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Case Report

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Comprehensive management of concurrent chronic lymphocytic leukemia and Evans syndrome: combinating rituximab, venetoclax and eltrombopag

Serkan Ünal

Department of Hematology, Kastamonu Training and Research Hospital, Kastamonu, Turkiye

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Corresponding Author: Serkan Ünal, sserkanunall@hotmail.com

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ABSTRACT

Chronic lymphocytic leukemia (CLL) and Evans syndrome represent complex hematologic disorders characterized by distinct yet interconnected pathophysiologies. This case report explores the diagnostic and therapeutic intricacies of managing concurrent CLL and Evans syndrome in a 59-year-old male patient presenting with fatigue and petechiae. Laboratory findings revealed severe hematologic derangements indicative of advanced CLL and autoimmune hemolytic anemia (AIHA). The diagnostic journey encompassed bone marrow analysis confirming CLL and Coombs positivity suggesting Evans syndrome, with careful exclusion of immune thrombocytopenia. Initial therapeutic interventions included steroids and intravenous immunoglobulin for AIHA, alongside eltrombopag for persistent thrombocytopenia. Subsequently, rituximab and venetoclax were initiated for CLL, leading to complete remission. The successful outcome underscores the importance of an integrated therapeutic approach in managing concurrent CLL and Evans syndrome, offering insights for future clinical management of complex hematologic disorders.

Keywords: Eltrombopag, CLL, Evans, ITP

INTRODUCTION

Chronic lymphocytic leukemia (CLL) and Evans syndrome represent two distinctive yet interconnected challenges in the realm of hematologic disorders, encompassing a spectrum of complexities in diagnosis and management. CLL, characterized by the gradual proliferation of mature B lymphocytes, predominantly affects the elderly population and underscores the delicate balance between indolent progression and the potential for transformation into a more aggressive form.[1] On the other hand, Evans syndrome, a rare autoimmune disorder, presents an intricate interplay of immune dysregulation, manifesting as the simultaneous occurrence of autoimmune hemolytic anemia (AIHA) and immune thrombocytopenia (ITP). The coexistence of these conditions in a single patient poses unique clinical considerations, demanding a nuanced understanding of their individual pathophysiologies and the synergistic impact on the patient's health.[2]

As we embark on the exploration of this complex case, it is imperative to delve into the intricate molecular and immunological mechanisms underlying CLL and Evans syndrome. This case report not only serves as a documentation of a compelling clinical scenario but also contributes to the broader discourse on the evolving landscape of hematologic malignancies and autoimmune phenomena.[2] By examining the synergistic effects of CLL and Evans syndrome within the framework of a single patient's journey, we strive to provide insights that may inform future clinical approaches and therapeutic strategies for similar complex hematological presentations.

CASE

A 59-year-old male diagnosed with CLL presented with complaints of fatigue. The clinical picture was further complicated by the presence of petechiae. Laboratory findings provided quantitative insights into the severity of the patient's hematologic derangement. Hemoglobin levels were recorded at 4.7 g/dl, platelet counts at 15,000/µL, and lymphocyte counts at 125,000/µL. It has been observed that the spleen size is 16 cm, the Rai stage is 4, and there are widespread lymphadenopathies.

The diagnostic journey unfolded with a comprehensive assessment, including a bone marrow analysis revealing the characteristic features of CLL. Additionally, Coombs positivity and hemolytic anemia were observed, prompting the concurrent consideration of AIHA and the diagnosis of Evans syndrome. This dual diagnosis exemplifies the intricate nature of hematologic disorders and the need for a holistic approach

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in patient management. Notably, the diagnostic process included the evaluation of ITP as a potential component of Evans syndrome. The diagnosis of ITP was confirmed through bone marrow biopsy, which demonstrated normal or increased megakaryocytes, consistent with peripheral platelet destruction. Additionally, the bone marrow analysis showed lymphocytic infiltration characteristic of CLL. CLL is recognized as an important secondary cause of ITP, further emphasizing the link between the two conditions. Thorough exclusion criteria were applied to rule out other potential causes of thrombocytopenia.

The initial therapeutic interventions included standard doses of steroids (1 mg/kg/day) to address the autoimmune hemolysis component of Evans syndrome. During the initial phases of treatment, intravenous immunoglobulin (IVIG 1 gr/kg/day for 2 days) and steroids were employed for thrombocytopenia without achieving a satisfactory response. Consequently, eltrombopag (50 mg/day) was initiated. However, with the successful treatment of bone marrow involvement and CLL through the rituximab-venetoclax combination (rituximab 375 mg/m^2/day once for 28 days, venetoclax 400 mg/day everyday), Eltrombopag became unnecessary in the ensuing months following the reduction of lymphocytic infiltration observed in the bone marrow aspiration and the successful completion of rituximab-venetoclax therapy. This led to the complete resolution of thrombocytopenia, eliminating the need for eltrombopag in the management of secondary ITP.

Four months into treatment, the patient exhibited a positive therapeutic response. AIHA resolved, as evidenced by the achievement of Coombs negativity. Furthermore, a complete remission of lymphocytic infiltration in the bone marrow was observed, validating the effectiveness of the standardized therapeutic regimen (**Figure**).

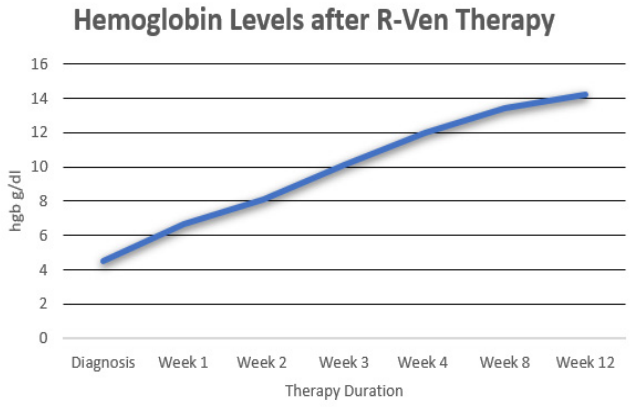


Figure. Hemoglobin levels after R-ven therapy

DISCUSSION

The presented case of a 59-year-old male with coexisting CLL and Evans syndrome encapsulates the intricate diagnostic and therapeutic challenges inherent in managing complex hematologic disorders. The initial presentation of fatigue, accompanied by night sweats, weight loss, and petechiae, prompted a thorough diagnostic investigation. The subsequent identification of severe hematologic derangement, marked by profound anemia, thrombocytopenia, and lymphocytosis, underscored the complexity of the case. The advanced Rai stage, enlarged spleen, and widespread lymphadenopathies indicated an aggressive form of CLL, further complicated by the presence of Evans syndrome.

This case exemplifies the need for a meticulous diagnostic evaluation and a tailored therapeutic strategy in managing the rare concurrence of CLL and Evans syndrome, considering potential ITP involvement.[2] The integrated therapeutic approach, incorporating eltrombopag, rituximab, and venetoclax at standard dosages, proved effective in achieving a favorable hematologic response. The successful outcome underscores the importance of a comprehensive understanding of concurrent hematologic disorders and the significance of an integrated therapeutic approach.[3]

CONCLUSION

In conclusion, our case highlights the importance of recognizing the diverse manifestations of CLL and the challenges presented by concurrent Evans syndrome, with careful consideration of ITP in the diagnostic process. The application of standardized therapeutic interventions offers a promising avenue for navigating the complexities of these hematologic disorders, providing valuable insights for future clinical management.

ETHICAL DECLARATIONS

Informed Consent

The patient signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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