Systemic Lupus Erythematosus as a Rare Cause of Anemia Resistant to Erythropoiesis-stimulating Agents

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Erythropoiesis-stimulating agents (ESAs) play an important role in the management of anemia in patients with chronic kidney disease, but the goals cannot be reached in 5% to 10% of the patients despite high-dose ESA treatment. In case of ESA resistance, all causes of anemia encountered in the general population should be carefully reviewed. We present a patient examined for ESA resistance that was diagnosed with systemic lupus erythematosus and subsequently showed improvement of anemia with systemic corticosteroids.

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INTRODUCTİON

Erythropoiesis-stimulating agents (ESAs) are important in the management of anemia in chronic kidney disease (CKD), but the goals cannot be reached in 5% to 10% of the patients despite high-dose ESA treatment.[1-2] We present a rarely seen case examined for ESA resistant-anemia that was diagnosed with systemic lupus erythematosus (SLE).

CASE REPORT

A 24-year-old woman who had been included in the hemodialysis program for 8 years was admitted to the emergency room with dyspnea. On physical examination, blood pressure was 140/90 mm Hg and the respiratory sounds were diminished at the basal parts of both lungs. Other findings were unremarkable. It was learned that the patient was hospitalized twice due to ESA-resistant anemia in the past 6 months and hyperparathyroidism was primarily considered. Parathormone level was 1186 pg/mL1 month before, and she had been on 60 mg/d of cinacalcet.

The laboratory findings are shown in the Table. Peripheral blood smear showed normochromic normocytic erythrocytes without atypical cells. Direct and indirect Coombs tests were negative. Serum protein and immunoelectrophoresis were reference ranges. Bilateral pleural effusion was seen on chest radiography. On echocardiography, there was pericardial effusion with a maximum dimension of 1.5 cm with normal left ventricle ejection fraction. With these findings in favor of hypervolemia, daily hemodialysis was performed and the patient lost 8 kg at the end of the 7th session. She still had dyspnea and pleural effusion

Laboratory Evaluation of the Patient

Test	Result	Reference Range
Blood leucocyte count, × 10^9/L	4.9	3.9 to 10.7
Blood lymphocyte count, × 10^9/L	1.08	1 to 4.8
Hemoglobin, g/dL	8.6	14 to 18
Mean corpuscular volume, fL	88.6	
Platelet count, × 10^9/L	132	130 to 400
Reticulocyte, %	1.4	0.5 to 1.5
Blood urea, mg/dL	119	17 to 43
Serum creatinine, mg/dL	5.78	0.84 to 1.25
Serum albumin, mg/dL	4	3.5 to 5.2
Lactate dehyrogenase, IU/L	166	25 to 248
Total bilirubin, mg/dL	0.4	0.3 to 1.2
Direct bilirubin, mg/dL	0.2	0 to 0.3
Serum vitamin B12, pg/mL	12	120.6 to 505
Serum ferritin, ng/mL	8.8	23.9 to 336.2
Serum iron, µg/dL	86	60 to 180
Iron binding capacity, µg/dL	137	155 to 355
Serum folate, ng/mL	6	3 to 17
Erythrocyte sedimentation rate, mm/h	36	0 to 20
Parathyroid hormone, pg/mL	430	12 to 88

Case Report

persisted.

At the end of the 2nd week of ESA treatment (recombinant erythropoietin, 150 IU/kg/w), hemoglobin level was 7.1 g/dL. The patient was consulted to the rheumatology clinic with a prediagnosis of SLE presented with polyserositis. Although serological tests were negative, the patient was diagnosed with SLE in accordance with the American College of Rheumatology's criteria, due to the presence of photosensitivity, psychosis, serositis, arthritis, kidney failure, and lymphopenia.[3]

The patient was administered 48 mg/d of methylprednisolone and 200 mg/d of hydroxychloroquine, and 2 weeks later, her dyspnea disappeared, the pleural and pericardial effusion decreased significantly, and hemoglobin level was 9.2 mg/dL. The patient's hemoglobin level was 12.5 mg/dL at the end of the 1st motnh after stopping ESA treatment.

DISCUSSION

According to the the National Kidney Foundation's guidelines, ESA resistance may be mentioned in the presence of one of these criteria: (1) a need for a continuous increase in ESA dose to provide a stabile hemoglobin level or a decrease in hemoglobin level with a stable dose of ESA; and (2) inability to increase hemoglobin level over 11 g/dL despite an erythropoietin dose of 500 IU/kg/w.[4] As our patient's hemoglobin level decreased despite recombinant erythropoietin at a dose of 150 IU/kg/w, it was consistent with the definition of ESA-resistant anemia.

Cardiovascular morbidity and mortality increase both due to inability to reach the target hemoglobin level and exposure to high ESA levels in patients with CKD.[5] The causes of ESA resistance are iron deficiency (including blood loss), vitamin deficiencies, hemolysis, hemoglobinopathies, malignancy, insufficient dialysis, hyperparathyroidism, myelosuppression, thyroid dysfunction, drugs, pure red cell aplasia, aluminum toxicity, malnutrition, infection, and inflammation.[6] These aforementioned causes were ruled out in our patient.

Anemia is a frequent disorder being encountered in the course of SLE. Chronic disease, iron deficiency, autoimmune hemolytic anemia, and concurrent renal insufficiency are the contributing factors to anemia.[7-8] The pathogenesis of chronic disease anemia includes decreased erythropoietin production or relatively decreased erythropoietin activity due to unresponsiveness of erythrocyte progenitor cells to erythropoietin. Inflammatory cytokines were shown to play a role in this process.[9-11] On the other hand, some antibodies including anti-erythropoietin antibodies may be detected in SLE, and this may result in partial ESA resistance.[12-14] It was reported that ESA need was higher in CKD patients with SLE when compared to other subgroups.[13,15,16] We could not comment on autoantibody-mediated ESA resistance in our patient since this was not investigated. As anemia and other clinical findings of our patient showed improvement with steroid treatment, we supposed that the anti-inflamatory effect of steroid was improved the ESA resistance. Similarly, Tzanakis and associates reported ESA-resistant anemia in 2 patients who were diagnosed with rheumatoid arthritis and vasculitis, which showed improvement after treatment with steroids.[17]

In conclusion, review of all etiologic factors in CKD patients might change the management of refractory anemia. It should be kept in mind that autoimmune diseases might be a cause of ESA-resistant anemia.

CONFLICT OF INTEREST

None declared.

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