Beyond myositis: The systemic complications of Antisynthetase syndrome

ABSTRACT

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| **Aims:** This case report aims to highlight the systemic complications and clinical challenges associated with Antisynthetase Syndrome (ASyS), a rare autoimmune condition characterized by antibodies targeting aminoacyl-tRNA synthetases.  **Presentation of Case:** A 65-year-old woman with a history of diabetes and hypertension presented with progressive muscle weakness, bilateral leg swelling, and respiratory symptoms. Diagnostic evaluations—including MRI, HRCT, muscle biopsy, and laboratory tests—confirmed necrotizing myositis and interstitial lung disease (ILD), consistent with ASyS. Despite treatment with high-dose corticosteroids and intravenous immunoglobulin (IVIG), the patient experienced persistent quadriparesis, respiratory compromise, and gastrointestinal bleeding due to gastric ulcers.  **Discussion:** This case illustrates the complex clinical spectrum of ASyS, with concurrent myositis, ILD, systemic inflammation, cardiac involvement, and gastrointestinal complications. Elevated muscle enzymes, severe anemia, leukocytosis, and the presence of mechanic’s hands supported the diagnosis. Management involved immunosuppressive therapy, broad-spectrum antibiotics, antifungal prophylaxis, and supportive measures. The patient’s partial response to treatment underscores the chronic, relapsing nature of ASyS. A multidisciplinary approach was essential for comprehensive care.  **Conclusion:** ASyS poses significant diagnostic and therapeutic challenges due to its multisystem involvement and variable presentation. Early recognition, aggressive immunosuppressive therapy, infection control, and organ-specific management are critical. Long-term multidisciplinary follow-up is necessary to monitor disease progression, mitigate complications, and improve patient outcomes. |

*Keywords: Antisynthetase syndrome, interstitial lung disease, myositis, autoimmune disease, intravenous immunoglobulin, multidisciplinary management.*

1. INTRODUCTION

Antisynthetase syndrome (ASyS) is a rare autoimmune disorder characterized by the presence of autoantibodies targeting aminoacyl-transfer RNA (tRNA) synthetases, which are essential enzymes in protein synthesis (Witt et al., 2017). Clinically, ASyS presents with a constellation of features, including interstitial lung disease (ILD), inflammatory myopathy (myositis), non-erosive arthritis, Raynaud's phenomenon, mechanic's hands, and unexplained fever (Patel et al., 2024) (Clevelend clinic, 2023) (Alfraji et al., 2021).

The heterogeneity in clinical manifestations often poses diagnostic challenges, necessitating a multidisciplinary approach for accurate identification and management (Wells et al., 2022). The hallmark of ASyS is the detection of antisynthetase antibodies, with anti-Jo-1 being the most prevalent (Witt et al., 2017). These autoantibodies are directed against specific aminoacyl-tRNA synthetases and are instrumental in diagnosing the syndrome (Wells et al., 2022). The presence of these antibodies correlates with distinct clinical phenotypes, influencing disease prognosis and therapeutic responses (Zanframundo et al., 2020) (Medicover hospitals, 2025).

Interstitial lung disease is a predominant and often initial manifestation of ASyS, significantly impacting morbidity and mortality. Pulmonary involvement can range from asymptomatic to progressive respiratory failure, underscoring the need for vigilant respiratory assessment in affected individuals (Patel et al., 2024).

Muscle inflammation, presenting as symmetrical proximal muscle weakness, is another core feature of ASyS. This myopathy can impair daily activities and quality of life, necessitating early intervention to prevent irreversible muscle damage (Opinc et al., 2021) (Tanboon et al., 2023).

The etiology of ASyS remains incompletely understood, with genetic predisposition, environmental exposures, and immune dysregulation implicated in its pathogenesis (Patel et al., 2024) (Galindo-Feria et al., 2022). Research continues to elucidate the mechanisms driving autoantibody production and tissue-specific manifestations (Galindo-Feria et al., 2022) (Medicover hospitals, 2025).

Management of ASyS is tailored to individual clinical presentations, primarily involving immunosuppressive therapies such as corticosteroids and disease-modifying antirheumatic drugs (DMARDs). Early and aggressive treatment is crucial, especially in cases with significant pulmonary involvement, to mitigate disease progression and improve outcomes (Zanframundo et al., 2020).

Given the complexity and potential severity of ASyS, a comprehensive, multidisciplinary approach is essential for optimal patient care. Regular monitoring and a personalized treatment strategy are pivotal in managing this multifaceted syndrome (Chan et al., 2024) (Rasendrakumar et al., 2022).

2. Presentation of case

A 65-year-old female, non-alcoholic, non-smoker with a mixed diet and a history of diabetes mellitus for five years managed on regular insulin therapy (Inj. Mixtard 14U – x – 10U s/c) and hypertension for five years controlled with Telmisartan (T. Telma 40mg OD), presented with complaints of right leg pain for one and a half months and bilateral leg swelling for fifteen days. The patient has been morbidly obese and bedridden for the past month due to progressive muscle weakness, which significantly affected her daily functioning. Given her worsening condition, she was taken to another hospital, where she was diagnosed with necrotizing myositis (immune-mediated), hepatopathy, coagulopathy, and right-sided pneumonia. In light of her deteriorating state, she was referred to this facility for further management, including intravenous immunoglobulin (IVIG) therapy.

On admission, the patient exhibited progressive paraparesis in bilateral lower limbs, along with truncal and neck muscle weakness, which raised suspicions of an underlying autoimmune or inflammatory muscle disorder. There was no significant family history of patients.

Extensive investigations were performed, including MRI of the spine which revealed degenerative disc thecal sac indentation from D6-D7 to D9-D10, causing compressive myelopathy, a potential contributor to her weakness. Muscle biopsy further confirmed necrotizing myositis, reinforcing the autoimmune-mediated muscle destruction.

High-resolution CT (HRCT) of the chest showed centrilobular nodules with patchy areas of consolidation in the right upper and middle lobes, along with segmental consolidation in the right lower lobe, suggestive of an infective etiology, specifically pneumonia.

An electrocardiogram (ECG) revealed sinus tachycardia, poor R-wave progression, and low QRS voltages, which raised concerns regarding possible cardiac involvement. Additionally, arterial blood gas (ABG) analysis reflected respiratory alkalosis with hypoxia, indicating respiratory compromise.

Laboratory investigations revealed several abnormalities. The patient was found to be anemic with hemoglobin levels fluctuating between 6.0 to 11.0 g/dL, requiring multiple packed cell transfusions during her hospitalization. Leukocytosis was evident, with white blood cell counts ranging from 19.8k to 32k, suggestive of a systemic inflammatory response. Further hematological analysis indicated neutrophilic leukocytosis with a left shift, indicating ongoing infection or inflammation and vitamin D deficiency. Coombs test results were negative, ruling out autoimmune hemolytic anemia. Elevated muscle enzyme levels, including creatine phosphokinase (CPK) ranging between 4435 to 6664 U/L, were indicative of severe muscle damage. Urine analysis revealed glucosuria, proteinuria, ketonuria, and bilirubinuria, with the presence of plenty of budding yeast forms, raising concerns about a possible secondary fungal infection, which necessitated antifungal prophylaxis.

Additional symptoms were developed during hospitalization, including suspected mechanic hands, shortness of breath on exertion, persistent cough, and arthralgia. These symptoms along with positive anti-Jo-1 antibodies confirmed Antisynthetase syndrome.

 

**Fig. 1. *Mechanic’s hands, a characteristic cutaneous manifestation of ASyS***

Given the multisystem involvement, treatment was initiated promptly. The patient was started on IVIG therapy at a dose of 0.4g/kg/day for several days, along with high-dose corticosteroids (Prednisolone 60mg OD and Methylprednisolone 60mg IV OD) to control immune-mediated muscle inflammation. Despite this, she continued to exhibit progressive quadriparesis with worsening truncal and neck muscle weakness, further supporting the diagnosis of antisynthetase syndrome or overlap myositis. The presence of persistent leukocytosis warranted the initiation of broad-spectrum antibiotics, including Meropenem (1g IV TID) and Ciprofloxacin (100ml IV BD), to cover for bacterial infections, especially given her respiratory compromise due to pneumonia. The patient also developed respiratory symptoms, requiring oxygen support and nebulization with Budecort. Blood cultures remained negative throughout, suggesting a non-bacterial cause of systemic inflammation, further pointing towards an underlying autoimmune process.

The patient also developed significant gastrointestinal symptoms two weeks after admission, including upper gastrointestinal bleeding, which was later confirmed via endoscopy. The Upper Gastrointestinal Endoscopy (UGIE) revealed two gastric ulcers with clear bases (1 x 1 cm and 0.5 x 0.5 cm) and erosive duodenitis, explaining the episodes of melena. She was managed with a combination of proton pump inhibitors (Pantoprazole 40mg IV BD) and mucosal protective agents (Sucralfate 15ml TID) to facilitate ulcer healing and prevent further bleeding. In addition to her gastric complications, she also developed symptoms of a urinary tract infection (UTI), prompting a nephrology referral. The presence of persistent burning micturition and urine abnormalities required additional antibiotics to prevent further complications.

Throughout the hospital course of 21 days, her diabetes was managed using HAI insulin according to a sliding scale, and Telma 40mg OD was continued for hypertension. She was also prescribed Pregabalin 75mg OD for neuropathic pain and physiotherapy to prevent muscle wasting and aid in maintaining some level of mobility despite her profound weakness.

By the time of discharge, the patient had shown mild improvement in muscle strength, with upper limb power improving to 3/5 and lower limb power at 2/5. However, she remained quadriparetic with persistent truncal and neck muscle weakness. Due to the nature of her condition, she was discharged with a planned tapering regimen of corticosteroids, beginning with Prednisolone 60mg OD for one week, gradually reducing over the following weeks to mitigate withdrawal symptoms and control disease activity. She was also prescribed ongoing supportive therapy, including Pantoprazole for gastric protection, Sucralfate for ulcer healing, Ciprofloxacin for UTI management, Spironolactone for edema management, Buscopan (hyoscine butyl bromide) for abdominal cramps, and iron supplementation (IFA PO OD) for anemia correction. The patient was followed up after 2 weeks. The patient had no fresh complaints, hence same course of treatment was continued.

This case demonstrates a variety of presentations for antisynthetase syndrome, an unusual autoimmune disease with myositis, interstitial lung disease and systemic inflammation. She needed aggresive immunosuppressive therapy, infection control, metabolic control and general supportive measures, all of which contributed to her stabilisation, given her unstable status at the time of presentation. Because there is a great risk of relapse of the disease, infections, and steroid-related complications, strict follow-up will be needed to assess her muscle function, respiratory status, and metabolic control. Ongoing physiotherapy and immunosuppression will be essential for preserving function and preventing progression. Multidisciplinary follow-up with participation of rheumatology, pulmonology, nephrology and rehabilitation teams is required to achieve optimal long term outcome in this patient.

3. discussion

Antisynthetase syndrome (ASyS) remains an elusive and complex condition considering it still falls under the spectrum of autoimmune diseases. Accompanying symptoms also include lung disease (ILD), myositis, arthritis, and other skin disorders which are speculated to be caused by the body's immune response (Witt et al., 2017). This case report is important because it discusses inadequately covered multi-system involvement in ASyS alongside the observably complex low-level diagnostic and effective treatment interventions.

The patient's clinical course highlights an important phenomenon regarding ASyS—the severity of associated muscle inflammation. Necrotizing myositis as confirmed by muscle biopsy alongside previously mentioned diagnosis corresponds with literature suggesting this to be on the higher end of estimates for myopathic involvement in 70 – 90% cases of ASyS (Tanboon et al., 2023). As noted previously, there is an available literature burden in ASyS regarding elevated muscle enzymes, and it becomes most apparent for creatine phosphokinase (CPK) which in this case was noted as being between 4435 to 6664 U/L strongly indicating breakdown of muscle structure in ASyS patients alongside expectation of such damage (Witt et al., 2017).

Another clinically important feature accompanying ASyS is the pulmonary one. The condition as described is consistent with the patient's ILD with patchy consolidation and centrilobular nodules on HRCT signifying early stages of pulmonary fibrosis. It has been shown that ASyS poses major risk for patients with ILD, coupling it as one of the leading causes for suffering from increased morbidity and mortality, alongside striking statistic of almost 70% of patients presenting with ILD upon first diagnosis (Patel et al., 2024). Preventing irreversible consequences, such as respiratory failure and pulmonary fibrosis, requires extensive early therapy using invasive procedures such as steroidal corticosteroids and IV immunoglobulin (Zanframundo et al. 2020).

The systemic inflammatory reaction is further supported by the presence of persistent leukocytosis (19.8k–32k WBC's), anaemia, and the increase in the inflammatory markers and confirms the autoimmune and inflammatory component of ASyS. The administration of broad-spectrum antibiotics to the patient (meropenem and ciprofloxacin) was performed to prevent secondary infections. In view of the broad-spectrum antibiotic cover, negative blood cultures, and the fact that the systemic inflammation had persisted, an on-going autoimmune rather than septic process was considered, in keeping with reports (Rasendrakumar et al., 2022).

Managing of further complications were unexpected such as GI complications i.e., upper GI bleeding; due to gastric ulcers. PPIs and sucralfate were required to heal the ulcers. This case also illustrated the systemic repercussion of ASyS, with renal function affected and the need for nephrology intervention. The glucosuria, proteinuria, and ketonuria were signs of a possible renal involvement, which is seldom reported in ASyS (Alfraji et al., 2021).

The management of ASyS, as illustrated in this case, demands a multifaceted strategy. Treatment with immunosuppressive therapy IVIG and steroid medication formed the foundation, whereas control of infections, respiratory care, physiotherapy, and other steps contributed to stabilization and recovery. Proactive plans are required to avoid exacerbation of the disease and address other associated issues, since recurrent ILD and progressive myositis are prevalent (Wells et al., 2022) (Sawal et al., 2021).

4. Conclusion

Antisynthetase syndrome (ASyS) is a complex autoimmune disease which may manifest with pleomorphic features, including myositis, interstitial lung disease (ILD), and systemic inflammation. The present case illustrates the challenges related to differential diagnosis of ASyS due to its differing clinical presentations. The patient was treated with intensive immunosuppressive therapy, strict infection control, as well as supportive therapy to maintain stability of the disease. Even though some recovery of neurological functions was noted, the patient’s remaining muscle weakness and relative respiratory function underscores the chronic nature and potential disablement of ASyS. To improve the patient’s outcome and halt indefensible disease advancement, multidisciplinary long-term care including rheumatology, pulmonology, and rehabilitation experts is fundamental.

Consent

All authors declare that ‘written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is submitted for review to the Editorial office/Chief Editor/Editorial Board members of this journal.

Abbreviations

**ASyS**: Antisynthetase syndrome

**ILD**: Interstitial lung disease

**IVIG**: Intravenous immunoglobulin

**tRNA**:Targeting aminoacyl-transfer RNA

**DMARDs**: Disease-modifying antirheumatic drugs

**CPK**: Creatinine phosphokinase

**UGIE**: Upper gastrointestinal endoscopy

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