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CASE REPORT

Demyelinating Polyneuropathy, Dermatomyositis, and Interstitial Pneumonitis Associated with Autoantibody Against Melanoma Differentiation-associated Gene 5

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Patients with serum anti-melanoma differentiation-associated gene 5 autoantibodies (anti-MDA5) are related to amyopathic dermatomyositis, especially in Asians. Here, we present a 46-year-old woman who was diagnosed with anti-MDA5-mediated demyelinating polyneuropathy clinically mimicking dermatomyositis. She had rapid progression of interstitial pneumonitis complicated with *Pneumocystis jirovecii* and *Aspergillus* pneumonia with septic shock. It is rare that patients with anti-MDA5-positive dermatomyositis present as demyelinating polyneuropathy.

Key words: Anti-melanoma differentiation-associated gene 5, polyneuropathy, dermatomyositis

INTRODUCTION

An autoantibody against anti-melanoma differentiation-associated gene 5 (anti-MDA5) is capable of recognizing long dsRNA structures or binding to viral RNA and contributes to type 1 interferon-mediated inflammation.[1] The anti-MDA5 is identified from the group of clinically amyopathic dermatomyositis initially and associated with rapidly progressive interstitial lung disease (ILD).[2] Here, we described the patient with anti-MDA5-positive dermatomyositis whose initial presentation mimicking demyelinating polyneuropathy.

CASE REPORT

The patient was a 46-year-old woman who had lived in Thailand for the previous 6 years. She developed orthopnea, general myalgia, and epigastric pain 2 months before this admission. Her symptoms resolved within 1 week. She had a sudden onset of left hemiparesis predominantly involving the lower limb, and magnetic resonance imaging of the brain showed no acute cerebral infarction. The hemiparesis subsided with conservative treatment. She had fever, erythematous skin rashes on both thighs, and swelling of the neck 1 month before this admission. She returned to Taiwan and was admitted for examinations. During hospitalization, weakness of the proximal limbs developed, followed by dysphagia and erythematous papules with pruritus on the thighs, trunk, and entire abdomen. A complete blood count revealed leukopenia. Biochemical test results are presented in Table 1. She underwent a bone marrow biopsy, but no abnormality was noted. She was referred to our hospital because of progressive weakness of the proximal lower limbs and severe myalgia.

On admission, the patient was alert and oriented, with fluent speech. Physical examination of the cranial nerve was normal. She had decreased strength of the trapezius muscle, sternocleidomastoid muscle, and proximal limbs, particularly the proximal part of the left lower limb, together with tenderness. There was no rigidity or tremor of any of the four limbs. There were symmetric normal proprioception, light touch, and pain sensation. The deep tendon reflex of all four limbs was mildly decreased. She had mild trunk ataxia with relatively normal tandem gait. There were no Kernig's, Brudzinski's, Babinski's,

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or Hoffman's signs. She presented with intermittent fever, scattered purpura over the fingertips bilaterally, and nail ulcerations [Figure 1]. Blood biochemistry results were as follows: creatine kinase 629 U/L (normal: 26–192 U/L), aspartate aminotransferase 241 U/L (normal: <40 U/L), alanine aminotransferase 85 U/L (normal: <40 U/L), and ferritin 2381 ng/mL (normal: 10–291 ng/mL) [Table 1]. Serum autoantibody tests were negative for antinuclear antibody (Ab), anti-Ro/La Ab, anti-Smith Ab, anti-ribonucleoprotein Ab, anti-double-stranded deoxyribonucleic acid Ab, anti-topoisomerase I Ab, anti-mitochondrial Ab, anti-Jo-1 Ab, anti-Mi-2 Ab, anti-centromere Ab, anti-fibrillarin Ab, anti-ribonucleic acid polymerase III Ab, and anti-PM/Scl Ab.

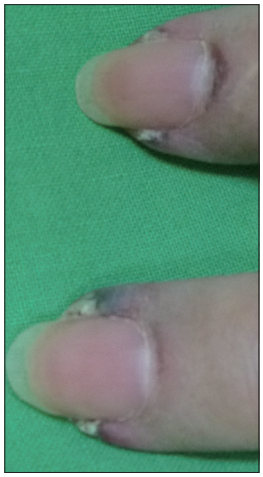

Figure 1: Nail ulcerations with scattered purpura on bilateral fingertips

Nerve conduction velocity assessment revealed a prolonged F wave and a motor-predominant axonal-type demyelinating polyneuropathy involving the median, ulnar, and peroneal nerves. Electromyography revealed normal insertion activities. The patient underwent muscle biopsy of the left proximal thigh, which revealed relatively normal skeletal muscle bundles with only scant inflammatory cell infiltration. She underwent lumbar puncture with an open pressure of 27 cm H_2O and a closed pressure of 8 cm H_2O. The cerebrospinal fluid (CSF) was clear and without white blood cells, and the protein and glucose levels were 30 mg/dL (normal: 15–45 mg/dL) and 50 mg/dL (normal: 40–70 mg/dL), respectively. CSF examinations, including microbial cultures and polymerase chain reaction (PCR) for *Mycobacterium tuberculosis*, herpes simplex virus, cytomegalovirus, enterovirus, and human papillomavirus, were negative. Blood analysis for screening neuropathy and myopathy revealed the presence of anti-MDA5.

This patient initially tolerated steroids, nonsteroidal anti-inflammatory drugs, and disease-modifying antirheumatic drugs (azathioprine). However, she developed exertional dyspnea. Chest radiography revealed bilateral infiltrates 4 weeks after admission [Figure 2a], which indicated rapid progressive severe acute respiratory distress syndrome (ARDS). She was mechanically ventilated and given veno–venous mode extracorporeal cardiopulmonary oxygenation support [Figure 2b]. Chest computed tomography revealed ground-glass opacities involving all pulmonary lobes, with interstitial thickening at the peripheral region [Figure 3]. Infectious work-up of the sputum demonstrated the presence of

Table 1: Selected laboratory values

	Reference range	1 month before admission	1 day after admission	2 weeks after admission	3 weeks after admission	4 weeks after admission (pneumonia)	After plasma exchange (5 sessions)
White blood cells ($\times10^3/\mu L$)	4.5-11.0	1.94	4.18	3.45	4.09	4.22	13.69
Percentage of neutrophils		68	73.5	79.7	88.1	94.9	80.4
Hemoglobin (g/L)	12-16	10.4	11	10.7	8.4	10.5	11.3
Platelets ($\times10^3$/mL)	150-400	152	216	150	263	66	76
AST (U/L)	0-40	44	241	101	90	92	199
ALT (U/L)	0-41	16	85	54	33	13	62
Total bilirubin (mg/dL)	0.3-1		0.4		0.4	1.6	2.4
CK (U/L)	26-192		629	352	213	130	52
LDH (U/L)	140-271		550	448	484	844	
Ferritin (ng/mL)	10-291		2381	1928	1821	2675	1959
CRP (mg/dL)			0.42	<0.1	6.44	29.23	4.01
BUN	7-25	13	16	22	16	29	32
Creatinine (mg/dL)	0.5-0.9	1	0.5	0.6	0.7	1.8	1.3

AST=Aspartate aminotransferase; ALT=Alanine aminotransferase; CK=Creatine kinase; LDH=Lactate dehydrogenase; BUN=Blood urea nitrogen; CRP=C-reactive protein

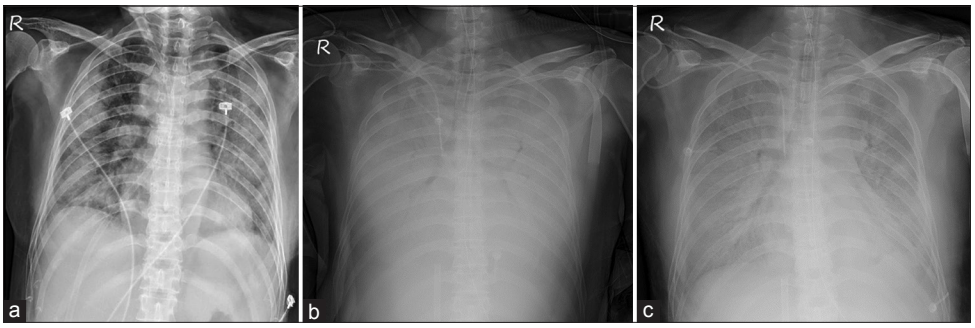

Figure 2: (a) Chest radiography revealing bilateral ground-glass infiltration of the peripheral lungs, (b) rapid progression of the consolidation shown on air bronchogram 2 days later, and (c) improvement in the pulmonary infiltration after five sessions of plasma exchange

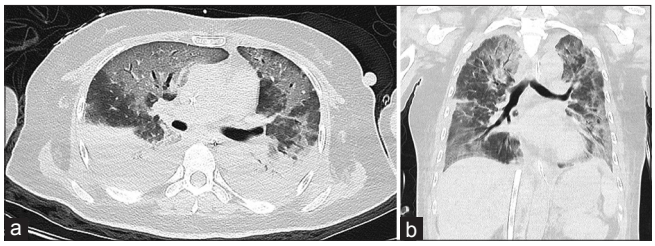

Figure 3: Chest computed tomography shows ground-glass opacities in all lobes of the lung with thickening of the interstitial lines in the peripheral lung region (a. Horizontal view of lower lung. b. Coronal view)

Pneumocystis jirovecii on PCR and *Aspergillus* galactomannan antigen. In addition to prednisolone, antibiotic treatment with sulfamethoxazole/trimethoprim and voriconazole was administered for P. *jirovecii* and *Aspergillus* pneumonia with septic shock. She underwent plasma exchange daily for five sessions to treat the anti-MDA5 Ab-mediated demyelinating polyneuropathy. One week after treatment, chest radiography and computed tomography demonstrated partial remission of the pulmonary infiltration and alveolar consolidation [Figure 2c]. Blood analysis showed improved oxygenation and reduced serum lactate levels. Nonetheless, she developed massive intracerebral and intraventricular hemorrhage, including severe compression of the brain stem. She received hospice care and eventually died.

DISCUSSION

Our patient was diagnosed with anti-MDA5-mediated demyelinating polyneuropathy and dermatomyositis based on her clinical presentation, neurological examination results, and the presence of serum anti-MDA5. Patients with dermatomyositis and serum anti-MDA5 can develop mucocutaneous phenotypes including Gottron's papules, oral mucosal pain, palmar papules with tenderness, and nail fold ulcerations.[3] According to a literature review, patients with serum anti-MDA5 have a high risk of rapidly progressive ILD.[2,4-7] There are more prevalent of ILD, especially rapidly progressive and life-threatening variant in Asian people than European and American people.[8] Hyperferritinemia may be a biomarker of poor outcome in acute progressive interstitial pneumonitis.[4]

Patients with anti-MDA5-positive dermatomyositis express nitric oxide synthase 2 (NOS2) in muscle fibers which can downregulate immune responses and associate with muscle regeneration.[9] The expression of NOS2 may explain the clinical hypomyopathic or amyopathic phenotypes. Interestingly, MDA5 knockout mice develop demyelination of the central nervous system after viral infection.[10] It is rare that patients with anti-MDA5-positive dermatomyositis present as demyelinating polyneuropathy.

In summary, our patient initially had a suspected virus infection followed by thyroiditis and lymphadenopathy. Serum anti-MDA5 Ab developed, which caused mucocutaneous symptoms including transient rash in the "holster" configuration, multiple nail ulcers, and demyelinating polyneuropathy in the absence of pathological myopathy. Rapid progression of interstitial pneumonitis complicated by *P. jirovecii* and *Aspergillus* pneumonia contributed to septic shock and ARDS. Clinicians should be aware that patients present demyelinating polyneuropathy combination with dermatomyositis-like mucocutaneous lesions and serum anti-MDA5 positive. It may be the symbol of hypomyopathic or amyopathic dermatomyositis with a poor prognosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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