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Case Report

Ethylenediaminetetraacetic acid-dependent pseudothrombocytopenia in a patient with systemic lupus erythematosus and lupus nephritis

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Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by several immunological abnormalities. We wish to communicate the case of a patient with SLE and lupus nephritis (LN) who developed pseudothrombocytopenia. Pseudothrombocytopenia can occur in patients with SLE and LN and should be considered when diagnosing patients with thrombocytopenia without bleeding.

Keywords: SLE, lupus nephritis, pseudothrombocytopenia

Introduction

We wish to communicate the case of a patient with systemic lupus erythematosus (SLE) and lupus nephritis (LN) who developed pseudothrombocytopenia.

Systemic lupus erythematosus is an autoimmune disease characterized by several immunological abnormalities (1). Laboratory testing may reveal leukopenia, anemia, and thrombocytopenia. Thrombocytopenia is a common and important manifestation of SLE, which is directly related to its morbidity and mortality. Growing evidence indicates that at least two types of autoantibodies, anti-glycoprotein IIb/IIIa (GPIIb/IIIa) and anti-thrombopoietin receptor (TPOR) antibodies, are involved in the major pathophysiologic mechanisms of thrombocytopenia in SLE (2). Thrombocytopenia in SLE may occur due to immune-modifying drugs, infection, thrombotic thrombocytopenic purpura (TTP), anti-phospholipid antibody syndrome (APS), disseminated intravascular coagulopathy (DIC), or marrow dysplasia (3) as well as rarely due to pseudothrombocytopenia.

Pseudothrombocytopenia is most frequently observed in association with autoimmune, neoplastic, cardiovascular, and chronic liver diseases (4). The disorder is caused by antibodies that recognize platelet antigens modified or exposed to the combined action of ethylenediaminetetraacetic acid (EDTA) and low temperature on platelet membrane glycoproteins (5). Methods for detecting pseudothrombocytopenia include the replacement of anticoagulants (sodium citrate and heparin) with EDTA and the determination of platelet aggregation through a microscope (6). Methods for detecting pseudothrombocytopenia also include the replacement of anticoagulants (sodium citrate and heparin) with EDTA to the other way, use the EDTA first as that was the culprit and the pseudothrombocytopenia was revealed by switching anticoagulants.

Case Presentation

A 48-year-old female patient reported weakness, fatigue, and pain in the wrists. On physical examination, skin and conjunctivae were pale and non-scarring localized alopecia was observed. The liver was palpable approximately 3 cm below the right costal margin. Laboratory studies revealed a white blood cell (WBC) count of 4000/μL, lymphocyte count of 600/μL, hemoglobin (Hgb) level of 6.5 gr/dL, hematocrit (Htc) of 18.5%, and a platelet (PLT) count of 210,000/μL. Peripheral blood smear revealed a few atypical lymphocytes. Furthermore, lactate dehydrogenase (LDH) levels were 832 U/L and the sedimentation rate was 132 mm/h. The patent was positive for anti-nuclear antibody (ANA; 1/3200 in granular pattern) and anti-dsDNA antibody (200 IU/mL). The activity of both the complements 3 (C3, 0.4 g/L) and 4 (C4, 0.05 g/L) was low. Urine tests revealed active sediment and 0.8 g/day proteinuria. Light microscopy of a kidney biopsy identified segmental endocapillary proliferation, including neutrophilic infiltration, thickening of the glomerular basement membrane, and wire loop lesions with tubular atrophy and interstitial fibrosis in some areas, which led to the diagnosis of LN and tubulointerstitial nephritis. Microscopy of a bone marrow biopsy

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revealed pronounced proliferation in all three hematopoietic series, megakaryocyte dysplasia in serial sections, and increased precursor granulocyte cells. Based on these findings, the patient was diagnosed with both SLE and LN.

The patient was treated with intravenous pulse methylprednisolone at 750 mg/day for 3 days, followed by 32 mg/day single-dose oral methylprednisolone and 1 g/month cyclophosphamide. At the sixth month of therapy, WBC count was 3810/µL, Hgb level was 9.3 g/dL, Htc was 29.1%, and PLT count was 69.000/µL. The PLT count then dropped suddenly to 9000/µL in 1 day. Physical examination did not identify focus of bleeding, petechiae, or purpura. The patient was given 40 mg of intravenous methylprednisolone as well as suspended thrombocytes. Both an EDTA and a citrate blood sample were taken and used for peripheral blood smears by Giemsa staining; thrombocytes were counted at room temperature. PLT counts differed between blood storage media that was stored in EDTA and yielded a PLT count of 9000/µL and citrate that yielded a normal PLT count. Although PLT clumping was observed in blood smears treated with EDTA (Figure 1), it was not observed in samples treated with citrate. Based on these results, the patient was diagnosed with SLE, LN, and pseudothrombocytopenia. Use of citrate as an anticoagulant enabled the identification of pseudothrombocytopenia by platelet clumping in a peripheral blood smear.

Discussion

Pseudothrombocytopenia has been identified in association with autoimmune diseases such as SLE (7) and rheumatoid arthritis (RA) (8). According to Irisawa et al. (7), pseudothrombocytopenia is closely associated with the disease activity of SLE. As our patient who had active SLE and LN was treated using cyclophosphamide, she did not receive thrombocytopenia inducing drugs. After the cyclophosphamide therapy her pseudothrombocytopenia continues in the active period of SLE and LN.

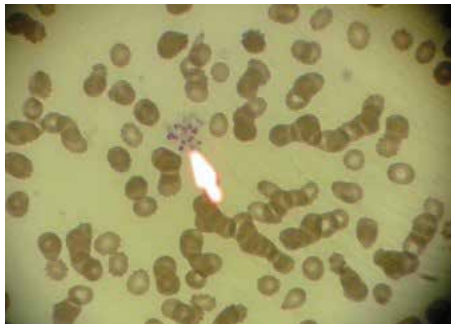

Figure 1. Peripheral blood smear anticoagulated with ethylenediaminetetraacetic acid (EDTA) showing platelet clumping (arrow)

SLE is a disease which has autoantibody responses to self-antigens. In addition, other autoantibodies that are not associated with SLE clinics are more frequently known to be positive in SLE patients when compared with the healthy population. As per this mechanism, the development of EDTA-dependent antiplatelet antibodies seems probable in SLE (9, 10).

Pseudothrombocytopenia may occur in patients with SLE and LN and severe thrombocytopenia related to SLE disease activity and it requires urgent investigation and treatment. In the absence of clinical signs of severe thrombocytopenia, EDTA-dependent pseudothrombocytopenia should be considered as a differential diagnosis and can be confirmed by peripheral blood smear demonstrating platelet clumping. Use of citrate as an anticoagulant confirmed EDTA-dependent pseudothrombocytopenia.

Ethics Committee Approval: N/A.

Informed Consent: Written informed consent was obtained from the patient.

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