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LETTER TO THE EDITOR

Splenectomy followed by administration of rituximab is useful to treat a patient with hairy cell leukemia-variant

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Dear Editor,

Hairy cell leukemia-variant (HCL-v) is a rare disease-category separated from hairy cell leukeimia (HCL) by the WHO classification [1]. The prognosis, characterized by splenomegaly, is relatively poor among splenomegalic B cell disorders including HCL and splenic marginal zone lymphoma (SMZL) [2]. Thus, a novel therapeutic modality has been explored for HCL-v patients.

Here, we show that splenectomy followed by rituximab monotherapy led to molecular complete response (CR) with an undetectable level of PCR-based immunoglobulin heavy-chain gene (PCR-based IgH) rearrangement in a patient with HCL-v.

A 67-year-old female presented with an abdominal mass. Computed tomography showed significant splenomegaly (Fig. 1a). Pancytepenia (WBC count, $1.88\times10^9/\mu l$; Hb, 10.8 g/dl; and platelet count, $121\times10^9/\mu l$) and atypical lymphocytes (4.0 %) were noted in peripheral blood. Hepatitis B virus antigen and hepatitis C virus antibody were negative. Soluble interleukin-2 receptor was 835 IU/ml. Bone marrow (BM) aspirate showed normocellularity, including increased medium- to large-sized atypical lymphocytes (5.0 %) with highly irregular nuclei, prominent nucleoli, and hairy projections (Fig. 1b). Moreover, monoclonal B cells with a predominant κ light chain infiltrated the BM. She was provisionally diagnosed with splenomegalic B cell disorder. Then, her bulky spleen was resected. Involved lymphocytes were morphologically consistent with atypical cells observed in BM (Fig. 1c, d). Cells that had infiltrated the spleen were positive for CD19, CD20, CD103, κ, and FMC7 and negative for CD5, CD25, CD10, CD38, and CD23 (Fig. 2). Karyotypic aberration including chromosome 14 and PCR-based IgH rearrangement was detected. Although WBC and platelet numbers in peripheral blood entered the normal range, lymphocytosis and the Hb level were not improved. PCR-based IgH rearrangement was detected in BM cells, and HCL-v cells still existed to the same extent as pre-splenectomy in BM. Thus, we chose additional therapy of rituximab. After four cycles of monthly rituximab (375 mg/m^2), the Hb level normalized. Furthermore, PCR-based IgH rearrangement became negative and there was no phenotypic evidence of BM involvement, leading to so-called molecular CR.

Patients with HCL-v have a poorer 5-year survival (50–60 %) than those with HCL (>90 %) or SMZL (80–90 %) [2]. Currently, independent prognostic factors of HCL-v include anemia, an older age, and mutation of p53 [2]. As the presence of any one of these can stratify patients with HCL-v into a high-risk group, she was consistent with this. Thus, although she underwent splenectomy, the Hb level little improved and the proportion of HCL-v cells in BM remained unchanged. Patients with HCL-v are resistant or show a limited response

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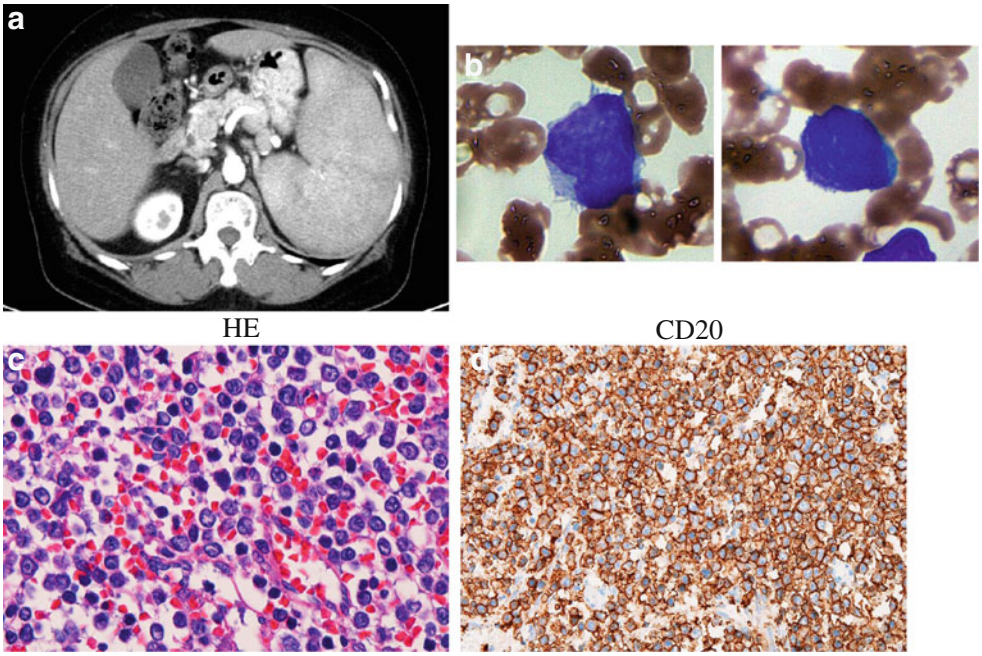

Fig. 1 **a** CT scan. **b** Morphology of cells in the BM aspirate on Wright staining. Blastic-type lymphocytes (*left panel*) and convoluted-type lymphocytes (*right panel*) were present. The latter type was predominant. **c** and **d** Morphology of cells in the spleen on hematoxylin–eosin (*left panel*) and anti-CD20 antibody (*right panel*) staining

to conventional therapy including pentostatin, cladribine, and interferon-α [3, 4]. Recent studies reported that rituximab is useful to treat patients with HCL-v [3–6]. Four-cycled rituximab therapy achieved CR, defined as the absence of hairy cells from the peripheral blood and BM along with the resolution of organomegaly and cytopenias [7]. Furthermore, PCR-based IgH rearrangement was absent, leading to so-called molecular CR, meaning deeper remission.

Here, we report that splenectomy followed by rituximab therapy induced molecular CR with an undetectable level of

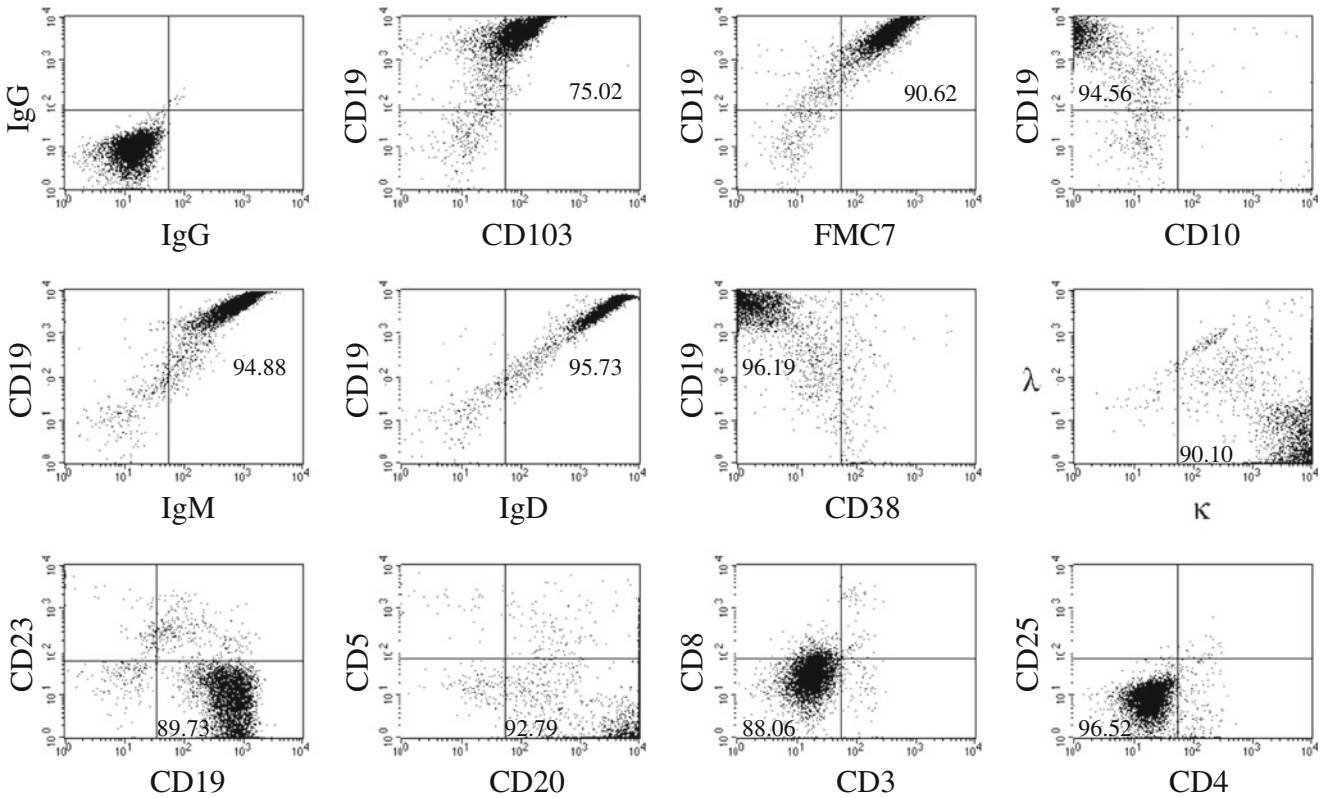

Fig. 2 Flow cytometric results of cells infiltrating the spleen. Cells infiltrating the spleen, minced with scissors, were subjected to Ficoll-density centrifugation and then flow cytometric analyses. Informed consent was obtained

PCR-based IgH rearrangement in a patient with HCL-v. These findings may shed light on a new therapeutic strategy for patients with HCL-v, ensuring a better prognosis.

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Conflicts of interest The authors declare that they have no conflict of interest.

References

1. Swerdlow SH, Campo E, Harris NL et al (2008) WHO classification of tumours of haematopoietic and lymphoid tissues, 4th edn. International Agency for Research on Cancer, Lyon
2. Hockley SL, Else M, Morilla A et al (2012) The prognostic impact of clinical and molecular features in hairy cell leukaemia variant and splenic marginal zone lymphoma. Br J Haematol 158:347–354
3. Robak T (2011) Hairy-cell leukemia variant: recent view on diagnosis, biology and treatment. Cancer Treat Rev 37:3–10
4. Jones G, Parry-Jones N, Wilkins B et al (2011) Revised guidelines for the diagnosis and management of hairy cell leukaemia and hairy cell leukaemia variant. Br J Haematol 156:186–195
5. Narat S, Gandla J, Dogan A, Mehta A (2005) Successful treatment of hairy cell leukemia variant with rituximab. Leuk Lymphoma 46:1229–1232
6. Quach H, Januszewicz H, Westerman D (2005) Complete remission of hairy cell leukemia variant (HCL-v) complicated by red cell aplasia post treatment with rituximab. Haematologica 90:e72–e73
7. Grever MR (2010) How I treat hairy cell leukemia. Blood 115:21–28