

Rituximab for Refractory Anemia and Thrombocytopenia in a Patient with Systemic Lupus Erythematosus

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Abstract

Introduction: Hematologic manifestations of Systemic Lupus Erythematosus (SLE) such as hemolytic anemia, leucopenia and thrombocytopenia are among the common causes of morbidity and hospitalization among patients. This is a case report of a patient presenting with refractory cytopenias.

Case: The patient is a 42-year-old female, diagnosed with SLE, having met the Systemic Lupus Erythematosus International Collaboration Clinics Criteria for diagnosis Persistent serositis (pleural effusion and ascites) and worsening of anemia prompted treatment with oral corticosteroid (prednisone 1.0 mg per kg per day) which showed improvement of shortness of breath and pleural

effusion. Cytopenias persisted despite increasing IV pulse steroid to 6.0 mkg prednisone then further to 13 mkg prednisone. Rituximab given as 1.0 g infusion once every two weeks for two doses which resulted to improvement of anemia, thrombocytopenia and serositis.

Conclusion: Hematologic manifestations may present as life threatening complications of lupus. Most cases are responsive to corticosteroid therapy, however, in a few refractory cases, less used conventional treatment such as rituximab, may provide significant response.

Key words: systemic lupus erythematosus, ANA, rituximab

Introduction

Hematologic manifestations of systemic lupus erythematosus (SLE) are among the common causes of morbidity and hospitalization among patients. Manifestations including hemolytic anemia, leucopenia and thrombocytopenia can be either the initial presentation of the disease or the parameters used in monitoring disease flare and response to treatment. One study of 126 patients with SLE showed that 47% had neutropenia, 27% had thrombocytopenia, 20% had lymphopenia and 13% had hemolytic anemia. They commonly result from an immune mediated bone marrow failure, excessive peripheral cell destruction or certain drugs and infections.¹ Evidenced-based treatment algorithm is currently not in consensus especially for the second and third line treatment to systemic glucocorticoids.² The utility of rituximab, a chimeric monoclonal antibody which targets the surface marker CD20 on B cells, in the management of recalcitrant renal and non-renal (hematologic and cutaneous) manifestations of lupus remains off-label despite a number of case series and open label trials demonstrating beneficial results.³

Case Report

The patient is a 42-year-old female, known hypertensive with a one-year history of recurrent joint pains, rash, oral ulcers and Raynaud's disease who came in due to epigastric pain and shortness of breath. Patient developed low grade fever, cough and progressive shortness of breath prompting admission to critical care unit. Initial labs revealed Coomb's positive anemia (Hgb 8.2), WBC 5,400, platelet count of 202,000, bilateral pleural effusion and ascites on CT scan. Patient was initially managed with pneumonia treatment regimen and was given broad spectrum antibiotics. During the course of hospitalization, CBC monitoring revealed worsening of anemia and decreasing trend of platelet count despite adequate antibiotic treatment, hence the referral to rheumatology service. Serologies requested revealed positive ANA (1:5120 speckled pattern), positive Anti SSa and SSb, low C3, equivocal B2 glycoprotein IgG and strongly positive lupus anticoagulant. Persistence of serositis (pleural effusion and ascites) and worsening of anemia prompted treatment with oral corticosteroid (prednisone 1 mkg) which showed improvement of shortness of breath and pleural effusion, shifted to IV due to persistent abdominal pains. Cytopenias persisted, lowest at Hgb of 8.1 post transfusion of two units PRBC and platelet count of 71,000 despite increasing IV pulse steroid to 6mkg prednisone then further to 13 mkg prednisone. CBC was monitored for a week after pulse corticosteroid therapy while on oral 1 mkg prednisone equivalent before patient was started on Rituximab given as 1.0g infusion once every two weeks for two doses which resulted to improvement of anemia, thrombocytopenia and serositis. Patient was

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then discharged well on low dose oral corticosteroid and hydroxychloroquine.

Discussion

Rituximab is an IgG dependent chimeric monoclonal antibody that is composed of a murine variable and human constant regions. Rituximab binds CD20, a surface antigen whose expression is restricted to B cells. CD20 is a membrane associated phosphoprotein that regulates the early steps of B cell activation. Binding of CD20 by rituximab either modulates its expression or by causing substantial internalization of CD20. The use of rituximab for SLE has been defined in refractory lupus nephritis and in central nervous system involvement. Cyclophosphamide, the immunosuppressant of choice for most lupus life threatening conditions, has limited role in cytopenias because of its known bone marrow suppression effect.⁴ Mechanisms of B-cell depletion includes (1) antibody dependent cellular cytotoxicity or ADCC where an antibody coated cell is directly destroyed by the effector cell expressing Fc receptors, (2) through complement activation via the classical pathway and (3) induction of apoptosis of B cells. In NPSLE, as cited by Tokunaga in 2007, Rituximab rapidly improved refractory NPSLE, as evident by resolution of various clinical signs and symptoms and improvement of radiographic findings. The down regulation of functional molecules on B and T cells suggests that rituximab modulates the interaction of activated B and T cells through costimulatory molecules.⁴

Corticosteroids remain the mainstay of treatment in cytopenias associated with lupus. Other conventional therapies include azathioprine, cyclophosphamide and human normal immunoglobulin. Mycophenolate mofetil as a corticosteroid and cyclophosphamide-sparing agent has also been cited in studies.⁵

In autoimmune hemolytic anemia alone, corticosteroids are usually given as first-line treatment. A response to corticosteroids is observed in 70% to 85% of the cases. Rituximab, both as second-line and first-line therapy is now being proposed, with rituximab leading to response rates similar to splenectomy (≈70%). In some European centers, rituximab is currently a preferred second-line therapy of warm antibody hemolytic anemia in adults, although no prospective study supports this practice yet.⁶ More importantly, studies cited and reviewed were among patients with autoimmune hemolytic anemia in general and studies on patients with underlying SLE would have been more useful and conclusive regarding this discussion.

Conclusion

Hematologic manifestations of SLE are one of the important parameters that warrant aggressive treatment to prevent fatal complications. Most cases are responsive to corticosteroid therapy, however, in a few refractory cases, less used conventional treatment such as rituximab, a monoclonal antibody against CD20 receptor may provide significant response.

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