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CHRONİC LYMPHOCYTİC LEUKEMİA: IMMUNE DYSREGULATİON AND MANAGEMENT

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INTRODUCTION

Hypogammaglobulinemia is the most common immune disorder in chronic lymphocytic leukemia(CLL). In CLL patients, both humoral and cellular immune dysfunction and treatment-related immune dysregulation may occur.The most common cause of death in CLL patients is infections. Apart from anti-infective treatments given for infection, immunoglobulin(Ig) replacement can be performed.
Three CLL patients with different scenarios followed in our clinic were retrospectively examined. Immunoglobulin levels, infection status and the effectiveness of immunoglobulin replacement therapy(IGRT) and their relationship with each other were examined in outpatient clinic follow-ups.

CASE REPORTS

Case report 1
A 69-year-old male patient was diagnosed with CLL(RAI stage IV) in 2018. The patient was treated with Rituximab plus Bendamustine. Before the treatment, thepatient's IgG level was 516 gr/dl. During and after the treatment, the patient's IgG level was 355 mg/dl and 285 mg/dl respectively. Subsequently, the patient was monitored without any treatment or immunoglobulin replacement therapy.
Case report 2
An 84-year-old male patient was diagnosed with CLL(RAI IV) in September 2017. At the time of diagnosis, his IgG level was 1720 mg/dl.The patient received Rituximab plus Bendamustine treatment, and after the first cure, he was hospitalized due to neutropenic fever and lung fungal infection.The patient was treated with voriconazole, meropenem, and teicoplanin. His IgG level was 1120 mg/dl at that time. IgG levels measured during follow-up were 525 mg/dl, 496 mg/dl, and 639 mg/dl, respectively. During this period, the patient did not receive IGRT.
Case report 3
A 56-year-old female patient, who has asthma and Sjögren's disease, was diagnosed with RAI I SLL/CLL in 2018. At the time of diagnosis, her IgG level was 642 mg/dl. During the follow-up period, the IgG levels decreased to 377 mg/dl. In 2019 Rituximab plus Venetoclax treatment was started. Intravenous immunoglobulin (IVIG) was given the patient, who had pneumonia in the 6th month of treatment and did not respond to antibiotic treatment. Post-treatment IgG levels were below 500 mg/dl and frequent infections ,due to the patient's history, IVIG was given regularly.

DİSCUSSİON

Immune system dysregulation in CLL begins in the early stages of the disease and worsens during follow-up. One of the most frequently diagnosed immunological defects in CLL patients is hypogammaglobulinemia. Studies have reported that hypogammaglobulinemia develops in 10-44% at the time of diagnosis and 25-85% during the course of treatment (1-3).Immunoglobulin replacement therapy (IGRT) is a valuable and effective option for increasing IgG levels, limiting antibiotic use, and reducing the rate of serious and/or life-threatening infections in patients with primary and secondary immunodeficiency (4-7).Despite the fact that infections are the main cause of death in CLL patients and studies showing that IVIG can reduce the rate of infective events, IVIG did not provide any increase in survival in these studies (8,9).

CONCLUSIONS

There were three different scenarios in our patients. In our first case, IgG levels were low at the time of diagnosis and during treatment. In our second case, there was a fungal lung infection that required hospitalization and responded to antifungal treatment. IVIG was not given to these two patients. In our third patient, there was hypogammaglobulinemia before, during and at the end of treatment and IVIG was given regularly due to a history of frequent infections that did not respond to anti-infective treatments.
In conclusion, we think that hypogammaglobulinemia can be seen throughout the course of the disease in CLL patients, and immunoglobulin replacement should be administered to patients who do not respond to anti-infective treatments and whose IgG levels are lower than 500 mg/dl.

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