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CASE IMAGE

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A less common case of anti-MDA5 and anti-Ro52 antibody-positive juvenile dermatomyositis complicated with macrophage activation syndrome

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KEYWORDS

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The patient was a 10-year old girl, who was admitted to Qingdao Women and Children's Hospital with bilateral knee joint and hip joint pain accompanied by facial and ankle edema for 4 weeks, and eyelid edema accompanied by purplish red rash on the face and around the orbital area for 2 weeks. Physical examination showed the weight was 64 kg, consciousness clear, purple-red rash on the face and periorbital area, and patchy rash and pigmentation in the V area in the front and back of the neck, extensor joint skin Gottron (+), edema in face, eyelids, ankle joint, and bilateral respiratory coarse and no obvious rales, heart strong rhythm and no obvious murmur, no abdominal tenderness and rebound tenderness, untouched subcostal liver and spleen, bilateral knee and hip tenderness with limited mobility, bilateral Patrick sign (+), and muscle strength grade IV. Laboratory characteristics were listed in Table 1. Imaging of MRI (Figure 1A–D) showed swelling of soft tissues around the right knee joint with abnormal signal shadow, and abnormal signals in bilateral hip. Electromyography motor nerve conduction test showed atypical myogenic damage. Chest CT scan revealed multiple patchy shadows in the right lung and lower in left lobe indicating pulmonary inflammation. Thus the patient was diagnosed as juvenile dermatomyositis (JDM). Treatment (listed in Table 2) began with piperacillin tazobactam, azithromycin, methylprednisolone, and immunoglobulin. After the rash and facial edema reduced, methylprednisolone was adjusted. On Day 9, glutamine aminotransferase, aspartate aminotransferase, and ferritin levels were all significantly elevated, pulse therapy of methylprednisolone was administrated. On Day 12, pulmonary function test showed severe mixed ventilation function limitation, and high-resolution lung CT scan (HRCT) indicated lung lesions. Bone marrow smear showed well-differentiated macrophages phagocytosis of various kinds of blood cells (Figure 2A–D). In the base of the examination, the patient was finally diagnosed as JDM complicated with interstitial lung disease (ILD) and macrophage activation syndrome (MAS). Immediately, cyclophosphamide pulse therapy was given and once again on Day 13. However, the patient had recurrent high fever, headache, and hepatosplenomegaly on the night of Day 14,

Li Zhang and Haiqing Zhang contributed equally to this work.

TABLE 1 Patient laboratory characteristics.

Tests	Day1	Day 9	Day 13	Day 15	Normal range
Leucocyte count ($\times 10^9$/L)	4.94	4.01	2.09	1.87	4.0–10.0
Platelets ($\times 10^9$/L)	171	145	74	25	100–300
ALT (U/L)	47	93	1015	1668	7–40
AST (U/L)	118	137	2240	5056	13–35
Lactate dehydrogenase (U/L)	435	418	5168	9392	120–250
Creatine kinase (U/L)	205	261	312	529	26–196
Ferritin (ng/mL)	1213	3145	>40,000	>40,000	13–150
Triglyceride (mmol/L)	2.52	2.82	3.50	3.55	0–1.7
Fibrinogen (g/L)	3.25	2.23	1.77	1.65	2–4
Antibody titer mycoplasma pneumoniae	1:320				1:160
Myositis-specific autoantibodies (MSAs)	Anti-MDA5 antibody: Positive				Negative
Myositis-associated autoantibodies (MAAs)	Anti-Ro-52 antibody: Positive				Negative
Antinuclear antibody-IgG (ANA)	Positive				Negative
Epstein–Barr virus (EBV)	Anti-EBV NA IgG antibody: >50.00 AU/mL				0–2
CD3+CD4+ T-cell count (number/μL)	221				404–1612
CD3+CD8+ T-cell count (number/μL)	154				220–1129
CD16+CD56+ NK cell count (number/μL)	8				84–724
CD19+ B cell percentage (%)	31.94				9.23–18.15
Interleukin-6 (pg/mL)	12.23				<11.09
Interferon (pg/mL)	4.93				<3.56
Bone marrow smear	Hemophagocytes: Positive				Negative

all the laboratory results deteriorated. The patient was administrated with immunoglobulin and cyclosporine A on Day 14–15. Unfortunately, the patient's condition was almost uncontrolled, despite tocilizumab administration on Day 15. The patient's condition continuously deteriorated on Day 16. The patient presented convulsions and arrhythmias, the combination of plasmapheresis, continuous renal replacement therapy (CRRT), and high-dose methylprednisolone pulse therapy were all given. However head CT scan showed bilateral cerebral hemisphere sulcus widening and brain parenchymal atrophy on Day 18, the patient turned to a coma, and finally died due to multiple organ failure.

JDM is an idiopathic diffused vasculitis-like autoimmune system disorder. Classical presentation of JDM includes the pathognomonic dermatologic findings of a heliotrope rash and/ or Gottron papules. Studies have shown that children of JDM with anti-MDA5 antibodies and anti-Ro-52 antibodies tend to cause ILD leading to severity and worse prognosis, more severe in symptoms and survival.[1] In addition to ILD, macrophage activation syndrome (MAS) is another fatal complication of JDM. MAS is an acute life-threatening systemic inflammatory process with around 20% mortality. While recognized as a life-threatening inflammatory process, the diagnostic criteria for MAS have been difficult to clearly define. The underlying JDM leads to excessive activation and expansion of macrophages and T cells leading to a striking cytokine storm inflammation. Moreover patients with anti-MDA5 had significantly higher levels macrophage activation, which maybe because the autoreactive B cells not only produce autoimmune antibody but also activate pathogenic T cells to secrete pro-inflammatory cytokines inducing macrophage activation as reported.[2,3]

In this study, we report a patient with complexity of JDM with multi-organ system involvement, ultimately diagnosed with MDA5 and Ro-52 antibody-positive JDM complicated with MAS. Regarding treatment, combination of methylprednisolone, immunoglobulin, cyclophosphamide, plasmapheresis, CRRT, and tocilizumab were given; however, the patient rapidly deteriorated and died. It is possible that the delay in diagnosis and adequate control of the underlying JDM with MAS led to the

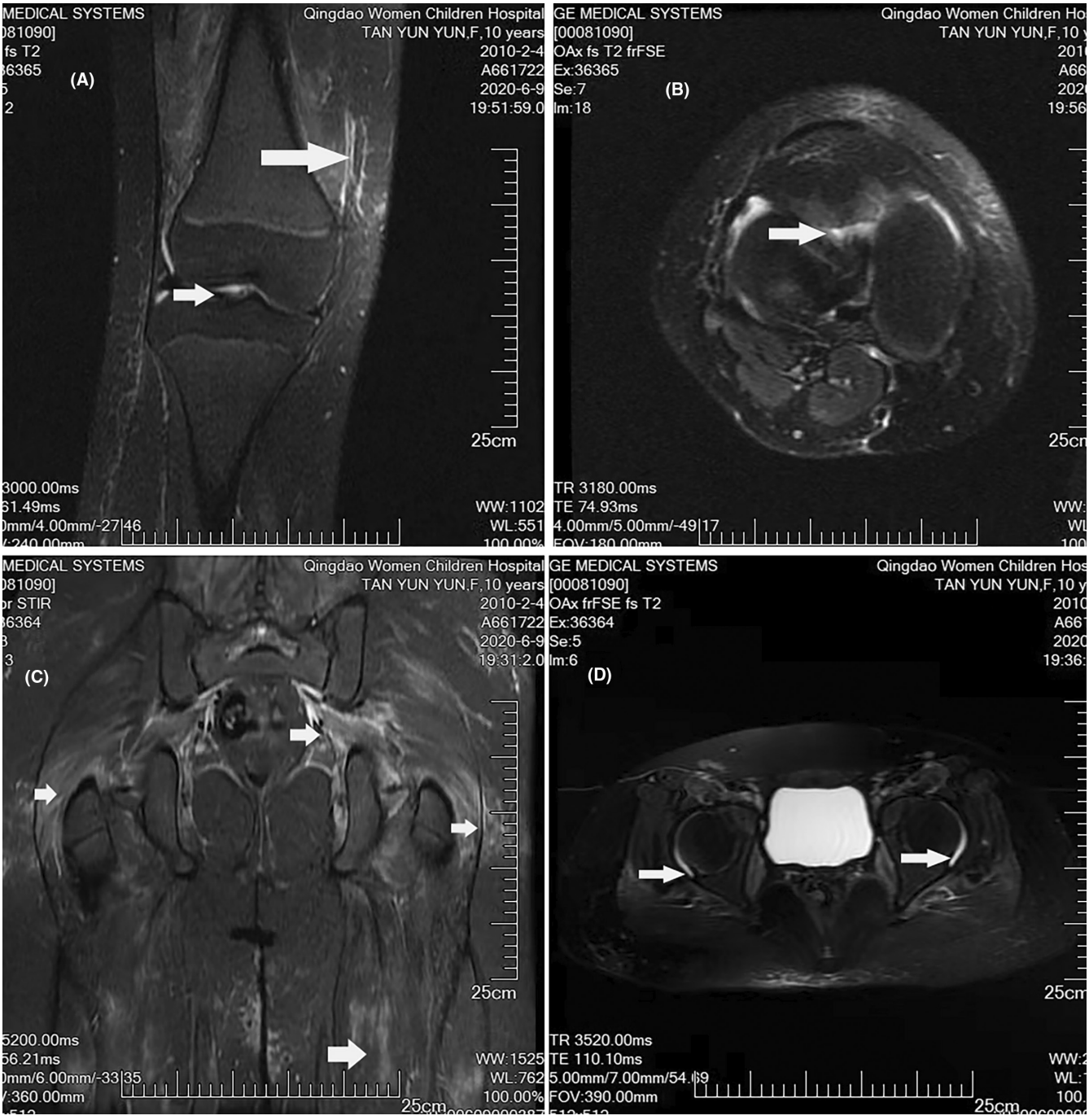

FIGURE 1 HRCT examination. (A, B) Soft tissue swelling with abnormal signal (arrows) around the right knee joint, and (C, D) diffuse abnormal signals (arrows) in bilateral hip.

hyper-inflammatory state in our patient's uncommon subtype of JDM. The results indicated more intensive therapy is required in addition to conventional management, immune regulators, such as IL-1R blockage, JAK inhibitor have been applied in some reported improved cases, among which the efficacy of RTX has shown excellent improvement in patients initially refractory to a combination therapy. Nevertheless, when and how to use immune regulators are needed to be answered in the future for inflammation control attaining to clinical remission.

TABLE 2 Patient drug administration.

Date	Drug	Dosage
Day 1–14	Piperacillin tazobactam	1.25 g/time×3 times/d
Day 3–7	Azithromycin	oral 0.25 g/d
Day 1–3	Methylprednisolone	80 mg/d
Day 1–2	Immunoglobulin	30 g/d
Day 4–8	Methylprednisolone	40 mg/d
Day10–12	Methylprednisolone	500 mg/d
Day 13	Cyclophosphamide	800 mg/m^2
Day14–15	Immunoglobulin	30 g/d and orally 75 mg/time, 2 times/d
	Cyclosporine A	
Day 15	Tocilizumab	240 mg/d
Day 16	Methylprednisolone	1 g/d
	Plasmapheresis, CRRT	

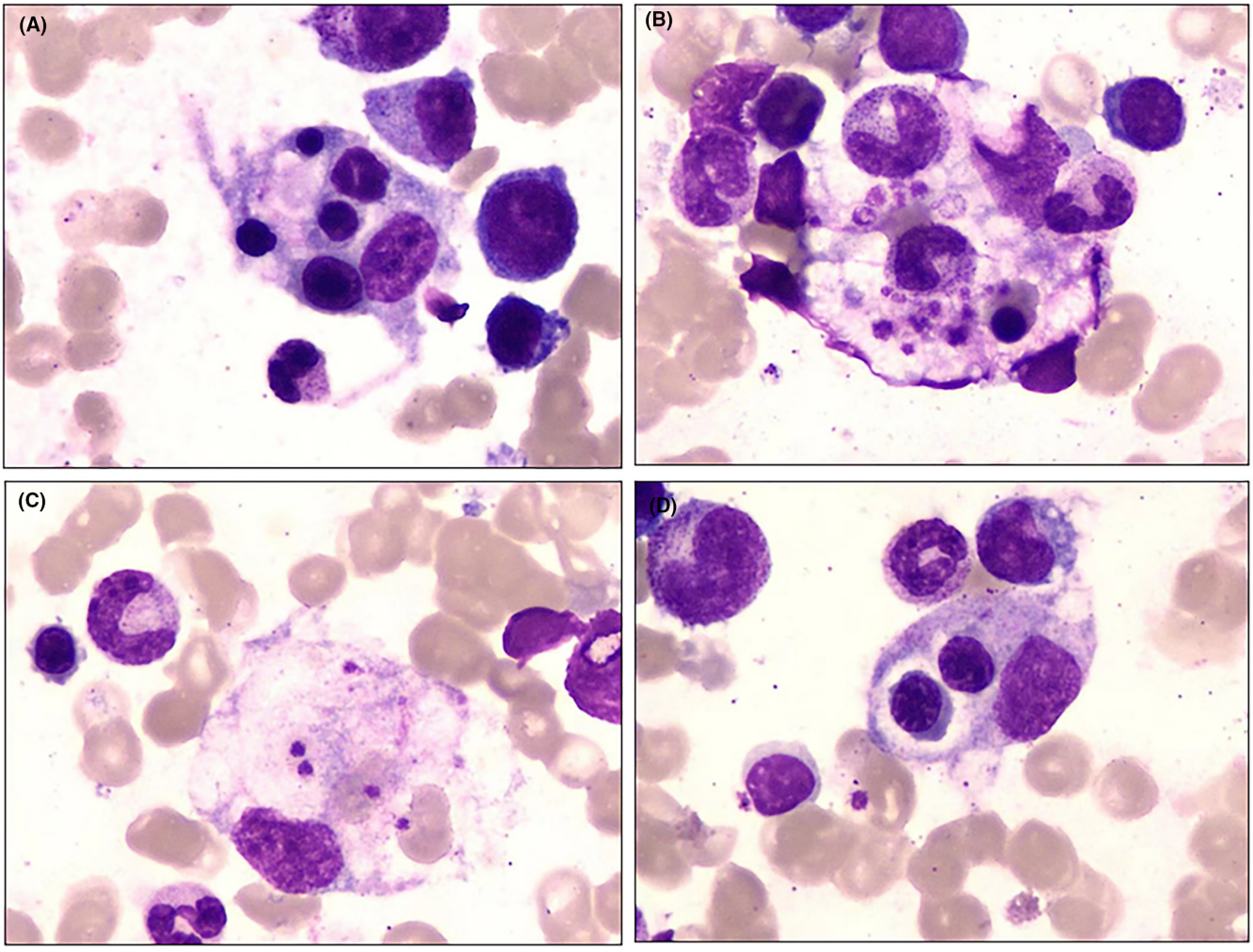

FIGURE 2 Bone marrow smears observed under microscope (10×100). It indicates phagocytosis of platelets, leucocytes, lymphocytes, and erythroblasts in phagocyte.

AUTHOR CONTRIBUTIONS

Li Zhang: Conceptualization; formal analysis; funding acquisition; investigation; validation; writing – original draft; writing – review and editing. **Haiqing Zhang:** Conceptualization; data curation; resources; supervision. **Shanshan Liu:** Data curation; resources; validation.

Ning Zhang: Investigation; methodology; project administration. **Yun Wang:** Conceptualization; data curation; resources; software; supervision.

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CONFLICT OF INTEREST STATEMENT

All the authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

CONSENT

Written informed consent was obtained from the parent of the patient to publish this report in accordance with the journal's patient consent policy.

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