Austin Oncology Case Reports

Open Access

Austin Publishing Group

Case Report

Autoimmune Hemolytic Anemia in Chronic Lymphocytic Leukemia Successfully Treated with Rituximab-Venetoclax: A Case Report

Martino E, Vigna E, Mendicino F, Caracciolo D, Botta C and Gentile M*

Department of Onco-Hematology, Hematology Unit AO of Cosenza, Cosenza, Italy

***Corresponding author:** Massimo Gentile, Department of Onco-Hematology, Hematology Unit AO of Cosenza, 87100, Cosenza, Italy

Received: April 09, 2021; **Accepted:** April 22, 2021; **Published:** April 29, 2021

Abstract

CLL is frequently complicated by autoimmune phenomena (up to 25% of patients) which are sustained by dysfunctions of the immune system. AIHA results the commonest form. In the past decade small molecules had dramatically change the therapeutic scenario of CLL. Their role in the setting of autoimmune phenomena has to be still elucidated. Here we report the case of a CLL patient harboring del (17p) in relapse of disease during ibrutinib therapy who experienced AIHA. Patient, refractory to steroids, achieved benefit from the administration of rituximab and venetoclax. The patient reached stable and long-lasting stabilization of hemoglobin values.

Keywords: CLL; AIHA; Venetoclax

Case Presentation

In June 2020 a 75 years-old man affected by CLL was admitted to the emergency department for repeated syncopal episodes and severe asthenia. He received a CLL diagnosis in April 2016. At baseline he showed a B/II stage according to Rai and Binet systems [1]. The biological assessment showed the absence of the expression of ZAP70, CD38 and CD49d, an unmutated *IGHV* mutational status, and both del (13q) and del (11q) at FISH analysis. In January 2017, for massive splenomegaly and lymph nodes the patient was enrolled in the GIMEMA multicenter phase 2 study (LLC1114) and received the combination of ibrutinib (420mg/day) and rituximab (six monthly cycles). After 21 months he achieved a complete remission. At the time of admission (38 months of ibrutinib therapy) the blood count showing anemia (hemoglobin 5.7 gr/dl) associated to intensely positive Direct Antiglobulin Test (DAT) with 3^+ reactivity with anti-IgG and hemolysis signs. A total body CT-scan confirmed a CLL progression, characterized by an increasing in abdominal lymph nodes (maximum diameter of 4 cm) and a splenomegaly (bipolar diameter 19 cm). A new FISH evaluation demonstrated the appearance of the del (17p). The patient received prednisone (1mg/kg/day) without clinical benefit.

At this time, we started a second line therapy with rituximab-venetoclax, according to Murano trial schedule [2]. As seen in Figure 1, we assisted to a progressive increase in hemoglobin values.

The patient recently completed the 6 cycles of rituximab-venetoclax and achieving a partial remission with a complete hematologic recovery (hemoglobin 12.2 gr/dl, platelet 209.000/mmc, WBC 4.010/mmc), normalization of hemolysis indices (DAT weakly positive). Total body CT-scan showed a reduction of the abdominal lymph nodes (diameter of 2 cm) and of the spleen (bipolar diameter 13 cm).

CLL is frequently complicated by autoimmune phenomena (up to 25% of patients) which are sustained by dysfunctions of the immune system [3,4]. AIHA results the commonest form [5].

In the past decade small molecules had dramatically change the therapeutic scenario of CLL. Their role in the setting of autoimmune phenomena has to be still elucidated. Indeed, the literature describes cases in which target drugs could induce or solve autoimmune cytopenias [6]. The majority of data concerns the role of ibrutinib and they come from post hoc analysis of clinical trials. Most of which suggest an effective control of the autoimmune phenomenon carried out by ibrutinib in refractory to first-line therapy patients [7]. Fewer and controversial data are available for venetoclax. We found only three cases of autoimmune cytopenias associate to CLL successfully treated with venetoclax [8,9]. Although, in our case we assisted to an increased hemoglobin value already during the ramp-up phase, we cannot exclude the synergic effect of rituximab.

Here we report the case of a CLL patient harboring del (17p) in relapse of disease during ibrutinib therapy who experienced AIHA. Patient, refractory to steroids, achieved benefit from the administration of rituximab and venetoclax.

The patient reached stable and long-lasting stabilization of hemoglobin values. More information about the relationship between autoimmune cytopenias and small molecules are essential, since the use of target therapy for CLL treatment is increasingly growing.

Contributions

E.M., M.G. designed the study; E.M., E.V., C.B., D.C., F.M., M.G. analysed and interpreted data, and wrote the manuscript; all authors gave final approval for the manuscript.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Citation: Martino E, Vigna E, Mendicino F, Caracciolo D, Botta C and Gentile M. Autoimmune Hemolytic Anemia in Chronic Lymphocytic Leukemia Successfully Treated with Rituximab-Venetoclax: A Case Report. Austin Oncol Case Rep. 2021; 4(1): 1013.

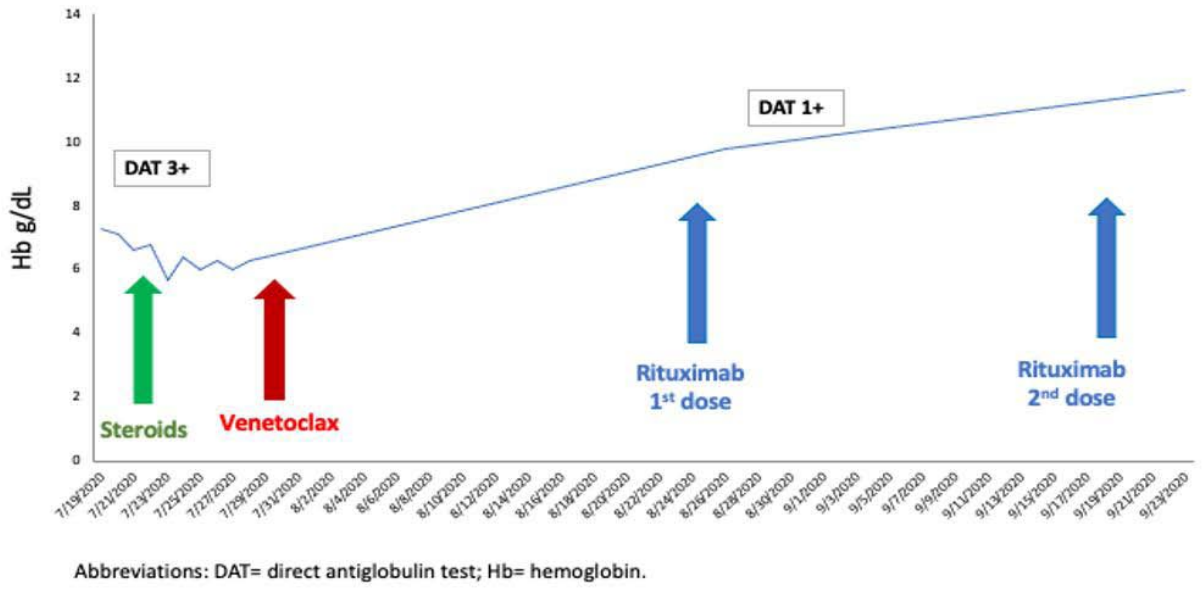

Figure 1: Hemoglobin values during therapy course.

Significance Statement

CLL is frequently complicated by autoimmune phenomena (up to 25% of patients) which are sustained by dysfunctions of the immune system. AIHA results the commonest form. Here we report the case of a CLL patient harboring del (17p) in relapse of disease during ibrutinib therapy who experienced AIHA and showed benefit from the administration of rituximab and venetoclax.

References

1. Hallek M, Cheson BD, Catovsky D, Caligaris-Cappio F, Dighiero G, Dohner H, et al. iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. Blood. 2018; 131: 2745-2760.
2. Roberts AW, Davids MS, Pagel JM, Kahl BS, Puvvada SD, Gerecitano JF, et al. Targeting BCL2 with Venetoclax in Relapsed Chronic Lymphocytic Leukemia. N Engl J Med. 2016; 374: 311-322.
3. Hamblin TJ. Autoimmune complications of chronic lymphocytic leukemia. Semin Oncol. 2006; 33: 230-239.
4. Rogers KA, Woyach JA. Secondary autoimmune cytopenias in chronic lymphocytic leukemia. Semin Oncol. 2016; 43: 300-310.
5. Fattizzo B, Barcellini W. Autoimmune Cytopenias in Chronic Lymphocytic Leukemia: Focus on Molecular Aspects. Front Oncol. 2020; 9: 1435.
6. Rogers KA, Ruppert AS, Bingman A, Andritsos LA, Awan FT, Blum KA, et al. Incidence and description of autoimmune cytopenias during treatment with ibrutinib for chronic lymphocytic leukemia. Leukemia. 2016; 30: 346-350.
7. Manda S, Dunbar N, Marx-Wood CR, Danilov AV. Ibrutinib is an effective treatment of autoimmune haemolytic anaemia in chronic lymphocytic leukaemia. Br J Haematol. 2015; 170: 734-736.
8. Lacerda MP, Guedes NR, Yamakawa PE. Treatment of refractory autoimmune hemolytic anemia with venetoclax in relapsed chronic lymphocytic leukemia with del (17p). Ann Hematol. 2017; 96: 1577-1578.
9. Gordon MJ, Maldonado E, Danilov AV. Refractory Autoimmune Cytopenias Treated With Venetoclax. Hemasphere. 2019; 3: e202.