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ANTI-SYNTHETASE SYNDROME: A CLINICIAN'S NIGHTMARE

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ABSTRACT
A 63-year-old male patient presented with complaints of generalized weakness, bilateral lower limb pain, swelling, and hyperkeratotic skin lesions. His myositis panel was positive for anti-KU and PL-12. Chest CT showed diffuse ground glass opacities with a non-specific interstitial pneumonitis pattern. This was suggestive of Anti synthetase syndrome. He was treated with Methylprednisolone for 3 days and later with Mycophenolic acid tablets. He was shifted to wards on the 9th day. On the 12th day, the patient was shifted back to the Intensive care unit (ICU) and he died due to bilateral aspiration pneumonia with multiorgan failure. The sudden deterioration of his condition could be due to rare complications such as pharyngeal paralysis and aspiration, myocarditis, or secondary infection. Diagnosing this myositis is difficult since the clinical features are so disparate and we should be aware of rare complications which can cause increased mortality.

KEYWORDS: Myositis, Anti-Synthetase, Autoimmune, Corticosteroids.

INTRODUCTION

Anti-synthetase syndrome is an autoimmune condition where autoantibodies are directed against Amino-Acyl transfer Ribonucleic acid synthetase (AtRNAs). It is associated with myopathy, interstitial lung disease (ILD), fever, Raynaud's phenomenon, arthritis, and a mechanic's hand.

CASE REPORT

A 63-year-old male patient presented with complaints of generalized weakness, pain in bilateral lower limbs, and breathlessness for 8-10 days. He was a known case of rheumatic mitral valve disease post-MVR (multiple valve repair) and replacement.

On initial evaluation, the patient was found to have anemia. There were petechiae and ecchymosis along with swelling in the lower limbs (Image-1). A provisional diagnosis of anemia with heart failure with probable cellulitis was made and admitted to the intensive care unit (ICU). Given his diffuse limb swelling antibiotics were initiated due to suspicion of cellulitis. Over the next 2 days, his anemia persisted and limb swelling with pain did not improve. There was progressive myalgia with swelling of the limbs. Hyperkeratotic skin lesions of both palms and feet (Image-2, Image-3), Creatine phosphokinase (CPK) level was sent which was normal. Lactate dehydrogenase (LDH) levels were also within normal limits. Peripheral smear showed microcytic anemia and a reticulocyte count of 1.4. He had increased indirect bilirubin levels with normal aspartate transaminase (AST) and alanine transaminase (ALT) levels. Tropical fever panel was also negative. His blood cultures showed no growth after 48-72 hours. Trans-esophageal echocardiography was done after intubation and mechanical ventilation, which showed normal valve function and no vegetation. Upper gastrointestinal endoscopy was also done which showed esophageal candidiasis and treated accordingly. Infective pathology was ruled out and antibiotics de-escalated.

Given the suspicion of myositis/ myopathy, a myositis panel was sent, and a chest and limb computed tomography (CT) scan was done. His myositis panel was positive for anti-KU and PL-12. This was suggestive of Anti synthetase syndrome which comprises ILD, joint

pathology along myositis. Chest CT (Image-4) showed diffuse ground glass opacities with a non-specific interstitial pneumonitis pattern and CT thigh showed normal muscle spaces with diffuse edema. A bone marrow biopsy was done after taking a hematology opinion, showing only a hyperstimulant marrow. A rheumatologist's opinion was sought and was started an injection of Methylprednisolone 500mg once daily for 3 days, later started with Mycophenolic acid tablets 360mg twice daily. His symptoms gradually improved and was successfully extubated. He was shifted to the wards on the 9th day. On the 12th day, he was shifted back to ICU because of breathlessness, type-2 respiratory failure, severe metabolic acidosis, and hypotension. The patient was intubated and ventilated but could not be revived. The sudden deterioration of his condition could be due to rare complications such as pharyngeal paralysis and aspiration, myocarditis, or secondary infection.

IMAGES

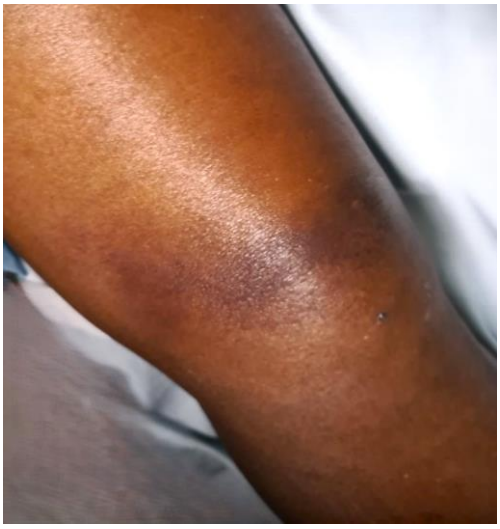

Image 1: Petechiae and ecchymosis along with swelling of the left thigh.

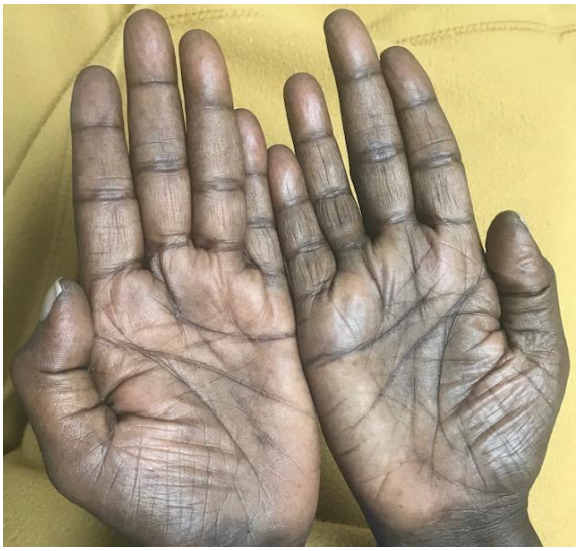

Image 2: Hyperkeratosis of the bilateral palm skin (Mechanic's hand).

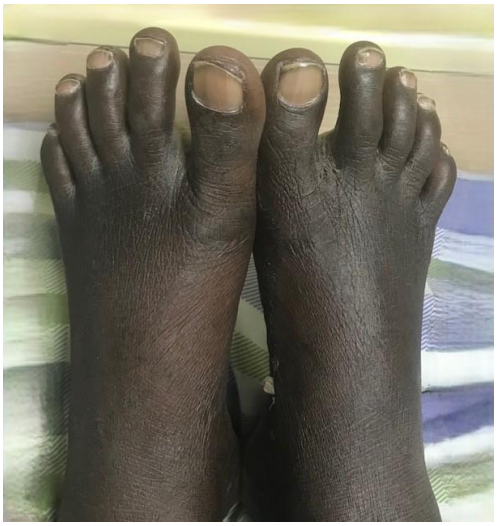

Image 3: Hyperkeratosis of the skin of bilateral foot (Hiker's foot).

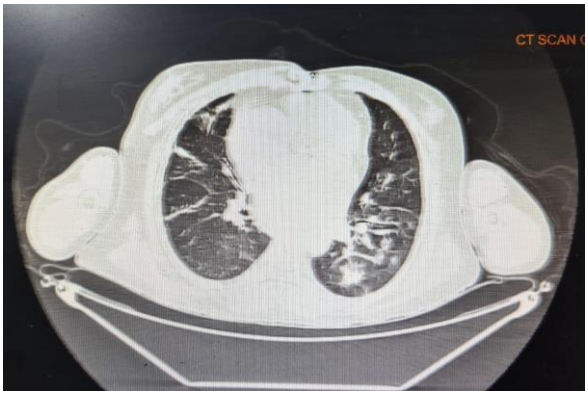

Image 4: Showing diffuse ground glass opacities with a non-specific interstitial pneumonitis pattern.

DISCUSSION

Anti-synthetase syndrome (ASyS) is a subtype of Idiopathic inflammatory myopathies. These autoimmune conditions include Dermatomyositis and polymyositis, Juvenile dermatomyositis, Amyopathic dermatomyositis, Anti-Synthetase syndrome, Immune-mediated necrotizing myopathy, and Inclusion body myositis. Anti-synthetase syndrome is a subtype of Idiopathic inflammatory myopathies. In ASyS, autoantibodies are directed against AtRNAs, an enzyme involved in protein synthesis, immune regulation, and gene transcription and silencing.

There are 8 different autoantibodies produced against AtRNAs.[1] The anti-Jo1 autoantibodies are more prevalent. The anti-Jo1 autoantibodies-associated patients have more myopathy than ILD as compared to non-anti-Jo1 autoantibodies patients who have more ILD symptoms.

The clinical features include myopathy, interstitial lung disease, arthritis (Triad), Raynaud's phenomenon, hyperkeratotic skin lesions (Mechanic's hand and Hiker's feet), fever, night sweats, and weight loss. Myopathy is seen in 90% of patients involving proximal

muscles and patients usually complain of myalgia, muscle tenderness, and difficulty in climbing stairs, and getting up from a sitting position. In 67-100% of cases, interstitial lung disease presents with cough and breathing difficulty.

Diagnosis is based on clinical suspicion and laboratory values. Muscle biopsy is not required routinely. High-resolution computed tomography (HRCT) thorax is used to diagnose ILD. The ILD patterns described are nonspecific interstitial pneumonitis, organizing pneumonitis, usual interstitial pneumonitis (UIP), and acute interstitial pneumonitis (AIP). The ASyS can overlap with rheumatic disease and may result in delayed diagnosis. Magnetic resonance imaging (MRI) of the muscle can identify muscle edema, scarring, and fatty replacement of muscle. Electromyography shows low-voltage polyphasic potentials.

The diagnostic criteria suggested by Connor et al.[2] include definitive criteria (presence of AtRNAs autoantibodies) and one of the minor criteria (fever, arthritis, Raynaud's phenomenon, ILD, and mechanic's hand).

Management mainly aims at antiinflammation and immunosuppression. Corticosteroids are the first line of treatment and for Immunosuppression mycophenolate, tacrolimus, and cyclophosphamide are used.[3] Prognosis depends upon early diagnosis and treatment. Due to diagnostic challenges, the ASyS has high morbidity and increased mortality. Multiple studies[4,5] have shown that in-hospital infection and complications related to cardiac and respiratory involvement are the leading causes of mortality. The mortality in our patient may be due to either pharyngeal weakness leading to aspiration pneumonia or myocarditis leading to multiorgan failure.

CONCLUSION

This case report highlights the importance of having high clinical suspicion of the disease and early diagnosis and treatment to reduce morbidity and mortality.

Conflict of Interest: None.

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Institutional Ethical Committee Approval Number: Our hospital Scientific committee has approved.

Informed Consent: Taken.

Author's contribution: All authors equally contributed to completing this case report (The literature search, data acquisition, data analysis, manuscript preparation, manuscript editing, and manuscript review).

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DECLARATION OF INTEREST: None declared.

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