Unravelling the link: anti-TIF1γ dermatomyositis associated with plexiform neurofibroma

Sirs,

Dermatomyositis (DM) is an idiopathic inflammatory myopathy clinically characterised by proximal muscle weakness and distinctive skin lesions, such as Gottron papules, V sign, and Holster sign. It can occasionally compromise the oesophagus, lungs, and heart. DM is well known for its association with certain malignancies, including ovarian, lung, pancreatic, gastric, and colorectal (1, 2). Plexiform neurofibroma, on the other hand, is typically a benign nerve sheath tumour that affects large nerves, presenting as elongated multinodular masses, often associated with neurofibromatosis type 1 (3). We present here the first report of a 48-year-old woman with a history of unresectable plexiform neurofibroma who subsequently developed inflammatory arthralgias and characteristic skin lesions of DM.

The patient was a 48-year-old woman diagnosed in 2008 with multiple plexiform neurofibromas affecting the right vulvopelvic area, extending into the lumbosacral and sciatic regions. She had previously undergone treatment with local alcoholisation and anti-hormonal therapy, with no improvement and surgical intervention was deemed unfeasible due to the mutilating nature of the procedure. The patient presented to the rheumatology clinic with a five-month history of inflammatory arthralgia affecting the hands, wrists, and knees, accompanied by erythematous and scaly lesions on the dorsal surfaces of her hands. Physical examination revealed Gottron papules, as well as fasciculations of the eyelids and tongue. Laboratory investigations showed mild leukopenia (neutrophil count of 1,600/mm^3 and lymphocyte count of 600/mm^3). Levels of muscle enzymes, liver function tests, and lactate dehydrogenase (LDH) were within normal ranges. Autoimmunity revealed antinuclear antibodies (ANA) at a titre of 1:160 with a fine speckle pattern, along with high titres of anti-TIF1γ. Electromyography (EMG) findings indicated mild, partial, and chronic axonotmetic injury to the right sciatic nerve, associated with the known plexiform neurofibroma. Computed tomography (CT) of the chest and abdomen showed no tumours other than the known plexiform neurofibroma. A muscle biopsy of the left biceps demonstrated perifascicular atrophy and perimysial lymphocytic infiltrates, consistent with DM (Fig. 1). A diagnosis of DM possibly associated with plexiform neurofibroma was established. The patient underwent a multidisciplinary evaluation involving dermatology, rheumatology and internal medicine. Treatment was initiated with prednisone 20 mg/day, methotrexate 10 mg/week and topical tacrolimus. Currently, 6 months later, the patient's articular and cutaneous symptoms have partially improved, continue with the same dose of methotrexate and is taking 12.5 mg/day of prednisone.

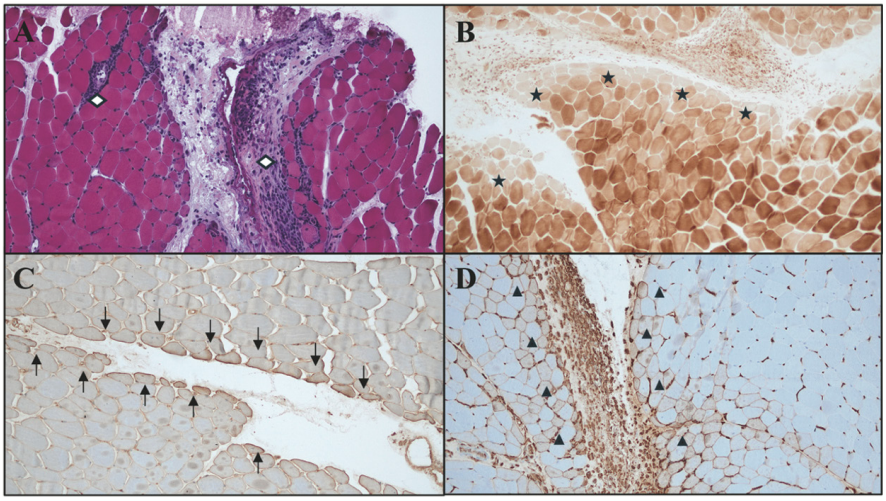

Fig. 1. Cross-sectional frozen muscle tissue with H&E staining showing perifascicular atrophy (**A**) and perivascular inflammatory infiltrate (**A**). COX-negative fibres are observed in the perifascicular area (**B**). Universal HLA-I immunostaining exhibits positivity with perifascicular predominance (**C**). HLA-DR immunostaining shows expression in the inflammatory cells and the perifascicular area (**D**).

Paraneoplastic DM is a distinctive subset of DM closely linked to an underlying malignancy, often presenting prior to cancer diagnosis. Clinical indicators suggestive of associated neoplasia encompass skin necrosis, onset in advanced age, dysphagia, cutaneous leukocytoclastic vasculitis, suboptimal response to conventional immunosuppressive therapies, and the absence of typical myopathic antibodies. Interestingly, the presence of interstitial lung disease appears to confer a protective effect. Notably, specific autoantibodies such as anti-TIF1γ and anti-NXP are commonly detected in these cases. Treatment strategies for paraneoplastic DM primarily involve managing the underlying malignancy alongside immunosuppressive agents to alleviate DM symptoms. This approach aims to address the pathophysiological mechanisms linking the two conditions while controlling inflammation and autoimmune manifestations (2). While paraneoplastic myositis has been documented in association with various malignancies, including neurological tumours, no previous cases linked to neurofibromas have been reported in the literature.

Plexiform neurofibromas, although typically benign, can impose substantial morbidity due to their expansive growth along nerve fibres, resulting in pain, disfigurement, and functional impairment through compression of adjacent structures (4).

In this case, anti-TIF1γ DM with prominent articular and dermatological manifestations occurred in the context of a non-malignant plexiform neurofibroma that remained unresectable due to surgical complexities. This case underscores a previously undescribed association between persistent plexiform neurofibroma and DM, emphasising the importance of recognising atypical presentations and exploring underlying pathophysiological links between chronic benign neoplasms and autoimmune processes. Further studies are warranted to elucidate the potential mechanisms underlying such associations and to guide optimal management strategies for similar clinical scenarios.

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Competing interests: none declared.

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