Anti-MDA5 antibody-positive juvenile dermatomyositis overlap with neuropsychiatric systemic lupus erythematosus: a case report

Sirs,

Overlap syndrome is defined as the presence of two or more recognisable rheumatic diseases (1). Prognostic factors include manifestations, such as interstitial lung disease (ILD) with juvenile dermatomyositis (JDM) and neuropsychiatric complications with systemic lupus erythematosus (SLE). This is the first report of a patient with overlap syndrome with JDM complicated by anti-melanoma differentiation-associated gene 5 (MDA5) antibody-positive rapidly progressive ILD (RP-ILD) and neuropsychiatric SLE (NPSLE).

A 9-year-old girl was admitted with malar rash, oral ulcers, Gottron's sign, and symmetric weakness of the proximal muscles of both legs, with no respiratory symptoms. Laboratory investigations revealed lymphopenia, thrombocytopenia, and hypocomplementemia with a raised erythrocyte sedimentation rate and elevated level of transaminase. The serum creatine phosphokinase level was 88 IU/L with an aldolase level of 27.4 IU/L. Urinalysis revealed neither haematuria nor proteinuria. The serum Krebs von den Lungen 6 (KL-6) level was elevated (1350 U/mL). Antinuclear antibodies were not detected, but antibodies to dsDNA and MDA5 were present. Chest computed tomography showed mediastinal emphysema and ground-glass opacity with bilateral peripheral lung field consolidation (Fig. 1A). Magnetic resonance imaging (MRI) of her lower extremities showed patchy inflammation in the muscle. We diagnosed overlap syndrome of JDM and SLE with ILD, and initiated methylprednisolone pulse therapy (30 mg/kg/dose once daily for 3 days); owing to deterioration of her respiratory condition 4 days after admission, continuous oxygen (5 L/min) was administered. Continuous infusion of cyclosporine A (2mg/kg/day) and intravenous immunoglobulin (400mg/kg/day for 5days) were also initiated. Her muscular and respiratory conditions gradually improved. However, she developed neuropsychiatric symptoms, including acute confusion, anxiety disorder, and psychosis. Mild cerebral atrophy and decrease in cerebral blood flow were respectively observed on MRI and single-photon emission computed tomography (SPECT) using the tracer [123I]iodoamphetamine. Rituximab (375mg/m^2 once weekly for 4 weeks) and plasma exchange (PE) were added to her treatment plan as her neuropsychiatric condition deteriorated. One month later, her neuropsychiatric symptoms resolved. Cerebrospinal fluid (CSF) anti-N-methyl-D-aspartate receptor subunit 2 (anti-NR2) antibodies, which were elevated on development of the neuropsychiatric symptoms, decreased on discharge from 10.0 to 0.95 U/mL (normal range <9.88 U/mL). The anti-MDA5 antibody index declined from 1520 to 0 (normal range <5) in parallel with improvements of the originally observed ground-glass appearance (Fig. 1B).

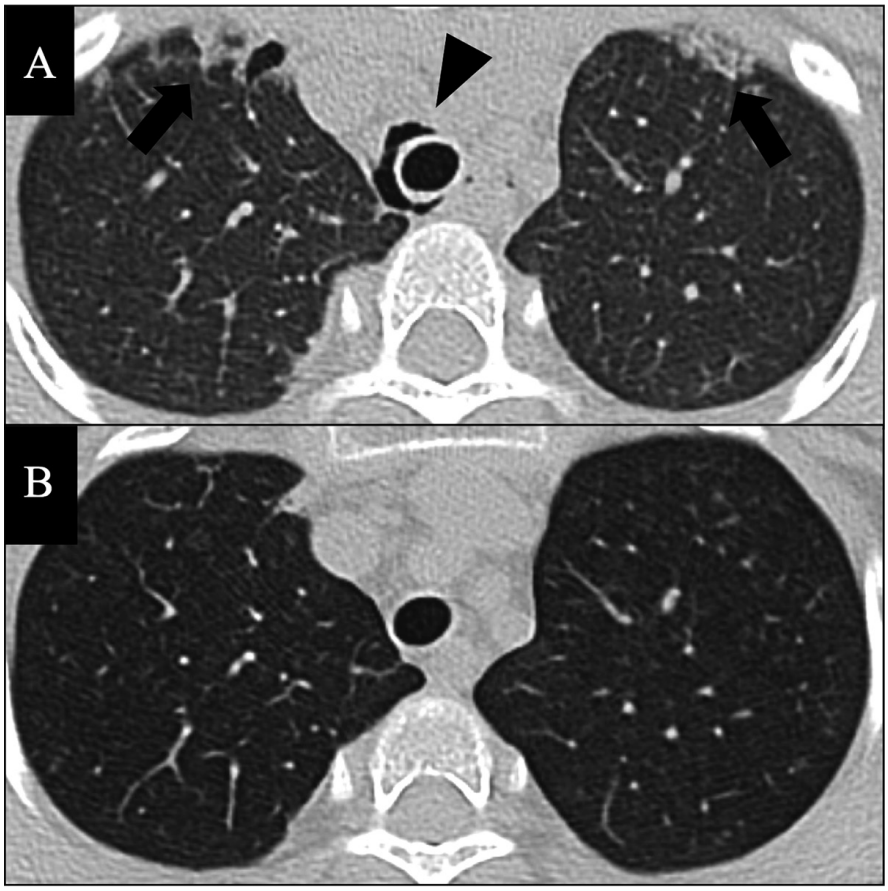

Fig. 1. Chest CT findings.
CT scans before treatment showing mediastinal emphysema (arrow head) and ground-glass opacities with bilateral consolidation (arrows) in the peripheral lung fields (A); resolution of previous changes after treatment (B).

The incidence of overlap syndrome was found to be 3.89 per 1000 children with rheumatological diseases in an Indian observational study (2). According to the EULAR/American College of Rheumatology (ACR) classification criteria (3), JDM is diagnosed without electromyography and muscle biopsy when a pathognomonic skin rash is present. The patient fulfilled the new criteria for JDM and the ACR (4) and Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus (5), and she was diagnosed with overlap syndrome with JDM and SLE. Anti-MDA5 autoantibodies were observed in 33% of Japanese JDM patients (6). The presence of these antibodies is associated with ILD, RP-ILD, and poor prognosis in JDM. Anti-MDA5 autoantibody titres are used to predict disease outcome in patients with dermatomyositis and RP-ILD (7). Higher titres of CSF anti-NR2 antibodies have been reported in patients with NPSLE compared to adult patients with SLE and non-inflammatory neuropathy (8). There has been no consensus on the treatment of overlap syndrome; it varies according to the severity of co-existing diseases and organ damage. Insufficient treatment results in poorer prognosis, while early aggressive treatment improves the outcome for JDM with RP-ILD and NPSLE. In our patient, methylprednisolone pulse therapy, cyclosporine, and intravenous immunoglobulin were administered for JDM with RP-ILD and SLE, but then NPSLE appeared.

Owing to the presence of various autoantibodies, rituximab and PE were chosen to deplete the B cells and eliminate the autoantibodies. Thereafter, JDM and NP-SLE symptoms disappeared and did not recur for two years.

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