



Anti-Ro52-positive antisynthetase syndrome (ASS): a case report and review of the literature

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Background: This study aimed to diagnose and treat a patient with anti-Ro52-positive antisynthetase syndrome (ASS), investigate the association between anti-Ro52 antibodies and ASS, and determine its clinical significance. The objective of this clinical report is to highlight this unusual syndrome to avoid incorrect diagnosis.

Case Description: A middle-aged woman presenting with obvious lung symptoms was admitted to our hospital. A physical examination revealed swollen joints in both hands, mechanic's hands, and normal muscle strength and muscle tone in all 4 extremities. A myositis-specific antibody panel, lung computed tomographic (CT) imaging, electromyography, and muscle biopsy were performed as auxiliary examinations, and appropriate treatment was administered after the confirmed diagnosis. The myositis-specific antibody panel yielded strongly positive results for anti-Jo-1 and anti-Ro52 antibodies, lung CT imaging revealed interstitial lung disease, electromyography revealed myogenic damage, and muscle magnetic resonance imaging revealed multiple inflammatory exudates. A definitive diagnosis of ASS was made, and glucocorticoid and immunosuppressant therapy were administered. After treatment, the patient's symptoms were alleviated, creatine kinase activity was reduced, and signs of disease activity and secondary tumors were not observed on a subsequent follow-up evaluation.

Conclusions: Anti-Ro52 antibodies, being myositis-associated antibodies, can lead to an atypical clinical presentation in ASS patients and are potentially associated with a poor prognosis. Therefore, thorough follow-up evaluation is required for such cases.

Keywords: Anti-Ro52 antibody; antisynthetase syndrome (ASS); myositis-associated antibody; interstitial lung disease; case report

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Introduction

Antisynthetase syndrome (ASS) is a subtype of idiopathic inflammatory myopathies primarily characterized by myositis, interstitial lung disease (ILD), Raynaud syndrome, mechanic's hands, pyrexia, and arthritis. The presence of anti-aminoacyl-tRNA synthetase antibodies in serum, the most common being the anti-Jo-1 antibody, serves as an immunological marker of ASS. Various clinical manifestations are associated with ASS, particularly a high risk of ILD and concomitant malignancies (1).

Anti-Ro52 antibodies are anti-nuclear antibodies recently identified as having varied clinical significance in several autoimmune diseases (2). Over the past few years, the high prevalence of anti-Ro52 antibodies in ASS has attracted increasing attention; however, relevant reports in China are relatively scarce. Therefore, this study reports the case of a patient with anti-Ro52-positive ASS and reviews the relevant literature to enhance understanding among clinicians of such diseases. We present the following case in accordance with the CARE reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-787>)

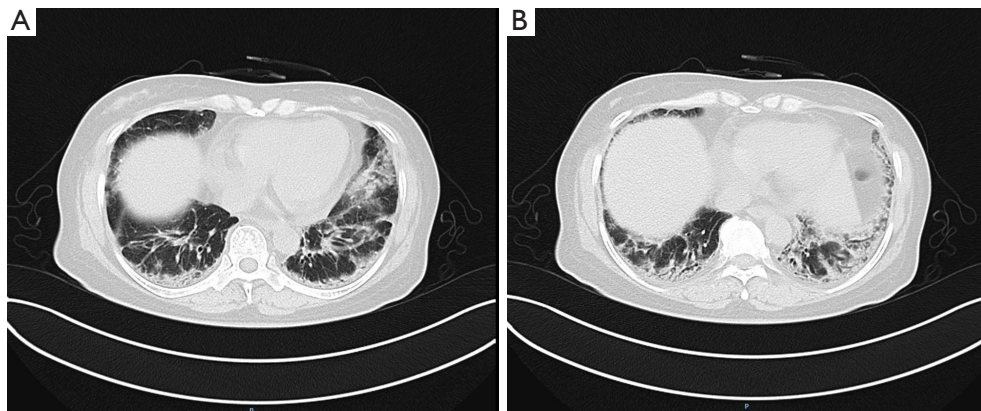


Figure 1 Lung computed tomographic scans of the antisynthetase syndrome patient during the initial visit.

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Case presentation

Clinical data

In June 2020, a 54-year-old woman from Zhejiang Province, with no previous comorbidities and no past history of tobacco smoking and alcohol intake, presented to our department with a cough and expectoration lasting 2 months and dyspnea on exertion lasting a month. Two months before consultation, the patient developed a cough producing yellow sputum with no apparent cause. One month before consultation, the patient exhibited dyspnea after stair-climbing and sought medical attention at a local hospital. Chest computed tomographic (CT) imaging revealed interstitial lesions in both lungs, and bronchoscopy revealed an absence of bronchial abnormalities at various lobe segments. Bronchoalveolar lavage was performed on the lingula of the left lung. Cellular analysis of the bronchoalveolar lavage fluid indicated 60% neutrophils and 40% lymphocytes. Pathological evaluation using a biopsy specimen of lymph node station 4R revealed a small mass of lymphoid tissue. Because specific treatment was not administered at the local hospital, the patient sought further treatment at our hospital. Pyrexia, photosensitivity, hair loss, oral ulcerations, and Raynaud syndrome did not occur over the course of the disease. Her family history was also insignificant for any respiratory or other systemic pathology. Physical examination revealed coarse skin with keratinization, fissures and desquamation on the palm at the thumb side of both hands with changes characteristic of mechanic's hands, and coarse breath sounds with Velcro

crackles were heard in both lungs. In addition, there was grade 5 muscle strength and normal muscle tension in the upper and lower extremities, swelling in the proximal interphalangeal joints of both hands, and positive findings in the squeeze test. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). 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 editorial office of this journal.

Imaging data

High-resolution chest CT scans of the patient revealed ILD in both lungs and pericardial effusion (*Figure 1*).

Laboratory tests and other examinations

The patient had a normal creatine kinase level and an erythrocyte sedimentation rate of 72 mm/h. The patient tested positive for anti-Jo-1 (+++) and anti-Ro52 IgG (+++) antibodies through a myositis-specific antibody panel and had a severe pulmonary diffusing capacity disorder. Whole-body muscle plain magnetic resonance imaging revealed widespread inflammatory exudates in the thoracodorsal area, both buttocks, and the muscles and subcutaneous tissue in the lower extremities. Electromyography revealed myogenic damage in both the upper and lower extremities.

Bronchoscopy examination revealed smooth mucosa and an unobstructed tracheal lumen, general hyperemia,

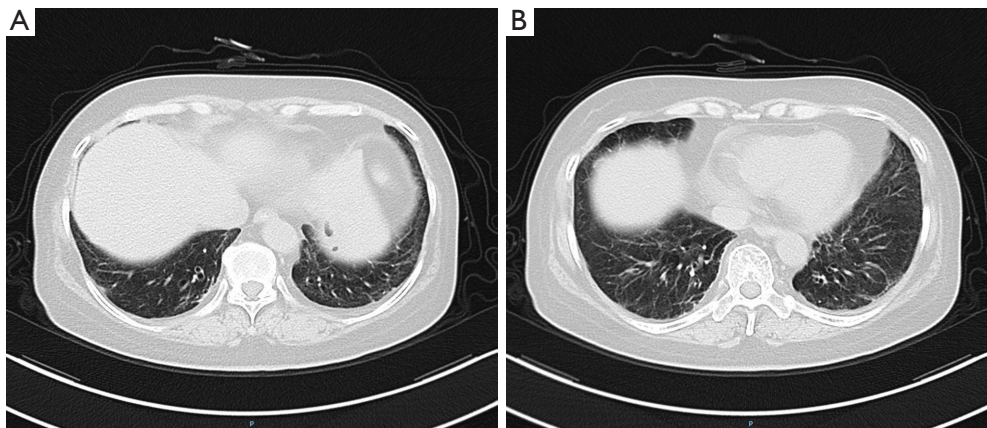


Figure 2 Lung computed tomographic scans of the antisynthetase syndrome patient after 6 months of treatment.

swelling, petechial hemorrhage upon contact, and an absence of masses or blockage in the bronchial mucosa of the left and right primary bronchi and the various lobe segments of both lungs. Based on the imaging results, bronchoalveolar lavage was performed on the lingula of the left lung and medial basal segment of the lower lobe of the left lung, and a brush biopsy sample was obtained from the lingula of the left lung. The bronchoalveolar lavage fluid was subjected to bacterial cell culture, fungal culture, acid-fast staining, GeneXpert assay, and liquid mycobacterial culture; all test results were negative.

Diagnosis and treatment

The patient was diagnosed with ASS in accordance with the diagnostic criteria for this disorder. Hence, 40 mg of intravenous methylprednisolone was administered daily, 75 mg cyclosporine was administered twice daily, and 200 mg pirfenidone was administered thrice daily. After 7 days of treatment, dyspnea symptoms on exertion were alleviated, while cough and expectoration persisted. Glucocorticoid therapy was then changed to 60 mg oral prednisolone acetate daily. Follow-up evaluation was conducted monthly at our department, and the glucocorticoid dosage was gradually reduced to 15 mg/day and maintained thereafter. Every month, 20 g/day immunoglobulin was administered intravenously for 5 days, and 0.8 g intravenous cyclophosphamide was administered once (cumulative dose, 4.8 g). The patient's symptoms gradually abated. During periodic follow-up evaluations, recurrence was not observed, the erythrocyte sedimentation rate and C-reactive protein level decreased steadily, the

creatinine kinase level remained normal, and no abnormalities in tumor markers were observed. The patient showed high adherence, we observed steroid diabetes and added hypoglycemic drugs, her blood glucose then decreased into normal range.

Figure 2 shows the chest CT scans of the patient obtained during the 6-month follow-up evaluation. *Figure 3* shows timeline for case presentation.

Discussion

ASS is an infrequent autoimmune disease. Clear diagnostic criteria for ASS are currently lacking worldwide. The hallmark characteristic of the disease is the appearance of myositis autoantibodies in patient sera (3). Currently, 11 different antisynthetase antibodies have been identified, with the anti-Jo-1 antibody being the earliest and most common antisynthetase antibody known. Patients with different clinical subtypes of ASS have different clinical manifestations, serum markers, and lung imaging results; however, relevant reports are relatively scarce. In spite of a wide range of early diagnosis of ASS described in the literature, ASS with interstitial lung disease as an initial presentation has not been fully appreciated.

Anti-Ro52 antibodies were once considered a type of anti-SSA antibody. However, recent studies have reported that anti-Ro52 and anti-SSA antibodies constitute 2 independent antibody systems that are of different clinical significance (4). The linear immunofluorescence assay revealed that anti-Ro52 antibody-positive serum samples were negative for anti-SSA antibodies when the traditional indirect immunofluorescence assay was used (5). Therefore,

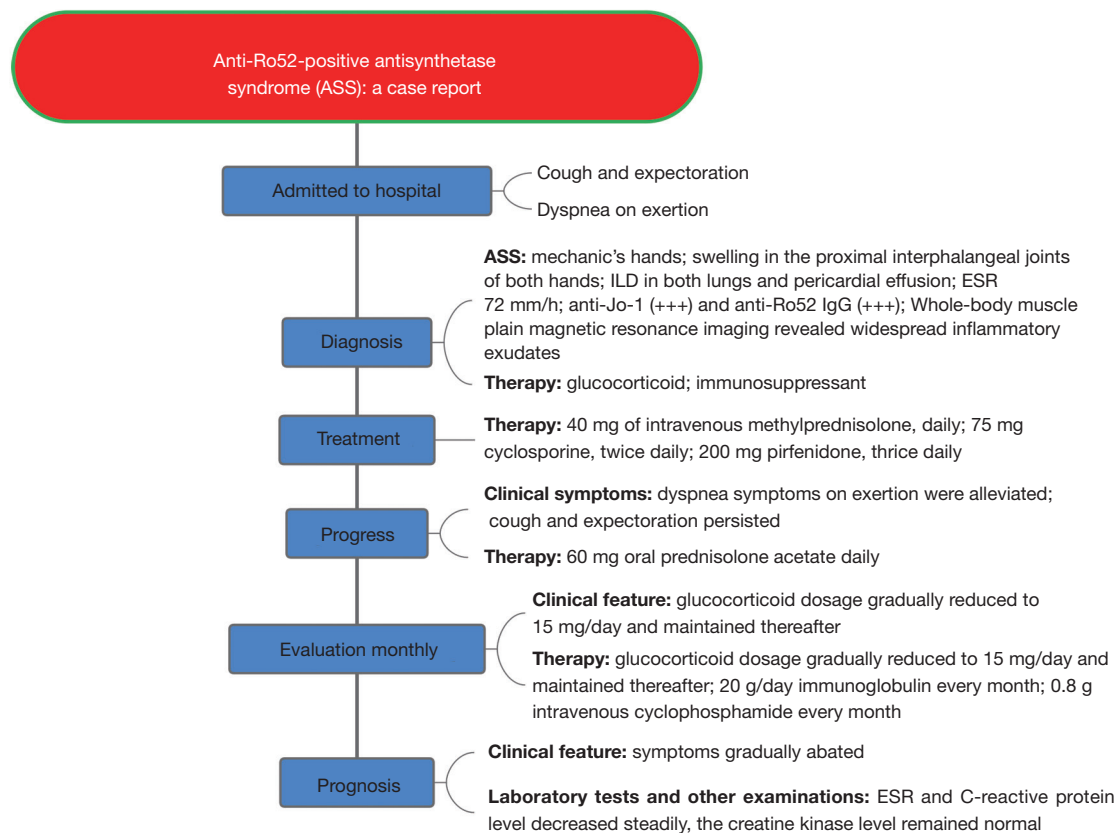


Figure 3 Timeline to show the diagnosis, treatment, progress, and prognosis. ILD, interstitial lung disease; ESR, erythrocyte sedimentation rate.

methods for detecting individual anti-Ro52 antibodies are critical in the clinical setting.

ASS patients are at a high risk of concomitant ILD and malignancies. Previous studies have reported that anti-Ro52 antibodies potentially lead to a more surreptitious onset and more rapid progression of ILD (6,7). A cross-sectional study conducted in India (8) reported that ASS patients testing positive for anti-Ro52 antibodies were at a significantly elevated risk of ILD. The clinical data of the present patient, who had milder myositis and exhibited ILD as the primary manifestation, are consistent with the aforementioned findings. Because ILD is a key determinant of ASS prevalence and ASS-related mortality (9), the risk of ASS should be considered for patients with idiopathic ILD and/or acute respiratory distress syndrome of unknown etiology to prevent misdiagnoses.

ASS patients are more prone to malignant tumors, probably owing to disrupted immune function. Numerous studies have reported that anti-Ro52 antibodies are generally present in patients testing positive for the anti-Jo-1 antibody and increase the risk of various cancers, primarily

digestive tract (mainly colon cancer) and gynecological (ovarian cancer and breast cancer) malignancies (4,10). The association between anti-Ro52 antibodies and cancer is potentially attributable to the location of the gene encoding the Ro52 antigen on chromosome 11 in humans. Furthermore, the p15.5 segment of chromosome 11 may harbor genes involved in cancer pathogenesis and progression (11). The aforementioned findings have been confirmed via a clinical study (5), and the correlations of anti-Ro52 antibodies with secondary tumors and a poor prognosis in ASS patients has been confirmed (12). However, further studies are required to determine whether such antibodies can serve as predictors of secondary tumors in ASS patients. Although malignant tumors were not detected in the middle-aged female patient in the present study during hospitalization and subsequent short-term follow-up evaluations, the presence of anti-Ro52 antibodies is an adverse factor and necessitates subsequent periodic follow-up evaluation.

This case did not show decreased muscle strength or muscle pain, and with normal creatine kinase, which also

increased the difficulty of diagnosis. Until we did a whole-body muscle plain magnetic resonance imaging, we found the basis for myositis. We searched for recent reports of ASS, but found no cases with completely normal creatine kinase. Whether the anti-Ro-52 antibody is associated with occult myositis is currently unknown, but this report can be used as a reference for clinical diagnosis. Muscle plain magnetic resonance imaging may be an examination that can be considered.

In conclusion, anti-Ro52 antibodies constitute an independent antibody system and are associated with a poor prognosis among ASS patients. Clinicians should have a clear understanding of the association between anti-Ro52 antibodies and ASS, remain alert during patient diagnosis and treatment, and regularly evaluate joint injuries, ILD progression, and secondary tumors to further improve the prognosis of ASS patients. Furthermore, chances of misdiagnoses are more frequent among ASS patients with ILD as the primary manifestation. Therefore, for ILD patients, clinicians should be attentive to other manifestations including mechanic's hand, myasthenia, painful swelling of joints, and Raynaud syndrome, and perform extensive tests including the antinuclear antibody panel, creatine kinase levels, and electromyography to facilitate early diagnosis and treatment. Clinicians should acquire a comprehensive understanding of this disease and broaden their perspectives for its diagnosis and treatment to improve patient prognosis.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <https://atm.amegroups.com/article/view/10.21037/atm-22-787/rc>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-787/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures

performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). 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 editorial office of this journal.

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References

1. Uribe L, Ronderos DM, Díaz MC, et al. Antisynthetase antibody syndrome: case report and review of the literature. *Clin Rheumatol* 2013;32:715-9.
2. Lee AYS. A review of the role and clinical utility of anti-Ro52/TRIM21 in systemic autoimmunity. *Rheumatol Int* 2017;37:1323-33.
3. Connors GR, Christopher-Stine L, Oddis CV, et al. Interstitial lung disease associated with the idiopathic inflammatory myopathies: what progress has been made in the past 35 years? *Chest* 2010;138:1464-74.
4. Decker P, Moulinet T, Lopez B, et al. Clinical significance of anti-Ro52 (TRIM21) antibodies in adult patients with connective tissue diseases. *European journal of internal medicine* 2021;91:45-52.
5. Marie I, Hatron PY, Dominique S, et al. Short-term and long-term outcome of anti-Jo1-positive patients with anti-Ro52 antibody. *Semin Arthritis Rheum* 2012;41:890-9.
6. Chi S, Yuxin S, Hui H, et al. Myositis specific antibodies are associated with isolated anti-Ro-52 associated interstitial lung disease. *Rheumatology (Oxford)*, 2021.
7. Bauhammer J, Blank N, Max R, et al. Rituximab in the Treatment of Jo1 Antibody-associated Antisynthetase Syndrome: Anti-Ro52 Positivity as a Marker for Severity and Treatment Response. *J Rheumatol* 2016;43:1566-74.
8. Srivastava P, Dwivedi S, Misra R. Myositis-specific and myositis-associated autoantibodies in Indian patients with inflammatory myositis. *Rheumatol Int* 2016;36:935-43.
9. Zamora AC, Hoskote SS, Abascal-Bolado B, et al. Clinical

- features and outcomes of interstitial lung disease in anti-Jo-1 positive antisynthetase syndrome. *Respir Med* 2016;118:39-45.
10. Courties A, Lidove O, Maisonobe T, et al. Antisynthetase syndrome and lung carcinoma: a fortuitous association? *Rev Med Interne* 2014;35:271-3.
 11. Strandberg L, Ambrosi A, Espinosa A, et al. Interferon- α

- induces up-regulation and nuclear translocation of the Ro52 autoantigen as detected by a panel of novel Ro52-specific monoclonal antibodies. *J Clin Immunol* 2008;28:220-31.
12. Schmidt J. Current Classification and Management of Inflammatory Myopathies. *J Neuromuscul Dis* 2018;5:109-29.

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