Severe Thrombocytopenia As the Onset of Late-onset Systemic Lupus Erythematosus: A Case Report And Literature Review

Case Report

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Abstract— Systemic lupus erythematosus (SLE) is a chronic, potentially fatal, multisystem, autoimmune disorder that primarily affects women of reproductive age. The late-onset form, which occurs after the age of 50, can have a distinct clinical presentation reflected in differences in gender and ethnicity prevalence, clinical manifestations, organ damage, disease activity, and prognosis. We report the case of an 82-year-old woman with a history of cirrhosis, who presented with lower gastrointestinal bleeding and a progressive decrease in platelet count that could not be explained by her underlying condition. After an exhaustive diagnostic evaluation, late-onset SLE was confirmed. Late-onset SLE is a rare entity, generally with a benign course and lower disease activity. However, it has a lower survival rate due to its association with comorbidities, greater organ damage, ageing and longer exposure to traditional risk factors. A broad differential diagnosis is crucial, including unusual manifestations of rheumatic diseases, when common treatments for comorbidities fail to relieve symptoms in older patients.

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Keywords—Systemic Lupus Erythematosus, Anemia, Thrombocytopenia, Autoimmunity

Resumen— Trombocitopenia Severa como Debut de LES de Inicio Terdío: Reporte de Caso y Revisión de la Literatura

El lupus eritematoso sistémico (LES) es un trastorno autoinmune multisistémico, crónico y potencialmente fatal que afecta principalmente mujeres en edad fértil. La aparición después de los 50 años puede tener una presentación clínica variable en términos de prevalencia de sexo y la etnia, manifestaciones clínicas, daño orgánico, actividad de la enfermedad y pronóstico. Se presenta el caso de una mujer de 82 años de edad con antecedente de cirrosis que consultó por hemorragia de vías digestivas bajas con descenso progresivo plaquetario no explicado por condición de base en quien posterior a una búsqueda exhaustiva se llega al diagnóstico de LES de inicio tardío. El LES de inicio tardío es una entidad rara, generalmente con un curso benigno y menor actividad de la enfermedad. Sin embargo, tiene una tasa de supervivencia más baja debido a su asociación con comorbilidades, mayor daño a órganos, envejecimiento y una mayor exposición a factores de riesgo tradicionales. Es crucial un diagnóstico diferencial amplio, que incluya manifestaciones inusuales de enfermedades reumáticas, cuando los tratamientos comunes para las comorbilidades no logran aliviar los síntomas en pacientes mayores.

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Palabras clave—Lupus Eritematoso Sistémico, Anemia, Trombocitopenia, Autoinmunidad

Introduction

Systemic lupus erythematosus (SLE) is a chronic, autoimmune disorder where genetic and environmental factors interact to trigger its development.[1] The disease is characterised by an exaggerated immune response mediated by T and B lymphocytes and a loss of immune tolerance to autoantigens.[2]

SLE affects approximately more than 3 million people worldwide. Due to the significant hormonal influence contributing to the pathogenesis of the disease, the prevalence is higher among women of reproductive age, typically between 15 and 45 years; however, SLE can also present in individuals over 50 years of age, referred to as late-onset SLE.[3]

Late-onset SLE (SLE-LO), which occurs after the age of 50 to 60, has a clinical course and symptoms that differ from those of the classic form and accounts for 2% to 12% of all cases. Although SLE is more common in women, SLE-LO is more common on men.[3]

Diagnosis in this population is challenging due to the non-specific nature of symptoms, comorbidities, polypharmacy, and the consideration of more likely differential diagnoses, which can lead to delays in disease identification.[4] We present the case of an 82-year-old woman who presented with gastrointestinal bleeding due to severe thrombocytopenia and was diagnosed with late-onset SLE after thorough investigation.

Case Report

An 82-year-old female with a medical history of hypertension, type 2 diabetes mellitus, and cirrhosis (Child-Pugh A) secondary to metabolic dysfunction-related steatosis, was on losartan, hydrochlorothiazide, and metformin with adequate disease control. She presented to the emergency department with a 15-day history of rectal bleeding that had worsened 24 hours prior to presentation. On physical examination, vital signs were within normal limits and she had pallor of the conjunctival margin without other significant abnormalities.

Initial laboratory results showed Grade IV anemia (according to WHO classification), moderate thrombocytopenia, normal white blood cell count, and a normal urinalysis (Table 1). Given the lower gastrointestinal bleeding, blood transfusions were administered, and a colonoscopy revealed diverticula in the sigmoid colon with signs of recent bleeding and internal, grade II hemorrhoids. Additionally, due to the cirrhosis history, an endoscopy was performed, which showed small esophageal varices without recent bleeding signs.

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After initial management, the bleeding resolved, but follow-up tests showed progressive thrombocytopenia (down to 4,000/mm³) and persistent severe anemia (hemoglobin 7.5 g/dL) despite transfusions, without signs of acute decompensation due to cirrhosis. As a result, the differential diagnosis was broadened.

Investigations for infectious, metabolic, and neoplastic diseases yielded negative results. However, chest and abdominal CT scans revealed bilateral pleural effusion, predominantly on the right (Figure 1), and ascites, which could not be explained by her cirrhosis history. Given these findings, an autoimmune study was conducted, revealing positive antinuclear antibodies (ANA), anti-Smith antibodies, and lupus anticoagulant along with complement consumption (C3). Anti-dsDNA antibodies were negative (Table 1).

Based on these findings, the patient met the EULAR/ACR 2019 classification criteria for SLE, including positive ANA, thrombocytopenia, serositis, complement consumption, positive lupus anticoagulant, and anti-Smith antibodies, yielding 10 out of 20 necessary criteria for classification. Immune-mediated destruction was considered the mechanism for thrombocytopenia, and she was treated with intravenous methylprednisolone pulses (500 mg daily for 3 days) and hydroxychloroquine (5 mg/kg/day), leading to an improvement in platelet count (21,000/mm³). Rituximab was considered, but the patient developed a new episode of severe gastrointestinal bleeding, leading to hypovolemic shock, cardiopulmonary arrest, and ultimately, death.

Discussion

SLE is a chronic autoimmune disease that can manifest with cutaneous, renal, haematological, neurological, and other symptoms at the time of diagnosis. It predominantly affects women of reproductive age, but can also occur in children and the elderly, where the clinical presentation tends to be more variable, making diagnosis more difficult.[3]

Due to the differences in clinical phenotypes, SLE is classified as early-onset (SLE-NLO) when diagnosed before age 50 and late-onset (SLE-LO) when diagnosed after 50.[5] These variations are reflected in differences in sex and ethnicity prevalence, clinical presentation, organ damage, disease activity, and prognosis. Several studies estimate the prevalence of late-onset SLE to range between 3% and 18%, although cases in patients over 65 years old are extremely rare.[4]

Late-onset SLE is characterized by a lower female predominance, insidious onset, fewer clinical manifestations, and a more benign course.[6] Despite this, it has a lower survival rate due to a higher frequency of comorbidities and greater organ damage, largely due to aging and prolonged exposure to classic vascular risk factors.[7,8] In our case, we speculate that the progressive thrombocytopenia could have been exacerbated by comorbidities, especially cirrhosis. While the relationship between SLE and portal hypertension is not fully understood, there are reports suggesting that autoimmune disease can worsen liver damage due to a

Test	Result
Hemogram	Leukocytes 9,470/mm³, Hemoglobin 5.01 g/dL, Hematocrit 15.4%, MCV 92.5 fL, MCH 30.1pg, RDW 18.2%, Platelets 67,000/mm³, MPV 14.5 fL, Neutrophils 55%, Lymphocytes 26.8%
Urinalysis	Proteins negative, Leukocytes 1-3 per field, Hematocytes 0-2 per field, Bacteria +
Hemolysis Profile	Haptoglobin 45 mg/dL, Total bilirubin 1.44 mg/dL (Direct 0.73 mg/dL, Indirect 0.71 mg/dL), LDH 232 U/L, Peripheral blood smear shows moderate hypochromia, dacryocytes and ovalocytes present, normal white blood cell series, decreased platelets with macroplatelets observed. Direct Coombs: Negative
Infectious Serology	HIV: Negative; VDRL: Non-reactive; HBsAg: Negative; Hepatitis C Antibody: Negative; Hepatitis A IgM Antibody: Negative; Epstein-Barr Nuclear Antigen IgG and IgM: Negative
Liver Function Test	Albumin 2.93 g/dL, AST 39, ALT 26, PT 14.9 sec (Control 10.5), INR 1.7, aPTT 40.9 sec (Control 28), Ammonia 83 mcg/dL, Alkaline Phosphatase 105 U/L, Ceruloplasmin 35.1 mg/dL (Normal)
Metabolic Panel	TSH 0.95 UI/mL, Vitamin B12 1132 pg/mL, Folic Acid 10.8 ng/mL, Ferritin 82.46 ng/mL, Total Iron 16.9 mcg/dL
Malignancy Testing	Flow cytometry normal, Protein electrophoresis: Normal
Autoimmunity Tests	**ANA by IFA Hep-2: 1/80 homogeneous pattern** **C3: 68 mg/dL, C4: 15.5 mg/dL** **Anti-Smith: 44.7 RU/mL**, Anti-dsDNA by IFA: Negative Anti-cardiolipins IgG: 6.5 RU/mL (Negative), IgM: 8.3 RU/mL (Negative), B2-glycoprotein I IgG <6.1 RU/mL (Negative), IgM <2 RU/mL (Negative), **Lupus Anticoagulant: 34.3 seconds (Positive)**, PCR: 1.32 mg/L

Table 1: **LABORATORY RESULTS** MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, MPV: Mean Platelet Volume, RDW: Red Cell Distribution Width, LDH: Lactate Dehydrogenase, HIV: Human Immunodeficiency Virus, VDRL: Venereal Disease Research Laboratory, HBsAg: Hepatitis B Surface Antigen, TSH: Thyroid Stimulating Hormone, ANA: Antinuclear Antibodies, Coombs: Direct Antiglobulin Test, aPTT: Activated Partial Thromboplastin Time.

chronic proinflammatory state and the formation of immune complexes affecting the hepatic vascular system.[6,9]

Common clinical manifestations of late-onset SLE include arthritis, oral ulcers, fever, photosensitivity, and malar rash.[10] In contrast to early-onset SLE, interstitial lung disease and diffuse alveolar hemorrhage are more prevalent in late-onset cases; however, lupus nephritis and neuropsychiatric manifestations are much less common.[11,12] Hematological involvement in elderly patients with SLE can be challenging to attribute to the disease due to comorbidities and polypharmacy. Recent meta-analyses have shown that autoimmune hemolytic anemia (AHAI), lymphopenia, leukopenia, and lymphadenopathy are more common in early-onset SLE compared to late-onset, with no significant differences in thrombocytopenia.[13] Although thrombocytopenia can be one of the most common initial presentations of SLE in the emergency department, it is not typically the initial manifestation in elderly patients.[5,14] This supports the unusual presentation of our patient, who presented with severe thrombocytopenia without the more common joint or skin symptoms seen in this age group.

Regarding immunological profiles, late-onset SLE has a lower prevalence of anti-dsDNA, anti-RNP antibodies, and hypocomplementemia compared to early-onset SLE.[8] However, findings regarding the behavior of antibodies in late-onset cases are inconsistent across different series.[7] In a study from Hanyang, all patients had positive ANA, with a higher frequency of anti-Smith antibodies and a lower positivity rate for anti-dsDNA and anti-RNP.[6] These findings align with what we observed in our patient. Additionally, in relation to antiphospholipid antibodies, a study documented lupus anticoagulant (LAC) in 11.6% of late-onset SLE patients, followed by anticardiolipin IgM in 4.3%, with no statistically significant difference when compared to early-onset SLE.[7] Our patient did not exhibit thrombotic manifestations suggesting the involvement of LAC beyond the thrombocytopenia.

It is essential to maintain a broad differential diagnosis, including unusual manifestations of rheumatic diseases, when treatments for common comorbidities fail to alleviate symptoms in elderly patients.[15] In our case, the significant hematological involvement due to anemia and severe thrombocytopenia could not be explained by cirrhosis alone, leading to an extended differential diagnosis. Ultimately, after excluding other infectious, metabolic, and neoplastic diseases, late-onset SLE was diagnosed.

In this clinical case, despite there being a partial hematological response with the use of high-dose glucocorticoids, it is evident that the etiology of thrombocytopenia is multifactorial, mainly due to autoimmune peripheral destruction, without underestimating the splenic sequestration and the decrease in thrombopoietin synthesis as a result from chronic liver disease9. We also considered that the patient could benefit from anti-CD20 therapy; however, during the clinical

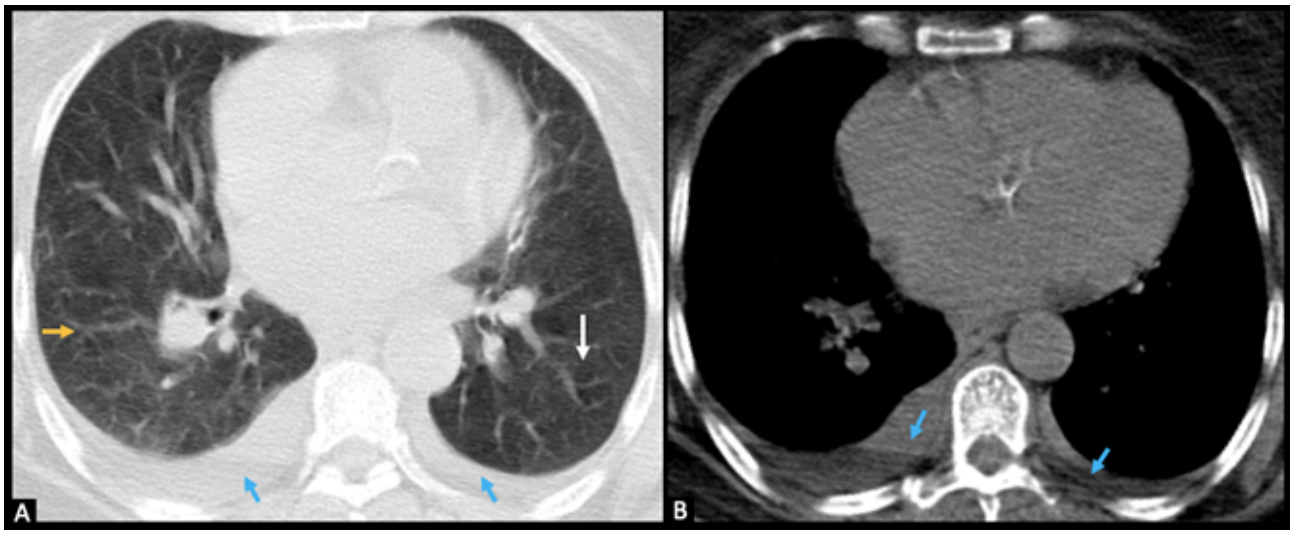

Figure 1: Simple chest CT scan. (A and B) Bilateral pleural effusion is evident, with homogeneous density, non-loculated, predominantly on the right (blue arrow), bilateral centrilobular emphysema (white arrow), and peribronchovascular interstitial opacities related to congestive findings (yellow arrow).

course, the activity of the SLE may have contributed to the increase in portal pressure, triggering severe gastrointestinal bleeding of variceal origin, without improvement after the transfusion of multiple blood products and the use of vasopressin analogues, leading to the loss of effective circulating volume and fatal outcome as a complication of cirrhosis.[16] These considerations highlight the need for a personalized therapeutic approach that takes into account both autoimmune manifestations and associated comorbidities.

Conclusion

Late-onset systemic lupus erythematosus is a rare disease with distinct clinical and immunological features compared with classic-onset SLE. In this case, the patient has a complicated clinical course due to the presence of portal hypertension and severe haematological involvement. These factors suggest that although late-onset SLE in older patients may have a more favourable clinical course, the presence of comorbidities such as chronic liver disease may complicate management and worsen prognosis. Early recognition and comprehensive management of multisystem manifestations are key in these patients, especially considering the high morbidity associated with autoimmune diseases in the geriatric population.

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Conflict of Interest

The authors declare to respect the ethical principles of research and to be free of any conflict of interest.

Patient consent

Informed consent was obtained and signed from the patient regarding the use of patient health information for the purposes of writing a case report publication.

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