Elevated liver enzymes: unusual presentation of anti-MDA5 antibody-associated juvenile dermatomyositis

Sirs,

Juvenile dermatomyositis (JDM) is the most common type of juvenile idiopathic inflammatory myopathy (JIIM). Anti-melanoma differentiation-associated gene 5 antibody positive juvenile dermatomyositis (anti-MDA5 JDM) is a subtype of JDM characterised by cutaneous ulcerations, arthritis, and progressive interstitial lung disease (ILD) that can cause significant morbidity and mortality (1-2). Diagnosis is challenging as it can present without classical JDM features (proximal muscle weakness, heliotrope rash and Gottron's papules). We report a case of anti-MDA5 JDM where diagnosis was delayed due to unusual presentation.

A 4-year-old male presented with chronic abdominal pain, arthralgia, bruises, oral ulcers, fatigue, intermittent fever, and recent history of COVID-19. Laboratory test results were notable for elevated aspartate aminotransferase (AST 667 Units/L), alanine transaminase (ALT 199 Units/L), gamma-glutamyl transferase (GGT 339 Units/L), total bilirubin (TB 1.72 mg/dL) and normal creatinine kinase (CK 32 Unit/L). Echocardiogram and cardiac enzymes, which were obtained with concern for multisystemic inflammatory syndrome (MISC), were normal. Non-accidental trauma (NAT) was ruled out given multiple ecchymoses (Fig. 1). AST, ALT, GGT and TB continued to rise (2,075 Units/L, 309 Units/L, 429 Units/L, and 6.06 mg/dL, respectively) while CK stayed normal. Abdominal ultrasound showed hepatomegaly. Liver biopsy revealed nonspecific extensive hepatocyte swelling and focal hepatocyte cholestasis. Ursodiol 20mg/kg/day, prednisone 2mg/kg/day, and azathioprine 20mg/day were initiated for presumed autoimmune hepatitis (AIH) without improvement of the cholestasis. Two months after initial presentation, the patient was readmitted with fever, weight loss, difficulty breathing, arm weakness, arthritis, and ulcers. Shoulder Magnetic Resonance Imaging (MRI) showed oedema and inflammation in the bilateral rotator cuff, deltoid, and surrounding soft tissues. Deltoid muscle biopsy showed atrophic and degenerative myofibres, predominant CD4-T-lymphocytes, increased expression of MHC Class I molecules, and capillaries with endothelial swelling, consistent with an immune-mediated myopathy. Skin biopsy of an ulcerating lesion showed perivascular and peri-adnexal dermatitis with increased dermal mucin deposits concerning for a connective tissue disorder. Chest computed tomography showed scattered peripheral tree-in-bud nodular opacities and symmetric intralobular septal thickening involving lower lobes, concerning for ILD. Myositis-specific autoantibody (MSA) profile from Oklahoma Medical Research Foundation came back positive for anti-MDA5, establishing a formal diagnosis of anti-MDA5 JDM.

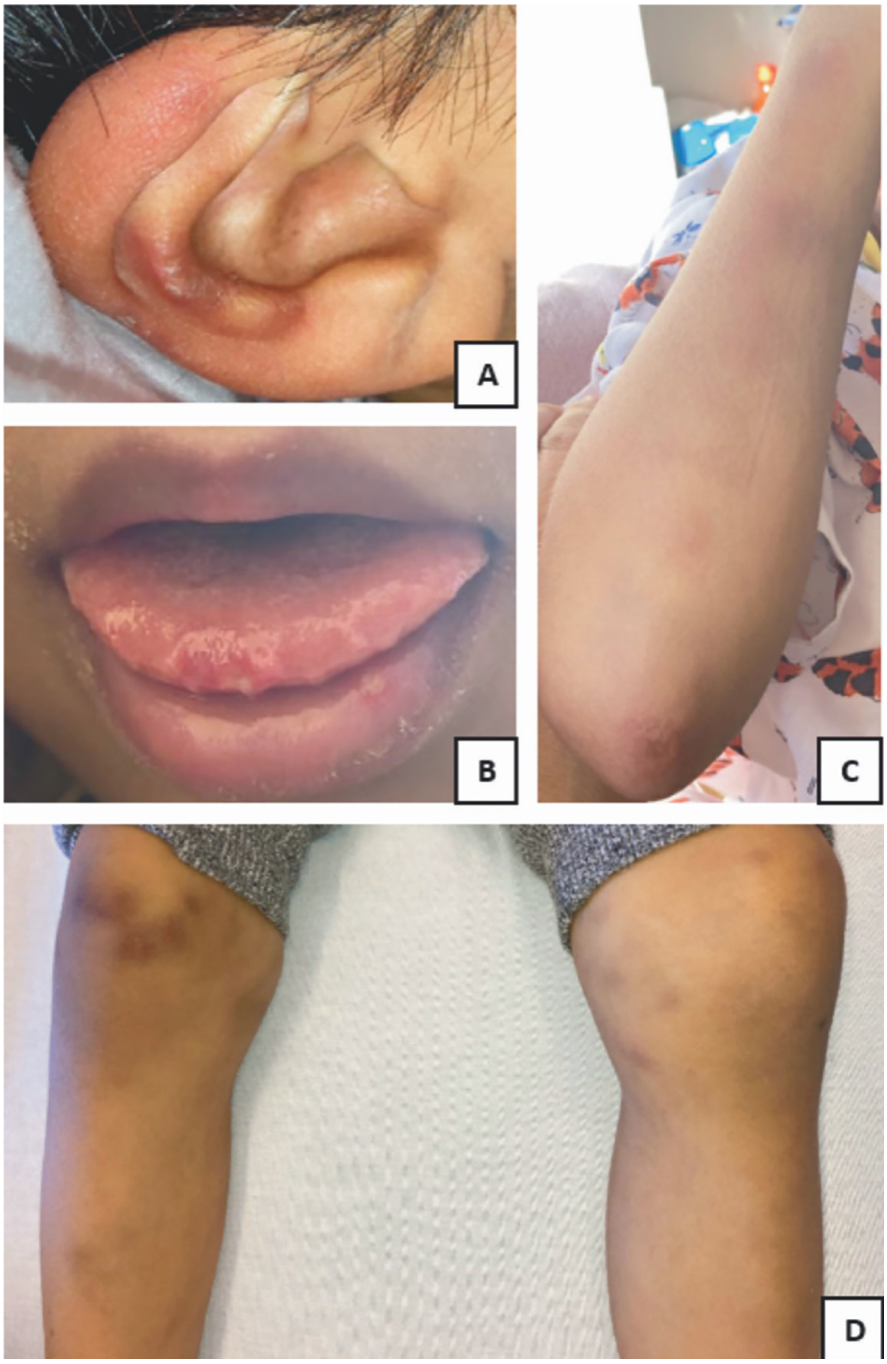

Fig. 1. Initial mucocutaneous features of the patient. **A**: Violaceous and ecchymotic thin papules and macules on helix. **B**: Circular erosion on lower mucosal lip and tip of tongue. **C-D**: Violaceous and ecchymotic thin papules and patches on right arm and bilateral lower extremities.

Anti-MDA5 JDM is a subtype of JDM differentiated by its atypical presentation of cutaneous ulcerations, arthritis, weight loss, milder muscle involvement, and progressive ILD (3). Prompt diagnosis and initiation of intensive immunomodulating treatment is important to avoid rapidly progressive ILD (4). Our patient underwent extensive work-up for differential diagnoses including MISC, NAT, and AIH. His elevated liver enzymes and hepatocyte changes were likely secondary to anti-MDA5 JDM. AIH and hepatocyte ballooning on liver biopsy have been described in anti-MDA5 dermatomyositis and polymyositis in adults (1, 5-6). To our knowledge, this is the first report of significant liver enzyme elevation as a component of initial Anti-MDA5 JDM presentation. Lack of prominent muscle weakness at presentation is concordant

with prior findings of amyopathic myositis and ILD in anti-MDA5 dermatomyositis patients (7). Our patient's arthralgia did not progress to arthritis until the time of diagnosis. Arthritis and arthralgia were common characteristics of anti-MDA5 JDM from the North American registry (89% and 88%, respectively) (1). MSA testing is emerging as a standard of care in evaluation for inflammatory myopathy and, as in this case, can be critical to establish the diagnosis**.** However, MSA testing takes a prolonged period (6-8 weeks) to result (8). The diagnosis of anti-MDA5 JDM can be aided by MRI and biopsies, especially in cases of fever or inflammation of unknown origin. This case illustrates that diagnosis of anti-MDA5 JDM can be challenging due to unusual presentation and demonstrates the importance of further studies surrounding the different clinical manifestations of anti-MDA5 JDM.

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