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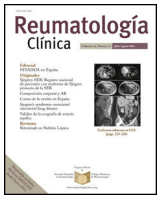

Case report

Severe and life-threatening onset of systemic lupus erythematosus

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ABSTRACT

Macrophage activation syndrome (MAS) is a potentially life-threatening complication of rheumatic diseases. We report a unique case of a previously healthy 20-year-old female presenting with MAS as first presentation of systemic lupus erythematosus. Remission was achieved with hydroxychloroquine, intravenous methylprednisolone pulse followed by oral prednisolone and cyclosporine. However, the management of MAS is still challenging, and the mortality rate remains high.

Una presentación grave y potencialmente fatal de lupus eritematoso sistémico

Palabras clave:
Lupus eritematoso sistémico
Síndrome de activación macrofágica
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RESUMEN

El síndrome de activación macrofágica (SAM) es una complicación potencialmente letal de algunas enfermedades reumáticas. Presentamos un caso único de una mujer de 20 años previamente sana que se presentó con SAM como primera manifestación de lupus eritematoso sistémico. Se logró una remisión completa con hidroxicloroquina, pulsos intravenosos de metilprednisolona seguido de prednisolona oral y ciclosporina. Sin embargo, el manejo del SAM sigue siendo un desafío y la tasa de mortalidad sigue siendo alta.

Introduction

Macrophage activation syndrome (MAS) is a underrecognized and potentially life-threatening complication of rheumatic diseases characterized by fever, pancytopenia, liver insufficiency, coagulopathy, and neurologic symptoms[1] and is thought to be caused by uncontrolled activation and proliferation of T lymphocytes and macrophages, leading to widespread hemophagocytosis and cytokine overproduction.[2,3]

Clinical observation

A previously healthy 20-year-old female presented with daily fever in the last 2 weeks, fatigue, anorexia, weight loss, polyarthralgia of the hands and dry mouth. She denied symptoms suggestive of infection, night sweats or swelling of the lymph nodes. No family history for rheumatic disease. Physical examination revealed normal vital signs except high temperature (38.8 °C), pallor of the skin, mild tenderness at proximal interphalangeal joints without swelling or deformities. Cardiopulmonary, abdominal and neurological examination was normal. Small red and painful patches were observed on her fingers. No axillary, cervical and inguinal adenopathy or peripheral edema were noticed. Laboratory workup showed pancytopenia (Hb 8.4 g/dL, WBC 1630/μL,

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platelet 108,000/μL), normal ESR and CRP, normal renal function, mild hypoalbuminemia (36.1 g/L), high AST and ALT (98 and 81 U/L, respectively), high ferritin (5075 ng/mL) and hypertriglyceridemia (357 mg/dL). High lactate dehydrogenase (LDH 1095 U/L), low haptoglobin (<8 mg/dL), positive direct coombs test, absence of schistocytes on the peripheral blood smear and reticulocytopenia were also observed. Coagulation tests showed normal prothrombin and activated partial thromboplastin time and hypofibrinogenemia (150 mg/dL). Urine analysis was normal. Blood cultures and serological tests for infectious diseases, namely for cytomegalovirus and epstein barr virus, were negative. Autoimmune workup showed positive ANA (1:1280, homogenous pattern), anti-dsDNA (>800 IU/mL), anti-Sm, anti-SS-A and anti-nucleosome antibodies and low complement levels (C3 54 mg/dL, C4 8 mg/dL). CT of chest, abdomen and pelvis showed cervical, axillary and retroperitoneal lymphadenopathy, hepatosplenomegaly with no focal lesions. No signs of infection or malignancy. Biopsy of axillary node showed *non-specific reactive lymphadenitis.* Bone marrow aspiration and biopsy were performed but the sample was inappropriate. Soluble CD25 in serum was only collected after 10 days of therapy. Even though, the level remained high (1187 U/mL, *N* 158–623).

New-onset of systemic lupus erythematosus (SLE) associated with MAS was diagnosed. MAS was diagnosed according to the HLH-2004 criteria and the *H*-score.[4,5] The patient started hydroxychloroquine 400 mg daily, intravenous methylprednisolone pulse (1 g daily for 3 days), followed by 1 mg/kg daily of oral prednisolone and cyclosporine 3 mg/kg daily. *Prophylaxis* for *Pneumocystis jiroveci*, calcium and vitamin D supplementation were also started.

A significant clinical and laboratory improvement was noticed with resolution of fever and constitutional symptoms, improvement of pancytopenia, hyperferritinemia, hypertriglyceridemia and hypofibrinogenemia. The patient was discharged after 3 weeks, with steroid tapering. At one year follow-up, a sustained remission was observed. Steroid was stopped and hydroxychloroquine 400 mg daily and cyclosporine 2.5 mg/kg daily were maintained.

Discussion

MAS is rarely associated with SLE and the incidence is 0.9–4.6%.[1,6] The mainstay of treatment is steroids.[1,7] Concomitant use of other agents, such as etoposide, cyclosporine, high-dose IV immunoglobulin and anakinra is useful in patients with severe, corticosteroid-resistant or refractory MAS.[7] Cyclosporine is a cyclic polypeptide immunosuppressant that suppresses the production of IL-2, IFN-γ TNF-α, IL-1 and IL-6, and also inhibits T lymphocyte activation.[8] This agent is effective for the induction and maintenance of remission in patients with MAS associated with rheumatic diseases, even in the cases of severe and corticosteroid-resistant disease.[9]

Early diagnosis is crucial since mortality remains high, even in patients undergoing treatment.[10] Here, we present an unusual, severe and life-threatening onset manifestation of SLE, MAS. Remission of the disease was achieved with corticosteroids and ciclosporine, with no adverse events reported, which corroborate the effectiveness, and also the safety, of this therapy.

Conclusion

Fever with constitutional symptoms and cytopenia can be clues to MAS and the level of suspicion should be high, to guarantee an early diagnosis. Looking for secondary causes of MAS, such as rheumatic diseases, is essential to ensure an accurate diagnosis and to select the appropriate treatment. However, a genetic predisposition can also exist and be related to dysregulated inflammasome activity (e.g., NLRC4 gene), and especially in situations with a positive family history of MAS, this should be investigated.

Conflict of interest

The authors declare they have no conflict of interest.

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