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HAEMATOLOGY IMAGES

Apoptotic abnormal lymphocytes as a possible early indicator of clinical response in patients with ATL

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A 63-year-old man was referred to our hospital with acute-type adult T-cell leukemia-lymphoma (ATL). The blood smear showed typical abnormal lymphocytes (Figure 1A). He received conventional induction chemotherapy. However, before the neutrophil count recovered, he had a significant increase in abnormal lymphocytes in the peripheral blood (PB). As there was insufficient recovery of normal hematopoiesis to use conventional salvage chemotherapy, we started the Enhancer of zeste homolog (EZH)1/2 inhibitor valemetostat. Even after the introduction of valemetostat, the absolute number of abnormal lymphocytes in the PB continued to increase. At this point, we noticed the presence of apoptotic abnormal lymphocytes with vacuoles in the blood smear (7 days after the introduction of valemetostat, Figure 1B). A few days later, on valemetostat, the absolute number of abnormal lymphocytes finally started to decrease and he achieved a partial response with continuous use of valemetostat.

This case highlights the unique morphological change in abnormal lymphocytes that preceded the objective clinical response in patients with acute-type ATL treated with valemetostat. EZH2 is the catalytic

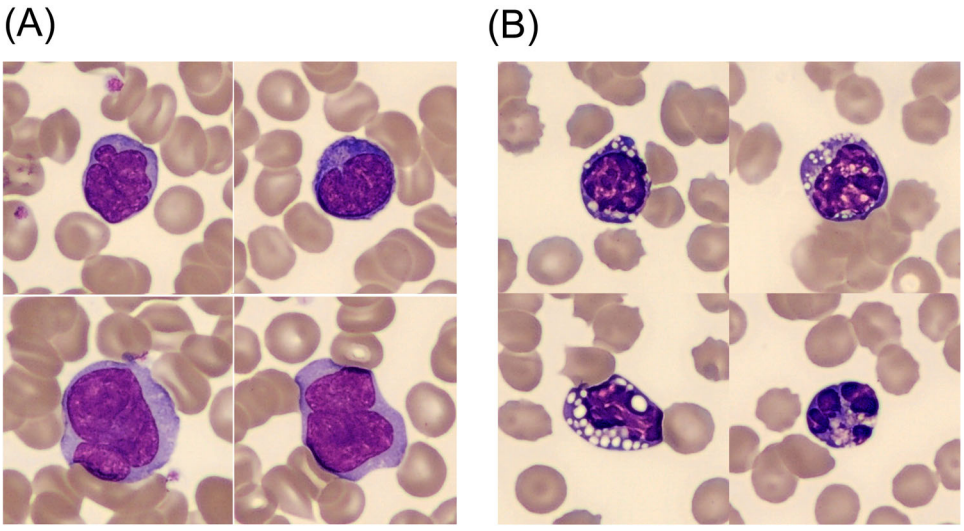

FIGURE 1 (A) Abnormal lymphocytes in the blood smear at diagnosis, and (B) apoptotic abnormal lymphocytes in the blood smear 7 days after the introduction of valemetostat.

subunit of polycomb repressive complex 2 (PRC2), which regulates downstream gene expression by trimethylation of lysine 27 in histone H3 (H3K27me3) [1]. Previous studies reported that EZH1/2 inhibitor valemetostat could induce apoptosis in HTLV-1-infected cells, ATL cells, and other cancer cell lines in vitro [2–4]. However, there are no data demonstrating that valemetostat could induce apoptosis in vivo when valemetostat is administered in humans.

Our findings suggest that the appearance of apoptotic changes in abnormal lymphocytes may be an indication of subsequent clinical response in patients with acute-type ATL. The additional work needs to be done to establish such a correlation and maybe develop this testing as a predictor for the clinical response. (see figure 1)

AUTHOR CONTRIBUTIONS

S.F. and R.S analyzed the morphology of ATL cells in peripheral blood smears and wrote the papers.

CONFLICT OF INTEREST STATEMENT

There is no conflict of interest to declare.

FUNDING INFORMATION

The authors received no specific funding for this work.

DATA AVAILABILITY STATEMENT

There are no available data to share.

ETHICS STATEMENT

Local ethics committee approval was obtained (Osaka International Cancer Institute, No.23021).

PATIENT CONSENT STATEMENT

Complete written informed consent was obtained from the patient.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

There were no data from other sources.

CLINICAL TRIAL REGISTRATION

The authors have confirmed clinical trial registration is not needed for this submission.

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