In conclusion, parainfectious myositis with preferential forearm involvement is important to recognize for its benign and self-limited course. Management is supportive. Comprehensive viral studies, including nasal and stool PCR plus convalescent serology, may help to identify the precise infectious agent in future outbreaks.

Ethical Publication Statement: We (the authors) confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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A CHILD WITH ANTIBODY-NEGATIVE IMMUNE-MEDIATED NECROTIZING MYOPATHY

Immune-mediated necrotizing myopathy (IMNM) is a recently recognized category of idiopathic inflammatory myopathies manifesting as symmetric proximal limb muscle weakness and high serum creatine kinase (CK) level, along with specific histopathological findings. IMNM is divided into 3 groups: anti–signal-recognition particle (anti-SRP); anti–3-hydroxy-3-methylglutaryl-CoA reductase (anti-HMGCR); and autoantibody-negative IMNM.[1] Thus far, most reported patients with IMNM have been adults.[2] Some pediatric patients were identified in 3 previous studies with limited information.[4–6] Rouster-Stevens and Pachman described 3 juvenile polymyositis patients with anti-SRP antibody.[7] Suzuki *et al.* reported 2 Japanese girls with anti-SRP myopathy.[8] Anti-HMGCR autoantibodies were detected in a total of 13 children with inflammatory myopathy in 2017.[9,10] We describe a boy with a diagnosis of antibody-negative IMNM who improved after treatment with intravenous immunoglobulin (IVIg).

An 11-year-old boy was admitted for evaluation of 3 weeks of acute-onset, progressive, proximal symmetrical weakness in all limbs. He had been vaccinated for influenza 3 weeks before he became symptomatic. His initial symptoms were trouble raising his arms. Over a few days, his family noted that he could barely rise from a chair. He had pain in his limb muscles. He lost 3 pounds, without changes in bowel or bladder habits or control, and had no diurnal variation in his weakness. His family denied any trauma, preceding febrile illness, rash, numbness, dysphagia, ptosis, diplopia, or dysarthria. The family also denied use of herbal medicines, or other toxic exposures. There was no family history of neuromuscular or autoimmune diseases.

On general examination, there was no skin rash or joint swelling. Neurologic examination revealed mild bilateral facial and eye closure weakness. He had diffuse hypotonia and atrophic hip- and shoulder-girdle muscles. Neck flexors and proximal limbs were weak, graded as 3/5 in the upper and 4/5 in the lower extremities. Deep tendon reflexes were 1^{+}.

The initial laboratory examination revealed an increased aspartate transaminase of 345 U/L (normal 13–39 U/L), alanine transaminase 384 U/L (normal 7–52 U/L), CK 13,006 U/L (normal 30–223 U/L), lactate dehydrogenase 1,950 U/L (normal 140–271 U/L), and aldolase 159 U/L (normal 3.3–10.3). Complete blood count; renal, hepatic, and thyroid functions; electrolytes; myoglobin in urine; erythrocyte sedimentation rate; C-reactive protein; and anti–streptolysin-*O* titers were all normal. Antinuclear and acetylcholine receptor antibodies were negative.

MRI with coronal and axial short-tau inversion recovery images showed extensive edema in both upper and lower

Key words: antibody negative, immune-mediated necrotizing myopathy, inflammatory myopathy, myositis, pediatric

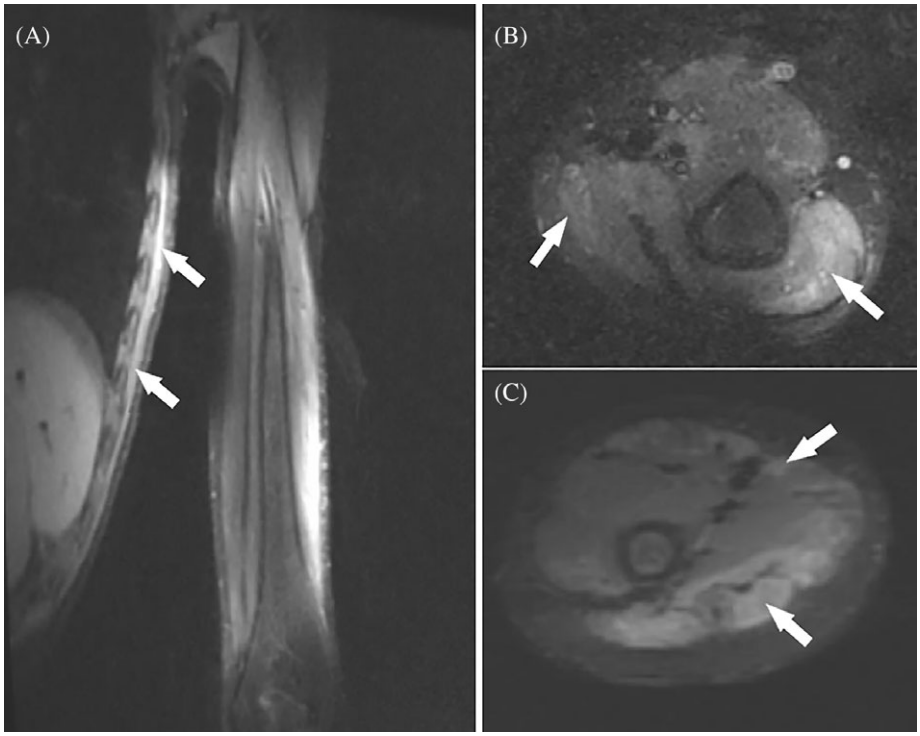

FIGURE 1. (A) Short-tau inversion recovery axial MRI sequences at the level of trunk muscles, showing muscle edema (white arrows). **(B)** Short-tau inversion recovery axial MRI sequence at the level of the femur, showing extensive muscle edema (white arrows). **(C)** Short-tau inversion recovery axial MRI sequence at the level of the humerus, showing extensive muscle edema (white arrows).

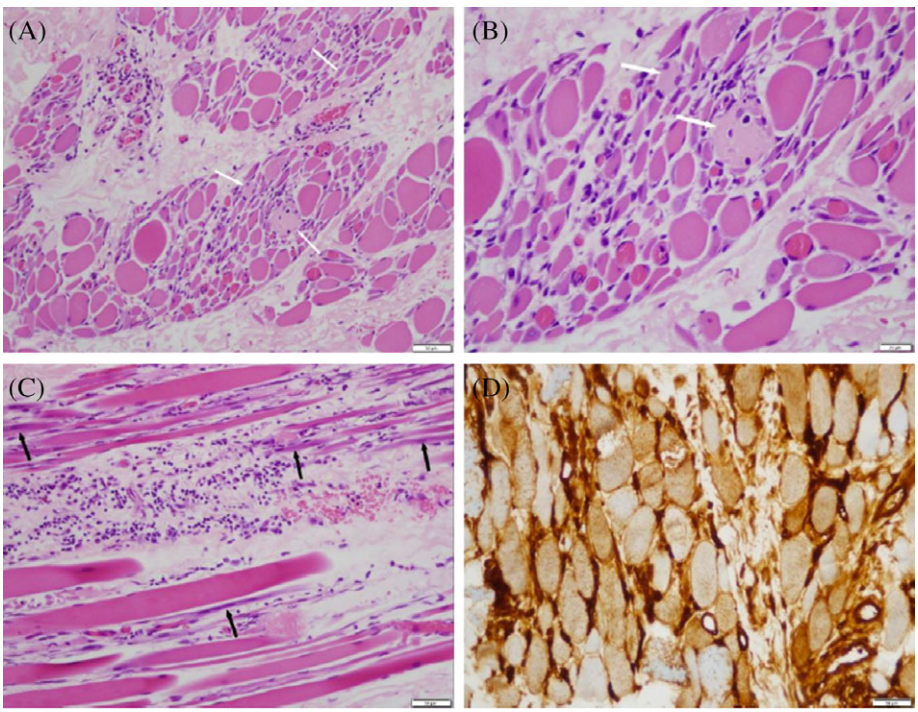

FIGURE 2. (A) Hematoxylin and eosin (H&E) paraffin section of a deltoid muscle biopsy demonstrates myofiber atrophy distributed throughout the fascicles; many of the atrophic myofibers are regenerating. Necrotic myofibers (white arrows) are distributed throughout this area. There is only minimal focal perivascular lymphocytic infiltration in this region (upper right quadrant). **(B)** Detail of a region included in the previous image **(A)**. White arrows indicate 2 necrotic myofibers. There is moderately severe myofiber atrophy. Some of the atrophic myofibers in this area are regenerating, as identified by their basophilic (slightly blue) cytoplasm and large nuclei. **(C)** This region of a paraffin H&E section has a focus of very mild perimysial lymphocytic inflammation. Multiple regenerating myofibers are present in this area, some identified by the black arrows. **(D)** The human leukocyte antigen class I immunohistochemistry study demonstrates labeling of the surfaces of myofibers and staining of sarcoplasm; this study is considered strongly positive, which provides evidence of an immune-mediated process. Scale bar = 50 μm in **(A)**, **(C)**, and **(D)**; **s**cale bar = 20 μm in **(B)**.

proximal extremity muscles and trunk muscles, compatible with myositis (FIG. 1).

Anti-Ro/La, dsDNA, thyroid peroxidase, anti-Smith, and anti-thyroid antibodies were all negative. Tests were negative for the following infections: Lyme; herpes simplex virus; human immunodeficiency virus; human T-lymphotrophic virus 1/2; adenovirus; coronavirus; human metapneumovirus; rhino/enterovirus; influenza A/B; Coxsackie virus; parainfluenza; respiratory syncytial virus; Bordetella; chlamydophila pneumonia; and mycoplasma.

Biopsy (FIG. 2) of the deltoid muscle demonstrated a necrotizing myopathy with scant focal inflammation and a positive human leukocyte antigen (HLA) class I immunohistochemistry study, the latter providing evidence of an immune-mediated disorder despite the paucity of inflammation. There were approximately 5 necrotic myofibers per low-power (100× magnification) field, which is considered to be a moderate degree of active myofiber necrosis, and at least twice that number of regenerating myofibers, all with a random distribution throughout the sample. Moderate nonspecific myofiber atrophy, some attributable to the regenerating myofibers, was present. There was no perifascicular patterning of the atrophy, necrosis, or regeneration, as would be characteristic of dermatomyositis. There were only a few isolated perimysial foci of scant lymphocytic inflammation. Features of polymyositis, such as endomysial inflammation and an attack by autoaggressive lymphocytes on non-necrotic myofibers, were absent. The (HLA) class I (or class ABC) immunohistochemistry study was strongly positive, demonstrating surface labeling and sarcoplasmic staining of all myofibers in the sample. Immunohistochemistry demonstrated no upregulation of utrophin, which is normal, and normal patterns of expression of dystrophin N-terminal, C-terminal, and rod domain epitopes, for α-, β-, and γ-sarcoglycan, and for laminin-2-α, β-dystroglycan, dysferlin, and emerin. Electron microscopy demonstrated no specific ultrastructural abnormalities within myofibers; there were only nonspecific pathological findings in a few necrotic myofibers.

Myositis antibody panel (RDL laboratory), including anti-SRP (via radioimmunoprecipitation assay), HMGCR (<20 units, enzyme-linked immunoabsorbent assay), Mi-2, PL-12, PL-7, EJ, OJ, Ku, U2snRNP, PM/Sc, Jo-1, U1-RNP, SS-A 52, fibrillarin, MDA-5, NXP-2, and TIF1-γ antibodies, were all negative.

Electrocardiogram, echocardiogram, pulmonary function tests, and chest X-ray were all unremarkable.

The patient was initially treated with methylprednisolone 1 g/day for 3 days, without improvement. After an initial loading dose of IVIg 2 g/kg, followed by 3 monthly 1-g/kg infusions, he recovered considerably and could dress himself, with 4/5 proximal upper extremity strength and 5/5 lower extremity strength. CK level decreased to 400 U/L.

Our patient's presentation was most consistent with IMNM, despite the lack of autoantibodies and acute symptom onset; this was unlike what was a reported in a series of 9 pediatric patients with necrotizing myopathy associated with anti-HMGCR antibody, of whom 5 showed a chronic disease course.[10] Most importantly, our patient had widespread muscle edema and atrophy on MRI, as well as necrosis > inflammation on biopsy, as described in IMNM patients.[3]

Other diseases, such as myositis, were excluded by the lack of histopathological features of polymyositis or dermatomyositis.[11] The muscle biopsy's normal immunohistochemical staining was inconsistent with a muscular dystrophy, although genetic testing for limb-girdle muscular dystrophy was not performed. Still, the rapid onset of symptoms and clinical response to IVIg would be highly unlikely in a muscular dystrophy, so this type of testing was not pursued. A paraneoplastic syndrome is possible,[12] but this would be unlikely in an individual of this age and clinical presentation. One may consider a viral or postviral-associated myositis, but there was no history nor any clinical and/or laboratory signs of an infection.

In conclusion, a high index of suspicion is necessary to diagnose pediatric IMNM, and our case report expands the phenotypical spectrum of IMNM in children. This case also highlights the importance of early recognition and correct choice of treatment to prevent rapid and severe disease progression.

Ethical Publication Statement: We (the authors) confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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