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Introduction

Chronic lymphocytic leukemia (CLL) is a hematological disease involving the clonal proliferation of mature and immunoincompetent B lymphocytes. Clinical manifestations are derived from lymphocytic and progressive bone marrow infiltration, lymph nodes and other tissues. The main manifestations include: asthenia, anemia syndrome, thrombocytopenia and infections. B symptoms are also common (> 38 °C unexplained fever, night sweats and unexplained weight loss). Adult leukemia has the largest incidence in Western countries, accounting for 20-40% of all. A total of 70% of patients are diagnosed after age 65, and it is more prevalent in men.

Venetoclax is one of the approved therapies for the treatment of CLL, a small molecule that acts as a BCL-2 antiapoptotic protein selective inhibitor. One of serious adverse reactions that can produce is the autoimmune hemolytic anemia (AIHA), a rare disease that affects all ages. Autoerythrocyte sensitization (coated autoantibodies) hemolysis is its main feature. Those autoantibodies are eliminated by the macrophage system, especially in the spleen. Diagnostic confirmation is based on a positive Coombs test result.

AIHA occurs because of medication, but it also may be secondary to systemic diseases, infections, primary immunodeficiencies or other autoimmune diseases.

AIHA is characterized by a decrease in hemoglobin levels and in acute or variable factors, depending on the patient. Initial treatment is based on corticosteroids for a long period. As a result, many patients develop resistance, thus the use of a second-line therapy with either rituximab, splenectomy or immunosuppressive drugs is required.

Case description

Male patient, 74 years old, diagnosed in September 2010 with Type B LLC, stage I according to Rai classification (lymphocytosis and lymphadenopathy) and stage B as rated by Binet (hemoglobin ≥10 g/dL; platelets ≥100,000 mm³/L and three or more affected lymphatic areas). Retired, active in rural life and no known drug allergies. As medical antecedents of interest, the patient presents prostate syndrome.

The patient received several treatment lines: alemtuzumab, six cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) and ibrutinib. After progression of the disease to all lines received, the patient presented a good general condition (ECOG-PS 0-1), and as a fourth-line treatment, venetoclax was requested through the application of Special Situations of the Spanish Agency for Medicines and Health Products (AEMPS by its Spanish acronym).

The drug’s administration requires a dose escalation from daily 20 mg to 400 mg in five weeks, close monitoring of analytical parameters and administration of concomitant medication for its high risk of tumor lysis syndrome.

KEYWORDS
Autoimmune hemolytic anemia; Venetoclax; Chronic lymphocytic leukemia.

PALABRAS CLAVE
Anemia hemolítica autoinmune; Venetoclax, Leucemia linfática crónica.
The patient was hospitalized to start treatment in March 2017 to prevent tumor lysis syndrome, where he was administered with high hydration, allopurinol 100 mg/day and rasburicase 0.2 mg/kg/day. These measures help eliminate toxic metabolites such as uric acid, potassium or phosphorus more quickly.

After hospitalization, the patient was discharged with the maximum dose of venetoclax, highlighting as adverse event a febrile neutropenia that was resolved with the temporary suspension of the drug and administration of filgrastim. After several days of treatment with corticosteroids without any hemoglobin improvement, tachypnea and asthenia that prevented him the development of daily activities were observed. He was administered with high hydration, allopurinol and rasburicase 0.2 mg/kg/day. These measures help eliminate toxic metabolites such as uric acid, potassium or phosphorus more quickly.

After hospitalization, the patient was discharged with the maximum dose of venetoclax and outpatient monitoring. AIHA was reported as a possible diagnosis to prevent further hemolysis. Treatment with venetoclax was suspended as it was found to be related to cause AIHA.

After several days of treatment with corticosteroids without any hemoglobin improvement, tachypnea and asthenia that prevented him the development of daily activities were observed. He was administered with high hydration, allopurinol and rasburicase 0.2 mg/kg/day. These measures help eliminate toxic metabolites such as uric acid, potassium or phosphorus more quickly.

The adverse reaction appears to be related to the use of venetoclax, although it can not be ruled out to be a secondary underlying pathology for the patient. The development of secondary autoimmune cytopenias in CLL is frequently observed, especially AIHA (10-15%) and thrombocytopenia (2-15%)..

The drug's withdrawal and initiation of treatment achieved an improvement in the patient's hemoglobin levels, as well as his clinical stability. For this reason, AIHA was mainly related to venetoclax. Naranjo algorithm9 was applied and the adverse reaction was reported as probable. This case reflects the possibility of developing AIHA with venetoclax and the importance of reporting adverse reactions to new drugs.

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Conflict of interests
No conflict of interest.

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