Beyond serological classification: severe multisystem muscle involvement and fulminant dysphagia in anti-Mi-2-positive dermatomyositis

Dear Editors,

Anti-Mi-2-positive dermatomyositis (DM) is associated with the classic DM phenotype with high creatinine kinase (CK) levels but generally considered a favourable disease subset with less frequent severe systemic manifestations compared with other myositis-specific autoantibody (MSA) subsets (1, 2). We report here the case of a patient with anti-Mi-2-positive DM who presented with the characteristic cutaneous findings but developed exceptionally severe multisystem muscle involvement, including fulminant dysphagia and gastrointestinal dysmotility, an uncommon and potentially under-recognised phenotype in this subgroup. Furthermore, we highlight differential recovery of muscle domains, a phenomenon that has not been specifically described previously.

A 55-year-old man with no significant medical history presented with a two-week history of progressive proximal muscle weakness and myalgia, followed by dysphonia and dysphagia. Examination revealed a heliotrope rash, Gottron papules and macules, periungual erythema, shawl sign and V-sign, together with severe proximal muscle weakness. Laboratory investigations demonstrated markedly elevated CK (15,734 U/L), alanine aminotransferase (689 U/L), aspartate aminotransferase (352 U/L), lactate dehydrogenase (928 U/L), myoglobin (3,682 ng/mL), and troponin T (1,010 ng/L). Antinuclear antibodies showed a fine speckled nuclear pattern (1:640), and immunoblotting identified anti-Mi-2 autoantibodies. Electromyography, muscle MRI and muscle biopsy were consistent with inflammatory myopathy. Swallowing assessment confirmed upper dysphagia. Positron emission tomography and serum tumour markers showed no evidence of malignancy.

The patient was initially treated with intravenous methylprednisolone pulses followed by oral methylprednisolone and azathioprine. Despite early treatment and improvement of skin manifestations, his condition rapidly deteriorated within days of admission with progressive proximal weakness, persistently elevated CK levels, and a further rising troponin T levels up to 4,697 ng/L. Echocardiography demonstrated a reduced left ventricular ejection fraction of 45%, suggesting possible myocarditis. Dysphagia worsened substantially, involving both the pharyngeal and oesophageal phases of swallowing (Fig. 1). Cricopharyngeal muscle spasm result-

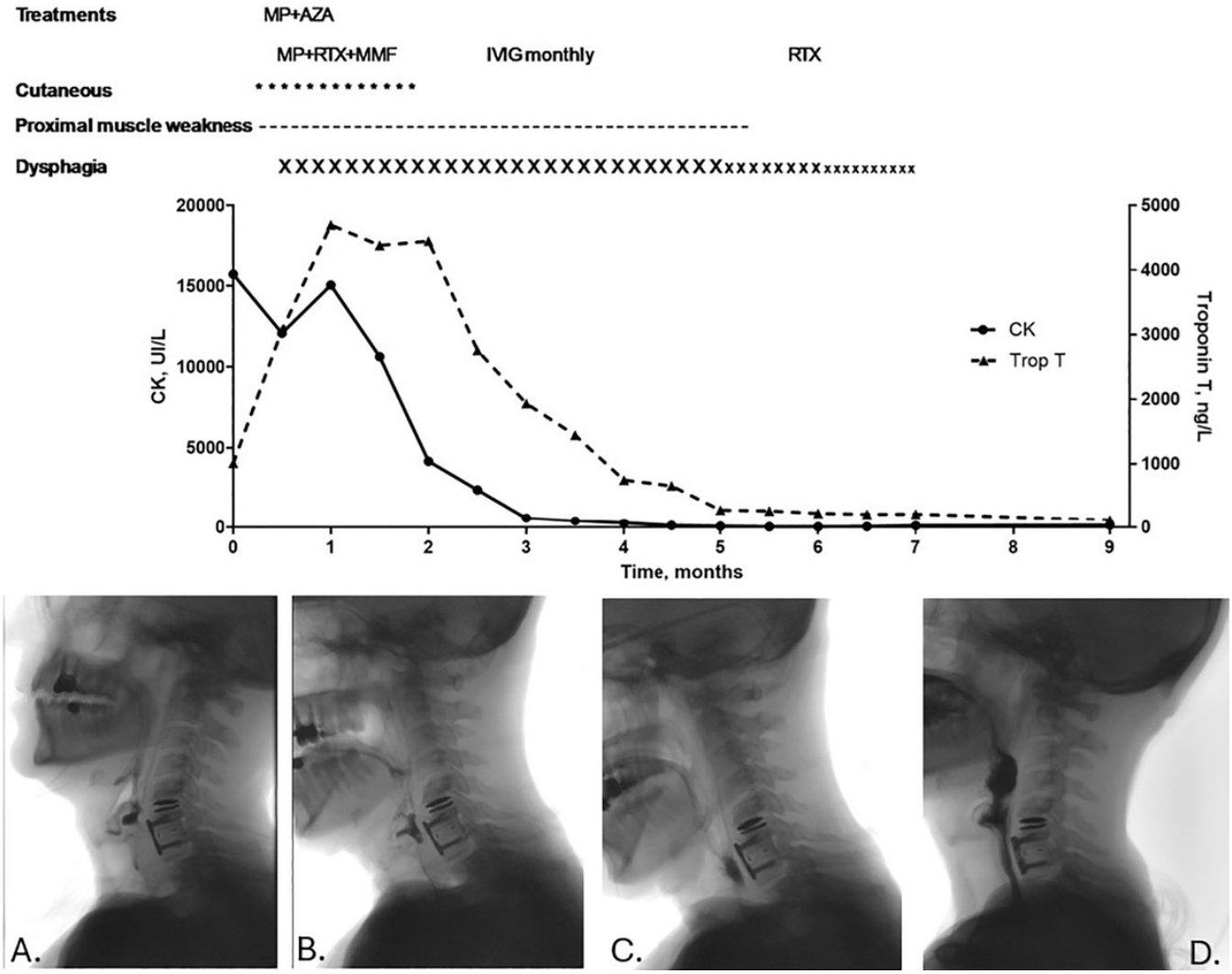


Fig. 1. Timeline of the disease course in anti-Mi-2 positive dermatomyositis, illustrating serum creatine kinase and troponin T levels, therapeutic interventions, and major clinical manifestations. Videofluoroscopic swallowing studies demonstrate severe pharyngeal and oesophageal dysfunction at presentation (**A-C**) with marked improvement after 6 months of treatment (**D**).

MP: methylprednisolone; AZA: azathioprine; RTX: rituximab; MMF: mycophenolate mofetil; IVIG: intravenous immunoglobulin; CK: creatinine kinase.

ed in functional oropharyngeal stenosis, causing complete inability to swallow and persistent salivary stasis. Methylprednisolone pulses were repeated, rituximab was initiated, and azathioprine was replaced by mycophenolate mofetil. Complete loss of oral intake necessitated nasogastric tube feeding, followed by jejunostomy placement. In parallel, gastrointestinal involvement was suspected, particularly gastrointestinal dysmotility. Together with severe dysphagia, these complications resulted in profound malnutrition and a 38% weight loss. Impaired clearance of oral secretions led to recurrent respiratory infections, culminating in aspiration pneumonia with severe respiratory distress requiring intensive care admission. Because of administrative constraints related to treatment access, intravenous immunoglobulin was initiated only during the intensive care stay. At that time, three months after admission, severe dysphagia persisted despite resolution of cutaneous manifestations and improving biochemical markers of muscle injury. Following treatment with monthly intravenous immunoglobulin and repeated rituximab over six months, combined with nutritional support, intensive physiotherapy and dedicated swallowing rehabilitation, the patient gradually improved. Muscle strength and swallowing progressively recovered, troponin T levels declined, and cardiac function normalized within nine months.

Although MSAs are highly specific and diagnostically valuable at the population level (3), substantial heterogeneity exists within autoantibody-defined subsets, limiting their ability to predict disease severity in individual patients. This case illustrates the broad spectrum of muscle involvement that may occur in anti-Mi-2-positive DM, affecting not only proximal skeletal muscles but also cardiac, pharyngeal, laryngeal and possibly gastrointestinal musculature. While these manifestations may share an inflammatory background, it remains unclear whether the same pathophysiological mechanisms underlie heterogenous domains of muscle involvement. Importantly, muscle systems demonstrated divergent responses to treatment (Fig. 1). While CK levels declined after three months, swallowing function and troponin T levels recovered much more slowly, suggesting distinct recovery trajectories across muscle domains that are not necessarily reflected by CK normalisation and improvement in limb muscle strength (4). This dissociation in recovery suggests that muscle involvement in DM cannot be regarded as a homogeneous process across different functional muscle domains. Whether this reflects intrinsic biological differences among limb, oropharyngeal and cardiac muscle, differential susceptibility to inflammatory injury, or the complexity of neuromuscular coordination required for swallowing remains uncertain. Dysphagia affects approximately one-third of patients with inflammatory myopathies, may lead to life-threatening complications and is associated with a poor prognosis (5). It has been reported most frequently in cancer-associated myositis and in patients with anti-NXP2, anti-TIF-1γ, anti-SAE1 and anti-SRP autoantibodies (5-7). In contrast, severe oropharyngeal involvement appears to be exceptionally uncommon in anti-Mi-2-positive DM.

This case highlights a marked dissociation between serological classification and clinical phenotype, contrasting with the expected disease trajectory of this otherwise favourable serological subset, and expands the recognized clinical spectrum of anti-Mi-2-positive DM to include extensive systemic muscle involvement. It underscores the limitations of antibody-defined phenotypes in fully capturing disease heterogeneity and emphasizes the importance of ongoing clinical reassessment. DM should be viewed as a multisystem disease in which cutaneous manifestations, muscle weakness, dysphagia, and cardiac involvement may follow distinct and asynchronous trajectories; improvement in one domain should not be interpreted as evidence of overall disease control. Careful clinical assessment, rather than serology alone, early recognition of severe systemic manifestations, prompt escalation of immunomodulatory therapy, and intensive multidisciplinary supportive care may play a critical role in improving patient outcomes.

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