

2. TWO CASES OF ANTI-MDA5 POSITIVE DERMATOMYOSITIS WITH RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE

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Introduction: Melanoma differentiation-associated gene 5 (MDA5) is a myositis-associated autoantibody. It is increasingly being recognised that this antibody presents with typical skin lesions and the potential for a rapidly progressive interstitial lung disease but without muscle involvement. We present two cases of patients with MDA5 positive dermatomyositis who both developed rapidly progressive lung disease and despite intensive treatment passed away.

Case description: A previously well 48-year-old Caucasian man presented with a few months history of inflammatory arthritis, Raynaud's and Gottron's papules. He also described exertional breathlessness and was found to have fine inspiratory crackles bibasally. An HRCT scan showed cryptogenic organising pneumonia (COP). Inflammatory markers and creatine kinase were normal but an extended myositis panel showed positive anti-MDA5 antibodies consistent with a diagnosis of amyopathic dermatomyositis. He was started on cyclophosphamide as part of a research trial, given iloprost and sildenafil for worsening digital ischaemia and commenced on home oxygen. He was admitted with worsening shortness of breath after the second cycle of cyclophosphamide and found to have pneumocystis jirovecii (PCP) positive sputum. He developed pyrexia with a positive influenza A swab and increasing oxygen requirements requiring transfer to ITU. Despite further antibiotics, antivirals, steroids, IV immunoglobulin and rituximab infusion he deteriorated further and died 13 days later.

The second patient was a 45-year-old Asian man. He was initially seen by dermatology with alopecia and a scaly rash on his face, elbow and hands. He was then diagnosed with early inflammatory arthritis and commenced steroids and methotrexate. He developed skin ulceration and respiratory symptoms with a CT chest showing features of COP. He was ANA negative but anti-Ro and anti-Scl-70 positive. He was given antibiotics, methylprednisolone and switched to mycophenolate mofetil. Whilst abroad he was admitted to hospital, diagnosed with anti-MDA5 positive amyopathic dermatomyositis and given methylprednisolone and cyclophosphamide. Cyclophosphamide was continued on his return to the UK, with PCP prophylaxis but he also required home oxygen. He was admitted to hospital with increasing breathlessness and given further methylprednisolone and treatment dose co-trimoxazole. Two weeks later he deteriorated further and repeat CT scan showed a pneumomediastinum. He received antibiotics, antifungals and rituximab but died after three days on ITU.

Discussion: Although in both cases it was recognised the patients had some form of inflammatory condition the diagnosis of anti-MDA5 positive dermatomyositis took some time. The lack of muscle involvement is typical and means clinicians need to give more thought to the possible diagnosis particularly when patients present with skin lesions and look specifically for MDA5 antibodies. These cases also show how rapidly the lung disease can progress. Being aware that a patient is MDA5 positive gives important information to the clinical team regarding the potential prognosis and in these cases it has been questioned whether these concerns were entirely relayed to the patients and their families. High serum ferritin, ground-glass opacities in all six lung fields and worsening of pulmonary infiltrates during therapy have been suggested as further poor prognostic factors.

Both patients presented particular challenges in trying to decide whether their deterioration was due to infection in the context of immunosuppression, disease progression or both and consequently full infection screens were performed including bronchoscopies at various points. Given how unwell both patients were all available treatments were considered. Once it was recognised how rapidly the lung disease was progressing they both received cyclophosphamide and rituximab. IV immunoglobulin was requested for both patients but only agreed for the first patient as he had proven PCP pneumonia.

Key learning points: Anti-MDA5 positive dermatomyositis commonly presents with typical mucocutaneous lesions (such as cutaneous ulceration, alopecia and oral ulcers) which can differ from those seen in classical dermatomyositis. It is important to consider the possibility of anti-MDA5 positive dermatomyositis in a patient with skin abnormalities and a normal CK, and in such circumstances request an extended myositis screen ensuring MDA5 is included. Patients who are MDA5 positive and have lung involvement often have rapidly progressive interstitial lung disease. Prognosis is especially poor when patients are admitted to ITU and worse than patients with anti-synthetase syndrome. Spontaneous pneumomediastinum can be a feature when the outcome is almost always poor in a ventilated patient. Treatment options are limited, generally aggressive immunosuppression is recommended when there is lung involvement and induction therapy with cyclophosphamide or rituximab has been tried. There are emerging reports of JAK inhibitors being used in dermatomyositis and so this may be something to consider in this subset of difficult to treat patients.

Consideration should be given to vaccinating against influenza and pneumococcal infections as soon as possible, together with PCP prophylaxis and aggressive treatment of superadded infections. When appropriate patients and relatives should be made aware of the potentially poor prognosis. It is important to work closely with other specialities such as dermatology, respiratory and when necessary ITU. Due to the complexity and severity of this condition an MDT approach is recommended.

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