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Case Report

A Case of Antisynthetase Syndrome Causing Critical Digital Ischemia

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Abstract:

Antisynthetase syndrome (ASS) is a heterogeneous group of systemic autoimmune diseases caused by autoantibodies against aminoacyl-transfer RNA synthetases. Although the hallmark characteristics of ASS include Raynaud phenomenon, critical digital ischemia and digital ulcers resembling systemic sclerosis are rarely reported in this condition. We hereby report an anti-Jo-1 positive ASS patient syndrome that demonstrated the typical clinical features of myositis, interstitial lung disease, "mechanic's hand", Raynaud phenomenon, intermittent fever and inflammatory arthralgia. She was initially treated with methylprednisolone and mycophenolate mofetil. During the follow up, she presented with critical digital ischemia causing severe cyanosis and digital ulcers. Upper extremity Doppler ultrasound was normal. Patient was hospitalized and intravenous iloprost infusion and acetylsalicylic acid were initiated. Unfortunately, patient developed a respiratory failure, she was intubated and was admitted to intensive care unit, where she passed away, before the efficacy of iloprost treatment could be assessed. This article also discusses the very limited amount of literature about ASS patients with severe digital ischemia.

Key words: Antisynthetase syndrome; critical digital ischemia; iloprost

Introduction

Antisynthetase syndrome (ASS) is a heterogeneous group of systemic autoimmune diseases caused by autoantibodies against aminoacyl-transfer RNA synthetases. The characteristic features of antisynthetase syndrome include inflammatory myopathy, interstitial lung disease, fever, arthralgia/arthritis, Raynaud's phenomenon, and a thickened, rough skin appearance on the lateral and palmar surfaces of the fingers, known as "mechanic's hand." It is more commonly seen in women than in men. The diagnosis of this syndrome is established by demonstrating the presence of antisynthetase autoantibodies, such as anti-Jo-1 in cases with interstitial lung involvement and/or myositis, or anti-threonyl-tRNA synthetase (anti-PL-7 and anti-PL-12) in cases with lung disease [1]. The majority of patients with anti-Jo-1 positive antisynthetase syndrome develops interstitial lung disease. Myositis is associated with significant proximal muscle weakness, affecting more than 90% of cases. Critical digital ischemia is a condition more commonly associated with systemic sclerosis. However, it has also been reported, though rarely, in patients with. antisynthetase syndrome [2]. In this case report, we report an antisynthetase syndrome patient with severe digital ischemia, while discussing the relevant literature on this rare but serious complication.

Case Report

A 56 years old female patient presented to the internal medicine outpatient clinic with complaints of muscle weakness, fatigue, and an unintentional weight loss of 10 kg over the past two months. Laboratory tests revealed elevated creatine kinase (CK) levels (2700 U/L), prompting hospitalization for further evaluation. Physical examination showed "mechanic's hands" in both hands and proximal muscle weakness in both upper and lower extremities. Electromyography (EMG) demonstrated myogenic involvement in proximal muscles, leading to a muscle biopsy from the deltoid muscle. The pathology report confirmed findings consistent with inflammatory myopathy. Laboratory tests were negative for antinuclear antibody (ANA) but positive for anti-Jo-1 in the extractable nuclear antigen (ENA) panel. Thoracic computed tomography (CT) revealed a bilateral ground-glass appearance consistent with interstitial lung disease. Upon further history taking, the patient reported intermittent fever, Raynaud's phenomenon, and arthralgias, leading to the diagnosis of antisynthetase syndrome. The patient was initially treated with a three-day course of intravenous pulse methylprednisolone, followed by oral prednisolone at a dose of 1 mg/kg (patient was 40 kg).

During follow-up, muscle strength improved, and creatine kinase levels declined. The steroid dose was gradually tapered, and the patient was discharged on oral prednisolone. Two weeks after initiating steroid therapy, mycophenolate mofetil (500 mg, twice in the morning and once in the evening) was added to the treatment regimen as a steroid sparing agent. Mycophenolate mofetil was selected due to its beneficial effects in myositis patients with interstitial lung disease. During an outpatient follow-up visit, severe cyanosis and digital ulcers developed at the fingertips of both upper extremities, prompting rehospitalization. Antiphospholipid antibodies were negative and bilateral upper extremity arterial Doppler ultrasound was normal. Due to the development of critical digital ischemia, the patient was started on acetylsalicylic acid and intravenous iloprost infusion. However, during this hospital stay, respiratory failure developed, necessitating an intensive care unit (ICU) admission and mechanical ventilation. Despite treatment, the patient's condition deteriorated, and she passed away in the ICU. Consequently, long-term follow-up and assessment of the response to digital ischemia treatment could not be conducted.

Discussion

The presence of typical clinical symptoms and positive anti-Jo-1 antibodies led to the diagnosis of antisynthetase syndrome in this patient. This case demonstrates that critical digital ischemia can occur in the course of antisynthetase syndrome, similar to systemic sclerosis, for which intravenous iloprost treatment was initiated. Early diagnosis and effective management of digital ulcers may prevent complications such as gangrene and amputation. In patients presenting with critical ischemia, including digital ulcers and gangrene, the antisynthetase syndrome should be considered in the differential diagnosis, alongside systemic sclerosis.

Since digital ischemia is not as frequently observed in antisynthetase syndrome, there is very limited amount of literature on the subject which consists of case reports and case series. Medline research using keywords "antisynthetase syndrome" and "ischemia" revealed only a total of 22 antisynthetase syndromes with 6 patients that are anti-Jo-1 positive [2-6]. In their systematic literature review concerning severe digital ischemia in patients with antisynthetase antibody positivity, Yoshida et al identified 12 antisynthetase-positive patients with severe digital ischemia from one case series and eight case reports. In addition they reported severe digital ischemia in 7 of their 100 ASS patients. Clinical features associated with severe digital ischemia in antisynthetase-positive patients included Raynaud's phenomenon, digital pitting scars, and nailfold capillary abnormalities. Outcomes of severe digital ischemia were generally favorable with vasodilators [6]. Our patient had Raynaud phenomenon but lacked digital pitting scars. We were unable to perform nailfold capilleroscopy to our patient. Response to vasodilators could not be assessed due to the deterioration in her respiratory function.

Due to its rarity, the treatment approach for critical digital ischemia in antisynthetase syndrome is typically based on the management strategies used in systemic sclerosis, in addition to immunosuppression/ immunomodulation (with agents including but not limited to glucocorticoids, methotrexate, mycophenolate mofetil, cyclophosphamide, rituximab and intravenous immunoglobulin). Xynogalas et al report critical digital ischemia in an anti Jo-1 positive antisynthetase syndrome patient that responded to treatment with a combination of immunosuppression by high dose glucocorticoids, rituximab, low molecular weight heparin, intravenous iloprost and acetylsalicylic acid [3]. Yehudina et al reported a 33 year old female ASS patient that was anti-Jo-1 whose digital ischemia did not adequately respond to many treatment modalities including immunosuppressives (methylprednisolone, methotrexate, cyclophosphamide) and vasodilators (including nifedipine, intravenous vasoprostane, intravenous iloprost, doxazosin, sildenafil) and antiaggregant (clopidogrel), which stabilied with repeated monthly intravenous immunoglobulin infusions and then further improved with rituximab [5]. Our patient was already under potent immunosuppressive treatment with methylprednisolone and mycophenolate mofetil for muscle and lung involvement of antisynthetase syndrome. When critical digital ischemia developed, we initiated vasodilator treatment with intravenous iloprost and antiaggregant treatment with acetylsalicylic acid.

Conclusion

In conclusion, critical digital ischemia resembling systemic sclerosis may develop isn ASS patients, which may necessitate intravenous vasodilator treatment in addition to immunosuppressive treatment. Early diagnosis of this potentially devastating condition and prompt, effective treatment can reduce the risk of necrosis and auto-amputation associated with critical digital ischemia, thereby decreasing morbidity in these patients.

Conflict of Interest:

None.

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