syndrome including polyarthritis, interstitial lung disease, myositis, Raynaud's phenomenon along with positive anti-Jo-1 antibody. This case report was reported in the form of SCARE 2020 criteria [6].

2. Case Presentation

A 29-year female presented to the Department of Rheumatology in our hospital with chief complaints of non-productive cough, dyspnea on exertion for 1 month. She gave a history of multiple joint pain for last 1 year involving bilateral interphalangeal and metacarpophalangeal joints, elbow, shoulder and knee joints, muscle weakness with muscle cramps for 4 months and history suggestive of Raynaud's phenomenon. There was no history of fever, chills, rash, dysphagia, or sicca symptoms. She was on anti-rheumatoid medication for multiple joint pain suspecting it to be rheumatoid arthritis in local hospital. She had visited many local hospital for the same complain however, she wasn't improved so, she visited our center. She had no other significant past history. Menstrual history was normal. She is a non-smoker nor she consumes alcohol. She had no known allergies and family history was not significant. On physical examination, temperature was 38 °C, oxygen saturation of 94% (on room air) and blood pressure of 120/70 mmHg. On examination there was metacarpophalangeal joint synovitis in the hands and wrists and proximal muscle weakness. Auscultation of chest revealed basal end inspiratory crepitations. Cardiovascular, abdominal and neurological system examinations were unremarkable.

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<https://doi.org/10.1016/j.amsu.2022.104571>

Received 16 July 2022; Received in revised form 30 August 2022; Accepted 4 September 2022

Available online 8 September 2022

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Routine investigations showed anemia (Hb 9.4 gm/dl) [Ref: 12–16 gm/dl], white blood cells (WBC) (9400/cumm) [Ref: 4000–11000/cumm] erythrocyte sedimentation rate (ESR) of 51 mm/hr [Ref: 0–20 mm/hr], C-reactive protein (CRP) was 56.1mg/L [Ref: <5mg/L], Brucella antibody test/titer was 1:80, SGOT (150U/L) [Ref: 5–40U/L], SGPT (80U/L) [Ref: 5–45 U/L], CPK (201U/L) [Ref: 39–238U/L] and Lactate Dehydrogenase (LDH) was 848 U/L [Ref: 140–280U/L]. RA factor test was negative while anti-CCP was 13 AU/ml [Ref: <10 AU/ml], anti-dsDNA was 9.6IU/ml [Ref: 0–25IU/ml], TSH was 9.30 μ IU/L [Ref: 0.35–5.5 μ IU/ml] and anti-TPO was 6U/ml [Ref: 5–34 U/ml]. In anti-neutrophilic antibody (ANA) reflex panel, ANA was 2+ with mixed pattern in titer of 1:160 and anti Jo-1 was 3+. Echocardiography was normal. Nail fold capillaroscopy showed dilated loop abnormality but normal capillary density indicating very early phase of Raynaud's phenomenon or scleroderma. The reverse transcriptase polymerase chain reaction (RT-PCR) test was done which was negative. Musculoskeletal ultrasonography (USG) with Power Doppler of right hand and peri-articular areas demonstrated mild inflammatory arthritis of wrist joint with tenosynovitis of 4th extensor compartment and flexor tendon of 2nd digit. High-Resolution Computed Tomography (HRCT) of chest displayed fibro bronchiectatic changes with inter and intralobular septal thickening in bibasal lung segments; patchy ground glass opacities with fibrotic changes in right middle and left upper lobe which are suggestive of fibrotic type of NSIP (Fig. 1).

This constellation of clinical manifestations of polyarthritis, interstitial lung disease, myositis, raynaud's disease along with positive anti-Jo-1 antibody, confirmed the diagnosis of Antisynthetase syndrome.

She was started on prednisolone 50mg once a day and gradually tapered each 10mg over 2 weeks. She was also on azathioprine 100 mg once a day. She also continued Hydroxychloroquine 300mg once a day. On 3 months of follow up. Dyspnea on exertion and dry cough was relieved, arthritis, muscle weakness Raynaud's phenomenon decreased significantly. She was suggested to take 5 mg of oral prednisolone, 200 mg hydroxychloroquine and 100 mg of azathioprine.

3. Discussion

ASS is a rare autoimmune disease characterized mainly by ILD, myositis, and arthritis reportedly in 90% of cases with other less common manifestations like fever, rashes, and Raynaud's syndrome have also been seen less commonly [3,7]. In the present case, polyarthritis, interstitial lung disease, myositis, Raynaud's disease along with positive anti-Jo-1 antibody was seen. As this syndrome is rare, epidemiologic studies are difficult to perform and true prevalence of anti-synthetase syndrome is unknown [8]. Early diagnosis is difficult because the clinical presentation is often nonspecific and many general practitioners lack acquaintance with this syndrome [8]. Similar was the case in our patient. She initially developed polyarthritis for which she was on anti-rheumatoid drugs for 1 year before she visited our center for other subsequent problems. So, clinicians must be familiar with this syndrome and all atypical rheumatoid arthritis should be tested for anti-Jo-1 antibody.

The hallmark of anti-synthetase syndrome is the presence of myositis-specific anti-synthetase antibodies [9]. Of the anti-synthetase antibodies, anti-Jo-1, an anti-histidyl-tRNA synthetase, is most common [9]. Anti-Jo-1 antibody is detected in 15%–25% of patients with polymyositis and in up to 70% of myositis patients with concomitant interstitial lung disease [10]. The patient reported herein had positive anti-Jo-1 antibodies.

Arthralgias and arthritis are common (50%), the most common form being a symmetric polyarthritis of the small joints of the hands and feet [8]. It is typically nonerosive but can sometimes be erosive and destructive [11]. Because inflammatory arthritis mimics rheumatoid arthritis, anti-synthetase syndrome should be considered in rheumatoid factor-negative patients presenting with polyarthritis. Our patient was also misdiagnosed as rheumatoid arthritis (RA) initially in other center and was on treatment for it.

The diagnosis of an inflammatory myopathy is based on clinical findings such as subacute development of symmetrical muscle weakness and signs such as laboratory investigations revealing skeletal muscle inflammation [12]. Creatinine phosphokinase (CPK) is mainly used to demonstrate skeletal muscle involvement. In the case described herein, she had muscle weakness and CPK was also very elevated.

ILD is the main pulmonary manifestation of ASS and the major cause of morbidity and mortality [3]. Patients usually present with dyspnea on exertion accompanied by dry cough [13]. In a study by Debray et al. on patients with anti-synthetase syndrome, ground glass opacities (100%), reticulation (87%) and traction bronchiectasis (76%) were predominant features and non-specific interstitial pneumonia (NSIP) was seen in 45% of cases [14]. Our patient developed clinical feature of ILD in later months with fibro bronchiectatic changes and patchy ground glass opacities which are the features likely of Fibrotic type of NSIP in HRCT.

Raynaud's phenomenon develops in about 40% of patients [8]. Some have nailfold capillary abnormalities [8]. Our patients also had Raynaud's phenomenon with dilated loop as abnormality in nail fold capillaroscopy.

Connors et al. and Solomon et al. proposed diagnostic criteria for the anti-synthetase syndrome. According to Connors et al., the presence of an anti-aminoacyl tRNA synthetase antibody is required as well as one or more of several clinical features, namely, Raynaud's phenomenon, arthritis, interstitial lung disease, fever and mechanic's hands [15]. According to Solomon et al., the presence of an anti-aminoacyl tRNA synthetase antibody is required plus two major or one major and two minor criteria, the major criteria being interstitial lung disease and polymyositis or dermatomyositis, the minor criteria being arthritis, Raynaud's phenomenon and mechanic's hands [16]. The patient described here fulfilled both the sets of criteria for the diagnosis of anti-synthetase syndrome proposed either by Connors et al. or Solomon et al.

Since, it is a rare disease no controlled clinical trials have been performed for the assessment of different treatment options. The response to immunosuppressive medications is generally favorable [5]. A combination of glucocorticoids and a steroid-sparing agent (usually mycophenolate or azathioprine) is initially used in AS syndrome-related

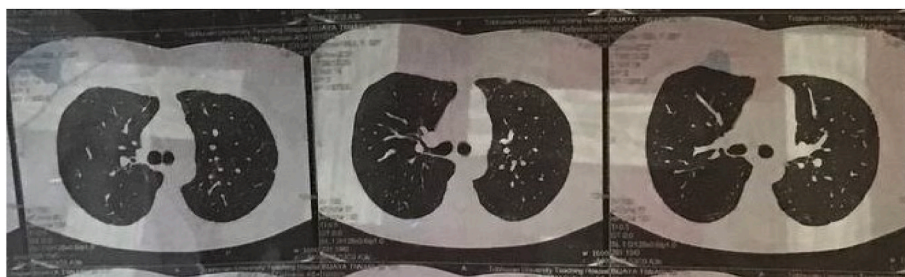


Fig. 1. HRCT of chest showing fibro bronchiectatic changes with inter and intralobular septal thickening in bibasal lung segments; patchy ground glass opacities with fibrotic changes in right middle and left upper lobe.

ILD of mild-to-moderate severity [17,18]. Our patient also improved with oral prednisolone and azathioprine. Cyclophosphamide is used for severe or rapidly progressive ILD [19]. Rituximab has also been used successfully for the treatment of refractory cases [20].

4. Conclusion

Antisynthetase syndrome's clinical manifestations can take many different forms and aren't always evident when the disease first manifests itself. The relevance of suspecting ASS in individuals presenting with unexplained ILD is emphasized in this case report. Interstitial lung disease is a frequent occurrence and is associated with a bad prognosis during the course of antisynthetase syndrome.

Ethical approval

None.

Please state any sources of funding for your research

No funding was received for the study.

Author contribution

KD, AC, and LR wrote the original manuscript, reviewed, and edited the original manuscript. KD, AC, LR, UR, SP, PK, PG, SKS, KKS, and SP reviewed and edited the original manuscript.

Please state any conflicts of interest

Authors have no conflict of interest to declare.

Registration of research studies

1. Name of the registry: None
2. Unique Identifying number or registration ID: None
3. Hyperlink to your specific registration (must be publicly accessible and will be checked)

Guarantor

Dr. Umesh Ray.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.104571>.

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