

Letter to the Editor

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Fasciitis as a disease manifestation in immune-mediated necrotizing myopathy with anti-signal recognition particle antibodies: a case report of two cases

Key message

- Fasciitis is a potential disease manifestation in patients with immune-mediated necrotizing myopathy.

SIR, Immune-mediated necrotizing myopathy (IMNM) is now classified as part of the group of idiopathic inflammatory myopathies, which are divided into DM, PM, inclusion body myositis and IMNM [1]. IMNM patients present with subacute or insidious onset of muscle weakness and highly elevated creatine kinase (CK) concentrations. The characteristic pathological features of IMNM comprise a lack of significant inflammatory infiltrates in muscle tissue despite the presence of muscle fibre necrosis, degeneration and regeneration [1, 2]. The pathogenesis of IMNM remains incompletely understood. We describe two cases of anti-signal recognition particle (SRP) antibody-positive IMNM patients with fasciitis.

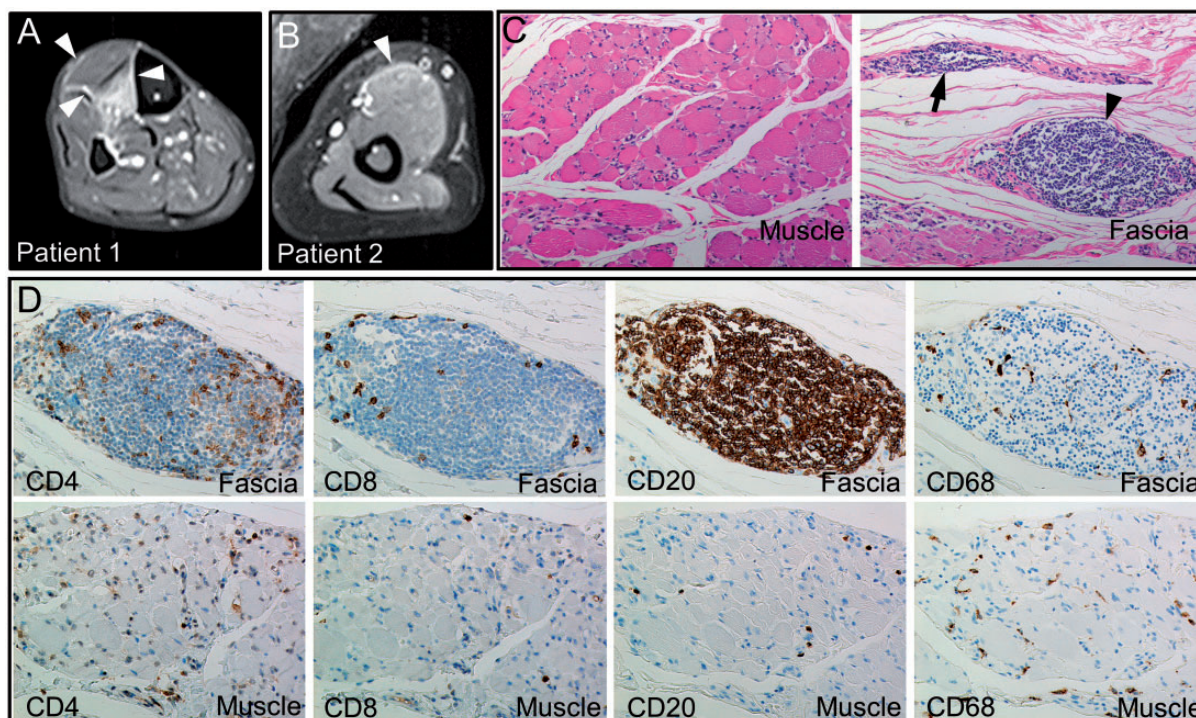
Patient 1 was a 68-year-old man who presented with muscle weakness of the lower extremities, dysphagia and an elevated CK concentration (5948 U/l). ANAs (speckled, discrete speckled and cytoplasmic pattern) were present at a titre of 1:640. Anti-SRP antibodies were detected by the commercial assay EUROLINE Myositis Profile 3 (immunoblots), and the positivity of anti-SRP antibodies was confirmed with an in-house ELISA [3]. The patient had combined pulmonary fibrosis and emphysema, but neither skin sclerosis nor RP. Short tau inversion recovery and gadolinium-enhanced fat-suppressed T1-weighted MRI revealed abnormal high signal intensity and enhancement, respectively, along the fasciae of the anterior tibial (Fig. 1A), gastrocnemius and soleus muscles and within these muscles. *En bloc* biopsy specimens including skin, subcutaneous tissue, fascia and muscle obtained from the anterior tibial muscle before treatment showed muscle fibre necrosis and regeneration with a few CD68⁺ macrophages and CD8⁺ T lymphocytes and no B lymphocytic infiltrates around the endomysium within the fascicles, whereas CD4⁺ T, CD8⁺ T and CD20/CD79a⁺ B lymphocytic infiltrates were distributed at perivascular sites in the fascia. The patient was treated with prednisolone 60 mg/day and improved, with normalization of his CK concentration after 3 months of treatment. Prednisolone

was gradually tapered; however, 7 months later, the patient relapsed with muscle weakness and an increased CK concentration (812 U/l). We increased the prednisolone dose from 17 to 30 mg/day and used high-dose IVIG 0.4 g/kg/day for 5 days. At 2 months after IVIG, his muscle weakness and increased CK concentration improved.

Patient 2 was a 29-year-old woman who presented with proximal muscle weakness and an elevated CK concentration (8880 U/l). The patient was positive for ANAs (cytoplasmic pattern) at a titre of 1:80, and anti-SRP antibodies were detected by both EUROLINE Myositis Profile 3 and the in-house ELISA. Short tau inversion recovery and gadolinium-enhanced fat-suppressed T1-weighted MRI showed abnormal high signal intensity and enhancement, respectively, along the fasciae of the biceps brachii (Fig. 1B) and quadriceps femoris muscles and within these muscles. Chest CT scans revealed the presence of mild ground-glass opacity in the lower lungs. *En bloc* biopsy specimens obtained from the biceps brachii muscle before treatment showed muscle fibre necrosis and regeneration, with small numbers of CD68⁺ macrophages, T and B lymphocytes around the endomysium within the fascicles (Fig. 1C). In the fascia, massive lymphocytic infiltrates, mainly consisting of CD20/CD79a⁺ B cells with a few CD4⁺ T and CD8⁺ T cells, were distributed in lymphoid follicle-like aggregates and at perivascular sites (Fig. 1C and D). The patient was given prednisolone at an initial dose of 40 mg daily in combination with tacrolimus 6 mg/day. After 5 months, the muscle weakness disappeared, and her CK concentration had decreased to 160 U/l.

In the present cases, fasciitis was found in addition to necrotizing myopathy. To date, fasciitis has not been recognized as a disease manifestation in IMNM because a muscle biopsy including the fascia (*en bloc* biopsy) is not usually performed for diagnosis of idiopathic inflammatory myopathies. We previously demonstrated that fasciitis was a common disease manifestation in patients with DM and anti-aminoacyl-tRNA synthetase antibody-positive patients (anti-synthetase syndrome) diagnosed with DM or PM by the Bohan and Peter criteria [4–7]. Fasciitis may also be a disease manifestation in patients with IMNM.

Regarding the inflammatory infiltrates in our cases, scant presence of macrophages and lymphocytes was noted around the endomysium within the fascicles, whereas significant B lymphocytic infiltrates were found at perivascular sites and in lymphoid follicle-like aggregates in the fascia. Many reports have described a few or no lymphocytic infiltrates in the muscle, whereas significant B lymphocytic infiltrates have not

Fig. 1 Fasciitis in patients with immune-mediated necrotizing myopathy, detected by MRI and *en bloc* biopsy

(A and B) Gadolinium-enhanced fat-suppressed T1-weighted MRI, showing enhancements (arrowheads) along fasciae and within muscles in patient 1 (anterior tibial muscle) and patient 2 (biceps brachii muscle). (C) Haematoxylin and Eosin staining of the biopsy specimen in patient 2, showing mononuclear infiltrates in lymphoid follicle-like aggregates (arrowhead) and at perivascular sites (arrow) in the fascia in addition to necrosis and regeneration of muscle fibres in fascicles. (D) Immunohistochemical staining of the specimen for patient 2, showing CD4⁺, CD8⁺, CD20⁺ and CD68⁺ cells in the fascia and muscle.

been reported in patients with IMNM. Preuße *et al.* [8] investigated the characteristics of cellular infiltrates in muscle tissues from patients with IMNM. They found that the majority of muscle biopsy specimens had no B lymphocytic infiltrates, with only 3 of 16 muscle biopsy specimens containing small numbers of B lymphocytes. These muscle findings are consistent with the present findings. However, significant infiltration of B lymphocytes was observed in the fascia of our patients, who were both positive for anti-SRP antibodies. Detection of anti-SRP or anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) autoantibodies suggests the involvement of an antibody-mediated autoimmune mechanism in the pathogenesis of IMNM [9]. The process of autoantibody production requires the presence of autoreactive B cells. Therefore, the lymphocytes, including B cells, observed in the fascia, which were located at perivascular sites and in lymphoid follicle-like aggregates, might be involved in the pathogenesis of IMNM.

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