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AUTOIMMUNE MYELOFIBROSIS REVEALING A SYSTEMIC LUPUS ERYTHEMATOSUS

Fatimaezzahra Bensalek, Hajar Joulal, Jaouad Yousfi, Mouna Zahlane, Leila Benjilali, Lamiaa Essaadouni

Department of Internal Medicine, University Hospital Centre Mohammed VI, Marrakech, Morocco

Corresponding author: Fatimaezzahra Bensalek **e-mail:** dr.f.bensalek@gmail.com

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease, characterised by multi-organ affections. Haematological involvement is a common manifestation of SLE, consisting of autoimmune peripheral cytopenia. Autoimmune myelofibrosis (AIMF) is a rare cause of cytopenia in SLE; it could precede or be concurrent with the diagnosis of SLE. There are few studies that describe this association.

Case description: We report a case of AIMF revealing the diagnosis of SLE in 34-year-old female, presented with episodes of gingival bleeding associated with peripheral inflammatory polyarthralgia, photosensitivity and deterioration of general condition. Clinical examination revealed a soft pitting oedema in the lower limbs. Laboratory investigations showed a pancytopenia, inflammatory biological syndrome, with positive 24-hour proteinuria and anti-native DNA antibodies. A bone marrow biopsy showed diffuse myelofibrosis associated with maturation disorders and no tumour infiltrate. Renal biopsy revealed proliferative glomerulonephritis class III with immune deposits.

Conclusion: The association of AIMF with SLE has been rarely reported, and it could be another cause for cytopenia in SLE.

KEYWORDS

Autoimmune myelofibrosis, systemic lupus erythematosus, corticosteroid therapy

LEARNING POINTS

- Autoimmune myelofibrosis can be associated with systemic lupus erythematosus (SLE), even though it is rare.
- This association should be considered when pancytopenia is not well controlled during SLE, prompting a bone marrow biopsy to confirm the diagnosis.
- The therapeutic management of this association is the same as that used in SLE.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease, characterised by multi-organ affections. Haematological involvement is a common manifestation of SLE, consisting of autoimmune peripheral cytopenia[1]. Autoimmune myelofibrosis (AIMF) is a rare cause of cytopenia in SLE[2]. It could precede or be concurrent with the diagnosis of SLE. There are few studies that described this association. We report a case of AIMF revealing the diagnosis of SLE in 34-year-old female.

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CASE DESCRIPTION

A 34-year-old North African female with a medical history of autoimmune myasthenia gravis, treated with acetylcholinesterase inhibitors and azathioprine, presented to the hospital with episodes of gingival bleeding associated with peripheral inflammatory polyarthralgia and photosensitivity. These symptoms occurred in the context of deterioration of general condition. There were no signs of a myasthenic flare-up. On physical examination, there was a soft pitting oedema in the lower limbs and gingival bleeding. The rest of the clinical examination was insignificant; there was especially no hepatosplenomegaly. The urine strips showed positive haematuria without proteinuria. Laboratory investigations showed a pancytopenia of 5.1 g/dl with no regenerative anaemia, thrombocytopenia of 12,000 mm^3, leukopenia of 1,220 mm^3, with neutropenia of 940 mm^3 and lymphopenia of 210 mm^3. There was inflammatory biological syndrome with elevated C-reactive protein (CRP) at 40 mg/l; the sedimentation rate was 19 mm/h and serum protein electrophoresis showed a beta gamma block with a significant polyclonal increase in immunoglobulins. The liver workup showed hepatic cytolysis with acute renal failure, while the thyroid workup was normal, and 24-hour proteinuria was positive at 5.88 g/24h. Viral serologies for hepatitis B, hepatitis C, HIV, syphilis, cytomegalovirus and Epstein-Barr virus were negative. The immunological workup showed complement consumption C3 at 0.54 g/l, normal C4 at 0.11 g/l and normal CH50 at 37 U/ml; anti-nuclear antibodies were not present, anti-native DNA antibodies were positive at 300 IU/ml, and anti-SSA and anti-SS-B antibodies were negative. Anti-b2-glycoprotein antibodies were not detected, and anti-cardiolipin IgG antibodies were positive at 36 U/ml with no evidence of circulating lupus anticoagulant.

A CT scan of the abdomen and pelvis was unremarkable, showing no evidence of splenomegaly. A cardiac echography and standard radiography of swollen joints were normal.

A renal biopsy was performed, revealing proliferative glomerulonephritis class III, with parietal-mesangial deposits of C1q ++ and low deposits of C3, IgG and IgA. To rule out a possible haematological malignancy, a myelogram was performed, and a white smear was found, with no pellets or bone marrow elements. A bone marrow biopsy was performed, showing diffuse myelofibrosis associated with a haematopoietic marrow with a grade estimated between 1 and 2, hypoplasia of the three haematopoietic lineages with maturation disorders and no tumour infiltrate. Testing for *JAK2* mutation was negative. In the absence of arguments in favour of a secondary solid tumour, the diagnosis of SLE revealed by a haematologic involvement of an AIMF was returned.

The patient was treated with a bolus of methylprednisolone at a dose of 1 g per day by intravenous infusion for 3 days, followed by oral corticosteroid therapy at a dose of 1 mg/kg/d combined with hydroxychloroquine at a dose of 400 mg/d; azathioprine, initially prescribed for myasthenia, was continued. With this treatment, the general signs and arthralgias disappeared. At 6 months, the patient was asymptomatic, and her blood cell counts had returned to normal, with haemoglobin at 13 g/dl, platelets at 190×103 mm^2, white blood cells at 7,200 mm^2 with polymorphonuclear neutrophils at 4,773 mm^2 and lymphocytes at 1,692 mm^2. A control bone marrow biopsy was not performed.

DISCUSSION

SLE is a classic multisystem autoimmune disease, which could affect all organs and tissues. Haematological involvement is a common manifestation of SLE, and it is one of the classification criteria of the American College of Rheumatology of SLE revised in 1997 and those of the Systemic Lupus International Collaborating Clinics developed in 2012[1,3,4]. AIMF was first described in 1994 by Paquette et al.[5]. Subsequently, cases of association with autoimmune diseases have been reported, especially with SLE and Sjögren's syndrome[3,4]. The pathogenesis of AIMF is incompletely understood. The lupus autoimmune process is supposed to induce an increase of platelet-derived growth factor, transforming growth factor β (TGFβ) and epidermal growth factor that stimulate fibroblasts, which overload collagen production and marrow fibrosis[6]. AIMF associated with SLE is rare. This association frequently affects women with an average age of 36 years, with an established diagnosis of SLE and presenting with bicytopenia or pancytopenia[7]. It is only occasionally found concomitantly with SLE, as in the case of our patient. In a comparison of cases found in the literature, hypocomplementaemia and anti-DNA positivity were the anomalies observed in most cases[8]. As far as treatment is concerned, there is no therapeutic consensus to date. AIMF is characterised by cortical sensitivity, leading to improvement or even normalisation of pancytopenia and regression of bone marrow fibrosis in most of the cases reported. The efficacy of immunosuppressive treatments such as azathioprine, cyclosporine, cyclophosphamide and mycophenolate mofetil has also been reported[7-9].

CONCLUSION

This work highlights the possibility of other causes for cytopenia in SLE. We therefore suggest evoking AIMF when cytopenia is not well elucidated during the course of SLE and performing a bone marrow biopsy to confirm the diagnosis. The mechanisms underlying this association are not yet fully understood. The therapeutic management of AIMF is generally the same as that used in SLE. Nevertheless, multidisciplinary management and an individualised approach to each patient are essential to optimise the results and quality of life of people suffering from this combination of diseases.

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