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Case Series

Case series on anti-melanoma differentiation-associated gene 5+ dermatomyositis associated with interstitial lung disease

Koya Pranathiya, Are Anusha, Kezia Sam, Anusha Manda*

Department of Pharmacy Practice, St. Pauls College of Pharmacy, Hyderabad, Telangana, India

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***Correspondence:**
Anusha Manda,
Email: mandaanusha961@gmail.com

ABSTRACT

Dermatomyositis (DM) associated with anti-melanoma differentiation-associated gene 5 (anti-MDA5) antibody is a rare autoimmune disease. Anti-MDA5, also known as anti-CADM-140 antibodies. DM affects the skeletal muscle, skin, joints, and lungs and is a form of idiopathic inflammatory myopathy (IIM). All the 5 dermatomyositis MDA5+ positive patients had rapidly progressive interstitial lung disease (RP-ILD). DM is classified into 2 types, classic dermatomyositis (CDM) and clinically amyopathic dermatomyositis (CADM). Anti-MDA5 antibody-positive as RP-ILD without signs of DM or CADM. RP-ILD in patients with CADM associated with antibodies to MDA5 has a high mortality rate. MDA5+ DM is diagnosed by DM rashes (Gottron's papules or Gottron's sign and heliotrope rash) and a positive anti-MDA5. RP-ILD includes acute/subacute interstitial pneumonia, which is a progressive deterioration associated with ILD. Immunosuppressives are effective agents for the treatment of anti-MDA5-positive RP-ILD of CADM.

Keywords: DM, Anti-MDA5+, ILD, CADM

INTRODUCTION

Dermatomyositis associated with anti-MDA5 antibody is a rare autoimmune disease.[1] MDA5, also known as interferon-induced helicase-1 (IFIH1), is a member of the retinoic acid-inducible gene I family of proteins like helicase (RIG-I or RLH) family of proteins, which function by recognizing single-stranded RNA viruses are involved in the innate immune response, including type I IFN production.[2,3] Anti-MDA5, also known as anti-CADM-140 antibodies.[4] Dermatomyositis MDA5+ positive patients have RPILD.[5] RP-ILD includes acute and subacute interstitial pneumonia, which is a progressive deterioration associated with ILD.[6]

DM is characterized by skin and muscle inflammation. RP-ILD is the major life-threatening complication in patients with DM.[7] RP-ILD has a 20-fold higher risk of developing in MDA5+ when compared to MDA5 negative DM, and it is the most important factor in predicting survival rate.[8-10] Dermatomyositis MDA5+ associated with RP-ILD patients presents with worsening dyspnea and cough, with radiographic deterioration causing hypoxia within 3 months of respiratory symptom onset.[11] Anti-MDA5-positive patients have RP ILD at a high frequency.[12,13] Rashes were observed clearly in a patient with Anti-MDA5-positive associated DM, but there will be mild or absence in muscle involvement or inflammation.[14] DM are classified into 2 types :CDM and CADM. It is a rare disease but a distinct type of IIM.[15-17]

The clinical features in adults of MDA5+ are DM rashes, amyopathic or hypo-myopathic muscle involvements and ILDs, Gottron's papules, Heliotrope rash, papules (frequently tender on the palm), plaques, nodules, and ulcerations. Painful ulcers are usually localized on the extensor surfaces of joints (fingers, elbows, knees).[18] The unique clinical entity has evolved and divided into two phases, i.e., the first phase nomenclature was CADM, and in the second phase, it is gradually transformed to MDA5+

DM, which is accepted by the experts.[19] Biomarkers to detect Dermatomyositis-MDA5 are serum myositis-specific autoantibodies, anti-MDA5 antibody, ferritin, surfactant protein-D, pulmonary high-resolution computed tomography (HRCT) findings of MDA5+ DM-ILD, serum neopterin, type I interferon.[20,21] Immunosuppressives are effective agents for the treatment of anti-MDA5-positive RP-ILD of CADM.[22]

CASE SERIES

Case 1

A 58-year-old female was admitted to the emergency department with complaints of poor appetite, fatigue, worsening cough, and dyspnea associated with facial rash for 1 week. She was diagnosed with dermatomyositis (MDA5+) with ILD in July 2021 for which rituximab 500 mg and cyclophosphamide 500 mg were prescribed. Given the progression of ILD and exertional desaturation, tacrolimus 1 mg and Nintedanib 100 mg were advised. However, because of poor tolerance both the drugs were stopped. Therefore, the plan was made to initiate the combination therapy of MMF with Tacrolimus at a low dose and titrate based on her tolerance.

Case 2

A 39-year-old male suffering from pain in multiple joints involving the small joints of the hands (proximal interphalangeal joints and metacarpophalangeal joints), early morning stiffness, shortness of breath (grade II), cough associated with minimal mucoid expectoration, rash on fingers was admitted in the emergency department. She was diagnosed with DM-anti MDA5 positive, early ILD. She was treated with drugs **i**nj. rituximab 500 mg infusion.

Case 3

A 38-year-old male was admitted with the chief complaints of high-grade fever, shortness of breath (grade III), and cough with scanty mucoid expectoration. He was diagnosed with dermatomyositis, RP-ILD-anti MDA5 positive, and HbsAg positive. He was treated with IV pulse steroids (Methylprednisolone 250 mg) and inj. cyclophosphamide 500mg. The patient had diffused consolidation with reticulonodular opacities in both mid and lower zones of the lung for which he was kept on oxygen support @ 8LPM with SPO2 95%.

Case 4

A 41-year-old male was admitted with chief complaints of skin rashes, generalized weakness, fatigue, and weakness in both lower limbs since 2 months. He was diagnosed with dermatomyositis anti-MDA5 positive, ILD, cutaneous involvement. He was started on with IV pulse steroids (Methylprednisolone 500 mg IV for 5 days), inj. cyclophosphamide (1st dose of inj. Endoxan 500 mg), HCQs 200 mg physiotherapy, topical medication (Excela max lotion + mometasone furoate cream) for the skin lesions, and other supportive medications.

Case 5

A 59-year-old female was admitted with chief complaints of shortness of breath for 3 months and cough for 3 months. She was diagnosed with dermatomyositis-SLE-Sjogrens syndrome overlapping with ILD. She was administered inj. Endoxan (inj. Cyclophosphamide 500mg IV infusion) and her symptoms improved it is planned to give her maintenance dose of inj. Rituximab.

DISCUSSION

Dermatomyositis is an autoimmune inflammatory disease affecting skin, joints, lungs, and underlying muscle tissue, involving degeneration of collagen, discoloration, and swelling, typically occurring as an autoimmune condition or associated with internal cancer. Genetic factors, which are an undefined viral trigger, lead to a sense of viral dsRNA by cytoplasmic pattern receptors. Virus-induced cell injury and lysis result in the release of Viral MDA5 complexes which are recognized by APCs and the helper T cells and B cells help in producing antibodies to MDA5.[22] Dermatomyositis autoantibody melanoma differentiation-associated gene 5 (anti-MDA5) was reported in patients with or without clinically amyopathic DM (dermatomyositis) (CADM) having RP-ILD and was originally called anti-CADM-140 antibodies. There was no rash of dermatomyositis reported, however, patients with anti-MDA5 antibody and skin rash were more likely to exhibit swelling of the hands, arthralgia/arthritis, skin ulcers, palmar papules, mechanical hands, hair loss, and oral mucosal ulcers. Furthermore, purpura and inverse Gottron signs suggestive of vascular injury are characteristic in patients with anti-MDA5 antibodies.[23,24] In our cases, we observed the skin rashes of CADM with anti-MDA5 antibody, the characteristic skin. Patients with RP-ILD usually have symptoms of cough and shortness of breath. In our cases, subjects were diagnosed with Dermatomyositis- MDA-5 positive, which is associated with ILD. They were admitted with chief complaints of pain in multiple joints, coughing, shortness of breath, and skin rashes. Immunosuppressive therapy is a standard and effective treatment for anti-MDA5-positive RP-ILD.[25] In our cases, dermatomyositis and ILD were treated with tacrolimus, nintetanib, steroids, inj. cyclophosphamide and Inj. Rituximab. The symptoms improved after treatment with inj. cyclophosphamide (inj. Endoxan 500 mg) followed by Inj. Rituximab.

CONCLUSION

Anti-MDA-5 DM is a rare autoimmune disease associated with RP-ILD. Anti-MDA-5 DM, also known as anti-CADM-140 antibodies. It affects skeletal muscle, skin, joints, and lungs. Patients with MDA5+ had RP-ILD at a high frequency, which is a major life-threatening complication. MDA5 + antibodies are caused by mutations

in the IFIH1 gene, which activates the production of MDA5 protein. This mutation leads to the varied MDA5 protein, which is non-functional and results in a storage deficiency of MDA5 activity. The clinical features in adults of MDA5+ are rashes, muscle involvement, ILD, Gottron's papules, heliotrope rash, plaques, nodules, and ulcerations. Patients diagnosed with MDA5+ with ILD are being prescribed rituximab along with Endoxan. In some cases, patients are given rituximab, an effective immunosuppressive therapy.

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REFERENCES

1. Briani C, Doria A, Sarzi-Puttini P. Update on idiopathic inflammatory myopathies. Autoimmunity. 2006;39(3):161-70.
2. Yoneyama M, Kikuchi M, Matsumoto K. Shared and unique functions of the DExD/H-box helicases RIG-I, MDA5, and LGP2 in antiviral innate immunity. J Immunol. 2005;175(5):2851-8.
3. Kato H, Takeuchi O, Sato S. Differential roles of MDA5 and RIG-I helicases in the recognition of RNA viruses. Nature. 2006;441(1):101-5.
4. Chitnis T, Khoury SJ. 20 Immunologic neuromuscular disorders. J Allergy Clin Immunol. 2003;111(2):S659-68.
5. Sato S, Hirakata M, Kuwana M. Autoantibodies to a, 140-kd polypeptide,CADM-140, in Japanese patients with clinically amyopathic dermatomyositis. Arthritis Rheum. 2005;52:1571-6.
6. Sakamoto N, Ishimoto H, Nakashima S, Yura H, Miyamura T, Okuno D, et al. Clinical Features of Anti-MDA5 Antibody-positive Rapidly Progressive Interstitial Lung Disease without Signs of Dermatomyositis. Intern Med. 2019;58:837-41.
7. Hoshino K, Muro Y, Sugiura K, Tomita Y, Nakashima R, Mimori T, et al. Anti-MDA5 and anti-TIF1-gamma antibodies have clinical significance for patients with dermatomyositis. Rheumatology. 2010;49:1726-33.
8. Chen Z, Cao M, Plana MN. Utility of anti-melanoma differentiation-associated gene 5 antibody measurement in identifying patients with dermatomyositis and a high risk for developing rapidly progressive interstitial lung disease: a review of the literature and a meta-analysis. Arthritis Care Res. 2013;65:1316-24.
9. Koga T, Fujikawa K, Horai Y. The diagnostic utility of anti-melanoma differentiation-associated gene 5 antibody testing for predicting the prognosis of Japanese patients with DM. Rheumatology. 2012;51:1278-84.
10. Moghadam-Kia S, Oddis CV, Sato S. Antimelanoma differentiation-associated gene 5 antibody: expanding the clinical spectrum in north American patients with dermatomyositis. J Rheumatol. 2017;44:319-25.
11. Wanlong W, Danting Z, Li GZ. Interstitial Lung disease in Anti-MDA5+ Dermatomyositis. Immunology. 2021.
12. Hoshino SSK, Satoh T. RNA helicase encoded by melanoma differentiation-associated gene 5 is a major autoantigen in patients with clinically amyopathic dermatomyositis. Arthritis Rheum. 2009;60:2193-200.
13. Nakashima R, Imura Y, Kobayashi S. The RIG-I-like receptor IFIH1/MDA5 is a dermatomyositis-specific autoantigen recognized by anti-CADM-140 antibody. Rheumatology. 2010;49:433-40.
14. Koga T, Fujikawa K, Horai Y, Okada A, Kawashiri SY, Iwa-moto N, et al. The diagnostic utility of anti-melanoma diferentiation-associated gene 5 antibody testing for predict-ing the prognosis of Japanese patients with DM. Rheumatology. 2012;51(7):1278-84.
15. Hoogendijk JE, Amato AA, Lecky BR, Choy EH, Lundberg IE, Rose MR, et al. 119th ENMC international workshop: trial design in adult idiopathic inflammatory myopathies, with the exception of inclusion body myositis, 10-12 October 2003, Naarden, The Netherlands. Neuromuscul Disord. 2004;14:337-45.
16. Bohan A, Peter JB. Polymyositis and dermatomyositis (second of two parts). N Engl J Med. 1975;292:403-7.
17. Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). N Engl J Med. 1975;292:344-7.
18. Narang NS, Casciola-Rosen L, Li S, Chung L, Fiorentino DF. Cutaneous ulceration in dermatomyositis: Association with anti-melanoma differentiation-associated gene 5 antibodies and interstitial lung disease. Arthritis Care Res (Hoboken). 2015;67:667-72.
19. Gerami P, Schope J, McDonald L, Walling H, Sontheimer R. A systematic review of adult-onset clinically amyopathic dermatomyositis (dermatomyositis sine myositis): a missing link within the spectrum of the idiopathic inflammatory myopathies. J Am Acad Dermatol. 2006;54:597-613.
20. Ye Y, Fu Q, Wang R. Serum KL-6 level is a prognostic marker in patients with anti-MDA5 antibody-positive dermatomyositis associated with interstitial lung disease. J Clin Lab Anal. 2019;33:e22978.
21. Kaieda S, Gono T, Masui K. Evaluation of usefulness in surfactant protein D as a predictor of mortality in myositis-associated interstitial lung disease. PLoS one. 2020;15:e0234523.
22. Chen Z, Cao M, Plana MN. Utility of anti-melanoma differentiation-associated gene 5 antibody measurement in identifying patients with dermatomyositis and a high risk for developing rapidly progressive interstitial lung disease: a review of the literature and a meta-analysis. Arthritis Care Res. 2013;65:1316-24.
23. Koichi Y, Aya Y, Megumi U, Shunichi K, Masafumi S, Hiroaki M. A case of anti-MDA5-positive rapidly

progressive interstitial lung disease in a patient with clinically amyopathic dermatomyositis ameliorated by rituximab, in addition to standard immunosuppressive treatment. Mod Rheumatol. 2017;27(3):536-40.
24. Fiorentino D, Chung L, Zwerner J, Rosen A, Casciola-Rosen L. The mucocutaneous and systemic phenotype of dermatomyositis patients with antibodies to MDA5 (CADM-140): a retrospective study. J Am Acad Dermatol. 2011;65:25-34.
25. Muro Y, Sugiura K, Akiyama M. Cutaneous Manifestations in Dermatomyositis: Key Clinical and Serological Features-a Comprehensive Review. Clin Rev Allergy Immunol. 2016;51(3):293-302.
26. Kameda H, Nagasawa H, Ogawa H, Sekiguchi N, Takei H, Tokuhira M, et al. Combination therapy with corticosteroids, cyclosporin A, and intravenous pulse cyclophosphamide for acute/subacute interstitial pneumonia in patients with dermatomyositis. J Rheumatol. 2005;32(9):1719-26.

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