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Early direct antiglobulin test negativity after bendamustine and rituximab treatment in CLL; two cases

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Running Head: DAT negativity after R-Bendamustine in CLL

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Dear Editor,

Autoimmune hemolytic anemia (AIHA) can emerge at any stage of chronic lymphocytic leukemia (CLL); furthermore patients can present with AIHA before diagnosis (1). Although direct antiglobulin test (DAT) positivity is one of the hallmarks of AIHA, it was also demonstrated to be associated with advanced disease (2) and poor prognosis (3), independent of hemolytic anemia in CLL patients (3). Here, we present two CLL patients with AIHA, whose DAT became negative shortly after receiving BR chemotherapy.

Case 1

A 69-year old male patient, who has been followed without treatment for CLL in Rai stage 2 for 6 months, presented with abdominal pain and jaundice. Laboratory tests were as follows: leukocyte: 55140/ μ L, lymphocyte: 51240/ μ L, hemoglobin: 5.3 gr/dL, platelet: 46000/ μ L, indirect bilirubin: 2.89 mg/dL, haptoglobin: 2 mg/dL, lactate dehydrogenase: 1585 U/L and DAT was positive for IgG (no titer provided). Imaging studies showed compressing conglomerate lymph node masses in the abdomen. The patient was started on steroid and bendamustin-rituximab (BR) treatments. Hemoglobin value rose to normal levels and DAT became negative after 3 cycles of BR. The patient received 6 cycles of BR and steroid was interrupted at the 5th month of treatment. The patient has been followed in remission for 1 year.

Case 2

A 75-year old female patient, who has been followed without treatment with the diagnosis of CLL in Rai 0 stage for 8 years, was admitted with weakness and fatigue. Laboratory tests were as follows: leukocyte: 78840/ μ L, lymphocyte: 67020/ μ L, hemoglobin: 6.3 gr/dL, platelet: 255000/ μ L, indirect bilirubin: 2.58 mg/dL, LDH: 504 U/L, haptoglobin: 1 mg/dL and corrected reticulocyte count: 5.2% and DAT was positive for IgG (4+). The patient was started on steroid treatment and subsequently BR therapy was added due to increased lymphocyte doubling time. After the first cycle, DAT titer dropped to 3+. Hemoglobin value rose to normal levels and DAT became negative after 3 cycles of BR. Steroid was ceased at 7th month of treatment; BR treatment was completed to 6 cycles. The patient has been followed in remission for 1 year.

Discussion

While standard approach in CLL patients with AIHA is steroids, systemic chemotherapy is recommended in refractory cases and in patients requiring treatment for CLL (1). Although first-line therapy in CLL patients is fludarabine-cyclophosphamide-rituximab regimen, the wide use of BR chemotherapy, especially in advanced-age patients, has brought up the application of this combination in patients with AIHA (4,5). In a recent study including 26 CLL patients who had AIHA and received BR, the response rate was 81 % for AIHA and 77 % for CLL (4). Similarly, our patients also responded well in terms of CLL and AIHA. But the most striking point was that, DAT became negative in a short period of time (after 3 cycles of BR).

In conclusion, besides its being a plausible option in advanced-age CLL patients, BR seems to be an important treatment of choice in terms of eliminating a poor prognostic factor DAT and assuring safe cessation of steroid treatment due to the achievement of DAT negativity.

Conflict of Interest

The authors declare that they have no conflict of interest

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