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CASE REPORT

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IVIG for refractory dysphagia in Antisynthetase syndrome: A truth hard to swallow

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Abstract

Refractory dysphasia could be the main symptom of Antisynthetase syndrome (ASS). IVIG may have a major impact in the successful treatment of dysphasia in patients with ASS. In our patient with ASS, IVIG treatment was an unreplaceable treatment option, and the patient regains her ability to swallow within 2 days.

KEYWORDS

anti-PL-12 antibody, Antisynthetase syndrome, case report, dysphasia, inflammatory myopathy, intravenous immunoglobulin

1 | BACKGROUND

Antisynthetase syndrome (ASS) is a rare inflammatory muscle disease (2–3 times more common in women than in men), related to dermatomyositis (DM) and polymyositis (PM).[1] The hallmark of ASS is the presence of serum autoantibodies directed against aminoacyl-tRNA synthetases (anti-ARS involved in protein synthesis).[2] including anti-Jo-, anti-PL-12, and other antisynthetase antibodies (ASAb).[1]

Antisynthetase syndrome is often misdiagnosed as idiopathic Inflammatory Lung Disease (ILD) or inflammatory myopathy not only due to the lack of awareness of the disease entity but also due to the lack of facilities for detection of anti-ARS antibodies.[3]

Dysphagia is a known complication of ASS and DM and has been reported in 18–20% of patients. We present a case of a young female with rapidly progressive dysphagia secondary to inflammatory myopathy treated with IVIG.

2 | CASE PRESENTATION

A 33-year-old woman presented with 6-month history of pruritic skin rashes, fevers, malaise, and 70-pounds weight-loss. Past medical history only included well controlled asthma. Family history was remarkable for SLE and scleroderma in two paternal cousins and leukemia in her grandfather. Extensive infectious workup was done in the past and she had received multiple courses of systemic antibiotic with no improvement.

On physical examination, she had bibasilar fine crackles in the lung bases. Her skin was remarkable for erythematous scaling papules located on the lateral aspect of most of her digit (*Image A*), psoriasiform raised skin lesions on both elbows (*Image B*), hyperkeratotic erythematous-flat papules on the dorsum of the metacarpophalangeal and interphalangeal joints (*Image C*) and maculopapular rash on her eyelids. Muscle strength was 4/5 in upper and lower extremities.

Laboratory studies showed elevated levels of ESR (63), CRP (3.140), ferritin (182), aldolase (12.3), but a normal CK. Given concerns for an underlying autoimmune condition, expedited rheumatologic workup was obtained and revealed positive cardiolipin, Anti-SSA, and Anti-PL-12 antibodies. She had negative antibodies to PL-7, EJ, OJ, Jo-1, Anti-smith, centromere, RNP, Scl-70, MPO, SSB, and SRP antibodies. Her Coomb's test was positive, along with an elevated PTT (36.3), but her remaining labs did not show evidence of active hemolysis. A skin biopsy was inconclusive but had findings that favored prurigo nodularis with evidence of perforation and atopic dermatitis. Although a skin biopsy is usually not required to make a diagnosis of DM, it can be helpful in distinguishing the rash of DM from other conditions that can mimic DM, such as eczema or psoriasis. We initiated glucocorticoid therapy, resulting in significant improvement of rash. She was discharged with oral prednisone 40 mg daily.

One month later, the patient returned with severe dysphagia, myalgias, and dyspnea. Now, her laboratory tests showed an elevated CK (4662), and ALT/AST (183/313). A deltoid muscle biopsy showed inflammatory myopathy consistent with dermatomyositis. A CT Thorax was preformed to assess her dyspnea, and this revealed interstitial fibrosis. To evaluate her dysphagia, she underwent a modified barium swallow study (MBSS) revealed an inability to swallow both solids and liquids.

Given the constellation of findings (ILD, arthritis, rashes, inflammatory myopathy, and anti-PL12-antibody), our patient was diagnosed with Antisynthetase syndrome. We escalated her therapy to intravenous SoluMedrol followed by prednisone, azathioprine, and hydroxychloroquine. This resulted in a resolution of her myalgias and an improvement of her CK to 800. However, there were no improvements in her dysphagia. A repeat MBSS was unchanged. Given concerns for a prolonged recovery period for our patient's dysphagia, we discussed potential for the need for a PEG tube. Before we proceeded with this plan, previous case reports in DM have shown improvement of dysphagia following months from being treated successfully with intravenous immunoglobulin. We administered a 2-day trial of IVIG (1 g/kg per day), to which our patient felt rapid improvement in swallowing and a repeat MBSS in 2 days, revealed successful passage of solids and liquids.

Because inflammatory muscle diseases can occur in association with underlying malignancy, we performed malignancy screening tests including CT chest/abdomen/pelvis and mammography. Screening for breast, colorectal, stomach, pancreatic, NHL, lung, and ovarian cancer was negative. Malignancy can also be detected within 12 months following diagnosis; thus, the screening tests were repeated in 1 year. Cancer screening was again negative.

3 | DISCUSSION AND CONCLUSION

In recent years, Antisynthetase syndrome has increasingly been recognized as an important cause of autoimmune inflammatory myopathy in a subset of patients with polymyositis and dermatomyositis,[4] but the understanding of its treatment options is still advancing.

The three major clinical criteria for the diagnosis of ASS include ILD, myositis, and arthritis. Presence of any one major criterion is sufficient to make the diagnosis of ASS. Minor criteria for the diagnosis of ASS include the presence of mechanic's hands, Raynaud's phenomenon and fever. The presence of “mechanic's hands” together with diverse skin lesions could be a clinical clue to the diagnosis of lung involvement with collagen vascular diseases, especially in antisynthetase syndrome.[5] Interstitial lung disease can affect 35–40% of patients and is often associated with the presence of an antisynthetase antibody.[4] Dysphagia is a serious symptom and at times presenting problem in patients with inflammatory myopathy. It may underlie the increased incidence of bacterial pneumonia, and nutritional deficit.

Whether the diagnosis of ASS can be made solely based on minor criteria is not clear. However, the obligatory criterion for the diagnosis of ASS remains the demonstration of anti-ARS antibodies in the serum.[3]

While initial therapy should be started with prednisone and azathioprine, treatment options for refractory cases remain unclear. Other immunosuppressants and immunomodulatory therapies have been used for steroid-refractory cases.[3] In 2006, a case report showed that treatment with rituximab according to the protocol used in rheumatoid arthritis resulted in a rapid resolution of myositis and other inflammatory features of Antisynthetase syndrome.[2]

There are limited amount of literature discussing the potential use of IVIG.[6] In 1993, a double blinded trial with 15 patients showed the benefit of once-a-month IVIG for 3 months in the treatment of refractory dermatomyositis.[7] A more recent case in 2018, a 53-year-old Korean male with dermatomyositis and severe dysphagia had significant improvement at 2 months from the IVIG therapy.[8]

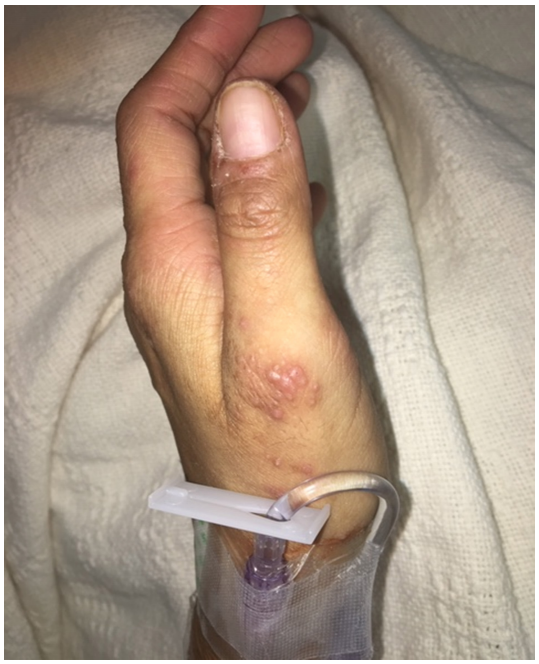
To our knowledge, high-dose IVIG and cyclophosphamide have been effective in a few cases of steroid-resistant dysphagia. However, there was no immediate improvement of dysphagia reported.[3]

Our case demonstrates the potential benefits of IVIG as a form of treatment for the disease. Limited literature has discussed the potential of IVIG, but our case specifically demonstrates drastic and rapid improvement of severe dysphagia in this setting. The administration of IVIG could be costly and requires close monitoring, but it may

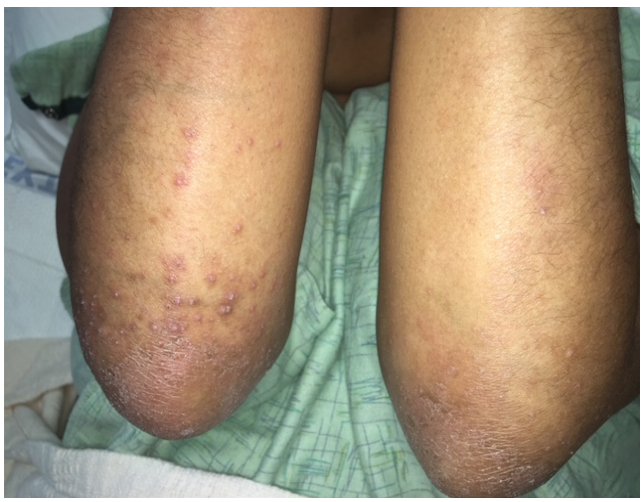
prove to have significant benefits that outweigh the risks and costs for patients.[6]

IVIG is also safer and could be better tolerated than corticosteroids or the other immunosuppressive medications and, despite the cost, may be considered the first-line drug for use as a steroid-sparing agent.[7]

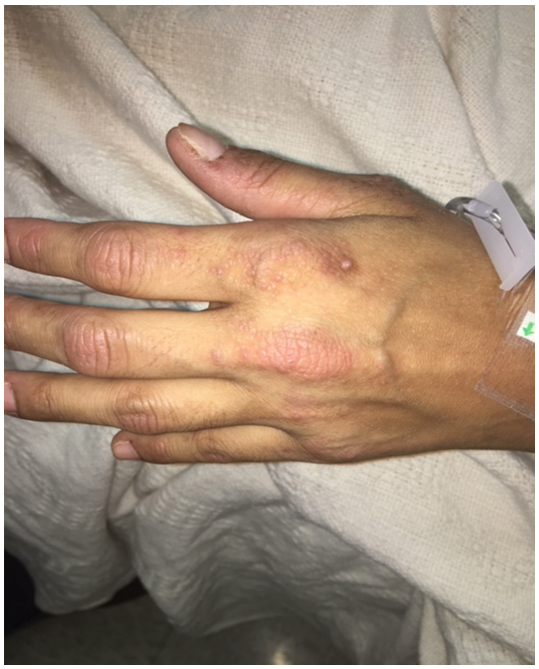
We believe that further investigation of the treatment of dysphagia and other clinical manifestations of Antisynthetase Syndrome with IVIG is well warranted.



A) Mechanic hands: Erythematous, scaling papules located on the lateral aspect of the second and third digits. Overgrown cuticles are seen containing multiple petite hemorrhages.



B) Psoriasiform raised skin lesions on elbows.



C) Gottron's papules: Violaceous, scaling papules on the skin overlying the joints.

AUTHOR CONTRIBUTIONS

Mais Alnoukari was involved primarily in management of patient and in the conception of the report, literature review, initial manuscript preparation, editing, and submission. Oziel Garza De La Garza, and Muhammad Shamim were involved in treating clinicians. Karrar Al Gburi, Niral Patel, and Henderson Lopez contributed to writing the report. Henry Kwang was involved in treating clinicians, reviewing the manuscript, and final approval.

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CONFLICT OF INTEREST

There are no conflicts of interest related to this case report.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONSENT

A written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

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REFERENCES

1. Cojocaru M, Cojocaru IM, Chicos B. New insights into Antisynthetase syndrome. *Maedica (Bucur)*. 2016;11(2):130-135.
2. Brulhart L, Waldburger JM, Gabay C. Rituximab in the treatment of Antisynthetase syndrome. *Ann Rheum Dis*. 2006;65(7):974-975. doi:10.1136/ard.2005.045898
3. Maturu VN, Lakshman A, Bal A, et al. Antisynthetase syndrome: an under-recognized cause of interstitial lung disease. *Lung India*. 2016;33(1):20-26. doi:10.4103/0970-2113.173055
4. Chatterjee S, Prayson R, Farver C. Antisynthetase syndrome: not just an inflammatory myopathy. *Cleve Clin J Med*. 2013;80(10):655-666. doi:10.3949/ccjm.80a.12171
5. Sohara E, Saraya T, Sato S, et al. Mechanic's hands revisited: is this sign still useful for diagnosis in patients with lung involvement of collagen vascular diseases? *BMC Res Notes*. 2014;7:303. doi:10.1186/1756-0500-7-303
6. Enk AH, Hadaschik EN, Eming R, et al. European Guidelines (S1) on the use of high-dose intravenous immunoglobulin in dermatology. *J Eur Acad Dermatol Venereol*. 2016;30(10):1657-1669. doi:10.1111/jdv.13725
7. Dalakas MC, Illa I, Dambrosia JM, et al. A controlled trial of high-dose intravenous immune globulin infusions as treatment for dermatomyositis. *N Engl J Med*. 1993;329(27):1993-2000. doi:10.1056/nejm199312303292704
8. Kwon KM, Lee JS, Kim YH. A case report of life-threatening acute dysphagia in dermatomyositis: challenges in diagnosis and treatment. *Medicine (Baltimore)*. 2018;97(17):e0508. doi:10.1097/md.0000000000010508

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