CASE REPORT

Clinically amyopathic dermatomyositis associated with anti-MDA5 antibody

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Accepted 18 December 2017

SUMMARY

Clinically amyopathic dermatomyositis (CADM) is a rare entity that presents with cutaneous manifestations of classic dermatomyositis but without muscle weakness or abnormal muscle enzymes. It is more common in young white and Asian females. A subset of patients with CADM has a specific antibody known as anti-MDA5.

These patients have a more aggressive course with distinct cutaneous features, pulmonary involvement and early death. Here, we present the case of a 64-year-old Caucasian male with no significant medical history who was admitted with marked weight loss and a painful rash for 6 months. Patient had no muscle weakness and his rash was characteristic of classic dermatomyositis. Skin biopsy was suggestive of dermatomyositis but muscle enzymes were normal. His serum was positive for anti-MDA5 antibody. Extensive workup failed to detect any malignancy but he did show non-specific interstitial pneumonia. He was treated with prednisone and mycophenolate with good clinical response.

BACKGROUND

Clinically amyopathic dermatomyositis (CADM) is a rare disease that has been recently recognised as a subgroup of dermatomyositis. CADM share similar cutaneous features of classic dermatomyositis but has no or minimal muscle involvement. CADM associated with anti-MDA5 antibody is a novel entity with a more aggressive course that has distinct cutaneous features compared with classic dermatomyositis. Also, lung involvement such as interstitial lung disease (ILD) and rapid progressive ILD (RPILD) are much more common than CADM not associated with anti-MDA5 antibody. A high index of suspicion is needed for prompt diagnosis and treatment since any delay in treatment could cause significant morbidity and even fatality.

CASE PRESENTATION

A 64-year-old Caucasian male with no significant medical history was transferred to our hospital from another centre with a 6-month history of weight loss, fatigue and a painful rash. The patient first noticed an erythematous rash in his upper back and then spread to his arms and legs. He was seen by a dermatologist and was treated conservatively; however, he developed polyarthritides affecting the small joints of his hands, associated with fatigue and prolonged high-grade fevers. Patient was admitted to an outside hospital to be evaluated for fever of unknown origin. He tested

positive for IgM to *Brucella melitensis* with a suspicious lesion on aortic valve on echocardiogram. Treatment for suspected *Brucella* endocarditis was started including rifampin, doxycycline and gentamicin; however, final confirmatory test for *Brucellosis* came back negative. Given lack of clinical improvement, a transoesophageal echocardiogram (TEE) was done and demonstrated a fixed calcified mass on aortic valve without evidence of vegetation. Repeated TTE demonstrated an aortic valve calcification. Blood and urine cultures were negative. His course was complicated by acute renal failure requiring temporary haemodialysis. Renal biopsy was consistent with acute tubular necrosis most likely due to gentamicin, well-known nephrotoxin and intravascular depletion. The urinalysis was unremarkable with no evidence of proteinuria or haematuria and his renal function improved with the cessation of gentamicin and with fluid repletion. Further investigation, with CT of the chest, abdomen, pelvic showed mediastinal and intraperitoneal lymphadenopathy with right-sided colitis. Colonoscopy showed non-specific findings of right-sided colitis with no significant pathology. Bronchoscopy with bronchoalveolar lavage and mediastinal lymph node biopsy showed non-specific reactive inflammation. As part of the workup for persistent fever, the patient underwent a bone marrow biopsy that was also unremarkable. Rheumatological workup revealed a positive Sjogren's Syndrome antibody (SSA) with a titer of 137 AU/mL (normal range 0–40 AU/mL) but other autoantibodies including antinuclear antibody, anti-Jo-1, scleroderma-70, anticentromere antibody, antineutrophil cytoplasmic antibodies and anticyclic citrullinated peptides were all negative. Skin biopsy (without immunofluorescence test) showed chronic non-specific cytotoxic dermatitis. The patient was empirically treated with prednisone 30 mg daily for possible autoimmune disease based on the positive SSA antibody and with some improvement of his joint pain and fever. He was transferred to our hospital for further evaluation.

On admission, patient had normal vital signs. On physical examination, the patient was found to have palmar erythema with scaling rash, erythematous violaceous plaques and papules on both hands, mainly over proximal interphalangeal and metacarpophalangeal joints, dorsum of the hands, elbows and legs, with periungual capillary dilatation on nailfold examination (figure 1). Lung examination revealed bibasilar crackles and

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To cite: Parperis K, Kiyani A. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-222060

Figure 1 Erythematous violaceous plaques and papules on both hands, mainly over proximal interphalangeal and metacarpophalangeal joints, dorsum of the hands, with periungual capillary dilatation on nailfold examination.

his muscle strength examination was intact (five out of five) throughout.

INVESTIGATIONS

Laboratory studies showed an elevated sedimentation rate level of 105 mm/hour (normal 0–20), C-reactive protein level of 10 mg/L (normal <4.9) and ferritin was 7800 ng/mL (normal 11–307). Further evaluation with chronic hepatitis panel, HIV, coccidioidomycosis serology and Whipple's disease were all negative. Serum complement levels, aldolase and creatine kinase (CK) were within normal range. A repeat CT chest scan showed bilateral ground opacities (figure 2), consistent with non-specific interstitial pneumonia (NSIP).

DIFFERENTIAL DIAGNOSIS

Differential diagnoses include primary dermatomyositis, paraneoplastic dermatomyositis, CADM, polymyositis, cutaneous T-cell lymphoma, acute febrile neutrophilic dermatosis (Sweet's syndrome), adult-onset Still's disease and Sjogren's syndrome complicated with lymphoma.

TREATMENT

Given the board differential diagnosis and the systemic nature of his disease, a repeat skin biopsy was obtained from the dorsum of the hand that revealed interface vacuolisation and increase dermal mucin, consistent with interface dermatitis

Figure 2 Chest CT scan shows bilateral lower lobes ground glass opacities.

(figure not shown), supportive the diagnosis of dermatomyositis. A myositis antibody panel testing was positive for the melanoma differentiation-associated gene 5 (anti-MDA5) antibody. Therefore, based on the positive test, normal muscle examination and enzymes, the presence of NSIP on chest CT scan, skin findings and biopsy, our patient was diagnosed with CADM associated with anti-MDA5 antibody. Our patient was started on prednisone 60 mg daily with weekly taper. Mycophenolate 1000 mg twice daily was added based on a case report that demonstrated efficacy of the above agent in a patient with CADM with MDA5 antibody and a recent study in patients with scleroderma and ILD showed that mycophenolate has comparable efficacy with cyclophosphamide and has a better adverse effect profile.¹²

OUTCOME AND FOLLOW-UP

His symptoms continued to improve with this regimen and he has not experienced any flares during clinic follow-ups. At his last clinic visit, the patient was symptom free.

DISCUSSION

CADM is a rare systemic inflammatory disorder manifested with the classic cutaneous features of dermatomyositis (Gottron's papules, heliotrope rash), for at least 2 years without any signs of proximal muscle weakness, with normal serum muscle enzymes and with no abnormalities on the electromyogram or muscle biopsy; however, a subset of patients may develop slight elevations of muscle enzymes (CK level of 400–500 UI/L).³ CADM is more common among white and Asian females in their fifth and sixth decades of life.⁴ A number of autoantibodies have been associated with CADM including the MDA5 antibody.⁵ MDA5 is an RNA-specific helicase that functions in recognising single-stranded RNA viruses.⁶ It recognises intracellular viral infection and initiates an immune defence response, including the release of type I interferons (IFNs) and modulates the subsequent adaptive immunity.⁷ Interestingly, an infectious process has been considered as a potential cause or triggering event for idiopathic inflammatory myopathies and the activation of MDA5 helicase by infection can explain the production of elevated levels of type I IFNs in a subset of patients with dermatomyositis.⁶ The CADM with the MDA5 antibody positivity has been associated with cutaneous ulcers, digital tip ulceration, ILD and rapidly progressive ILD (RPILD).^{8–9} These patients have a poor prognosis compared with patient without anti-MDA5 antibody with early death.¹⁰ Interestingly, high serum levels of ferritin, such as in our patient, have been reported to be associated with RPILD and a poor prognosis.¹¹ Based on the clinical presentation of our patient and his remarkable response to immunosuppression, we do not feel our patient has RPILD but seems to have a chronic form of ILD.

Like dermatomyositis, CADM can be associated with malignancies. Lung, breast, genitourinary, gastrointestinal and nasopharyngeal cancers are the most commonly associated malignancies with CADM.¹²

Management of anti-MDA5-associated CADM can be challenging, especially in patients with chronic ILD and includes corticosteroids, immunosuppressants like calcineurin antagonists and biologics. A recent case report favours the use of mycophenolate as the primary treatment in patients with ILD and CADM with the anti-MDA5 antibody.¹ In addition, patients with RPILD and respiratory failure might benefit with the use of basiliximab or cyclophosphamide.^{13 14} Furthermore, the use of direct haemoperfusion using polymyxin-B immobilised fibre column therapy

has showed some promise as a potential therapeutical option in patients with CADM positive to anti-MDA5 and RPILD.¹⁵

In summary, CADM is a rare disease that shares cutaneous manifestations of dermatomyositis but without muscle involvement. Anti-MDA5-associated CADM is a novel entity that has a more aggressive course with distinct cutaneous findings and ILD. Management is challenging and most patients finally succumb to their disease.

Learning points

- ▶ Clinically amyopathic dermatomyositis (CADM) is a rare systemic inflammatory disorder manifested with the classic cutaneous features of dermatomyositis but without signs of muscle involvement.
- ▶ CADM with the MDA5 antibody positivity has been associated with cutaneous ulcers, digital tip ulceration, interstitial lung disease (ILD) and rapidly progressive ILD (RPILD).
- ▶ Management of anti-MDA5-associated CADM remains challenging, especially in patients with ILD and includes corticosteroids, immunosuppressants and biological agents.

Contributors Both authors have participated in the preparation of this manuscript and contributed to the planning, conduct, reporting, conception and design, acquisition of data or analysis and interpretation of data.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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