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LETTER TO THE EDITOR

Chronic lymphocytic leukemia with plasmacytic differentiation

Kirill A. Lyapichev[1] · Habibe Kurt[1] · Narittee Sukswai[1,2] · Sergej Konoplev[1] · Carlos E. Bueso-Ramos[1] · Joseph D. Khoury[1] · Yang O. Huh[1]

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Dear Editor,

A 71-year-old woman was initially diagnosed with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) at age 63. The original bone marrow biopsy demonstrated 60% involvement by lymphoma with no unusual morphological presentation. Flow cytometry study showed the immunophenotype consistent with CLL/SLL with lambda light chain-restriction. CD38 and ZAP70 were negative. Additionally, FISH and molecular studies demonstrated monosomy of chromosome 12, del13q, and TP53 gene deletion. Due to persistence of the neoplasm, despite on original treatment with idelalisib plus rituximab for 5 years, the patient was placed on ibrutinib and venetoclax therapy. The post-therapy evaluation was scheduled and performed at our institution. The bone marrow biopsy showed markedly increased number of atypical lymphocytes with interstitial and nodular distribution pattern involving approximately 50% of marrow cellularity. Interestingly, in addition to lymphoma cells, occasional large round cells with eosinophilic globular cytoplasmic inclusions were noted (Fig. 1a × 200 and insert × 1000). The inclusions were positive for periodic acid–Schiff (PAS) special stain. Bone marrow aspirate also showed scattered larger cells with similar cytoplasmic globular inclusions (Fig. 1b × 1000). To confirm the prior diagnosis of CLL and compare with original biopsy, the immunohistochemical study for LEF-1 was performed and showed positive expression in both cases: the original (Fig. 1c × 400) and the most recent biopsy (Fig. 1d × 400). Remarkably, neoplastic cells with cytoplasmic inclusions were focally positive for LEF-1 as well. This finding would support the clonality of previously diagnosed CLL and neoplastic cells with globules (plasmacytic cells), as previously was shown as a support for true transformation from CLL to classic Hodgkin lymphoma [1]. It is important to mention that there were no indications of a transformation to Hodgkin's lymphoma or Richter syndrome. Although earlier it was demonstrated that differentiation of CLL cells into immunoglobulin-secreting (plasmacytoid) cells can lead to a decrease in LEF-1 expression, in our case we still can appreciate the positive staining in the neoplastic cells [2]. Additionally, the small-sized lymphoma cells were identified and showed positivity for CD5/PAX5 dual stain (Fig. 1e × 1000), IgM, and MUM1 (Fig. 1f × 1000). The large, mononuclear cells showed similar immunophenotype which were positive for MUM1 (Fig. 1f × 1000), CD5/PAX5 (Fig. 1e × 1000), and IgM (in cytoplasmic globules). Both CLL cells and large mononuclear cells were negative for CD20, CD138, IgG, IgA, and CD163. Large mononuclear cells were consistent with clonal plasmacytoid cells with lambda light chain restriction by in situ hybridization studies. By flow cytometric analysis, the CLL cells also showed surface lambda light chain-restriction. Similar phenotype with the same immunoglobulin light chain restriction and LEF-1 staining suggested that CLL cells and plasmacytoid cells are clonally related.

Eren et al. showed that bone marrow biopsy might provide useful information for treatment plan [3]. In addition to treatment decision, our data stated that bone marrow biopsy also provides critical value to reach the correct diagnosis. To our knowledge, CLL with plasmacytic differentiation is very rare entity with unclear etiology. It may be easily misdiagnosed as other B cell lymphomas with plasmacytic differentiation such as lymphoplasmacytic lymphoma [4]. In this case, the plasmacytoid cells did not show the usual plasma cell features, like CD138 positivity. We believe that plasmacytic differentiation in CLL could be related to the prior ibrutinib and venetoclax treatment which required additional future investigation and extra attention from pathologists, during bone marrow evaluation.

✉ Yang O. Huh
yhuh@mdanderson.org

[1] Department of Hematopathology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA

[2] Department of Pathology, Chulalongkorn University, Bangkok, Thailand

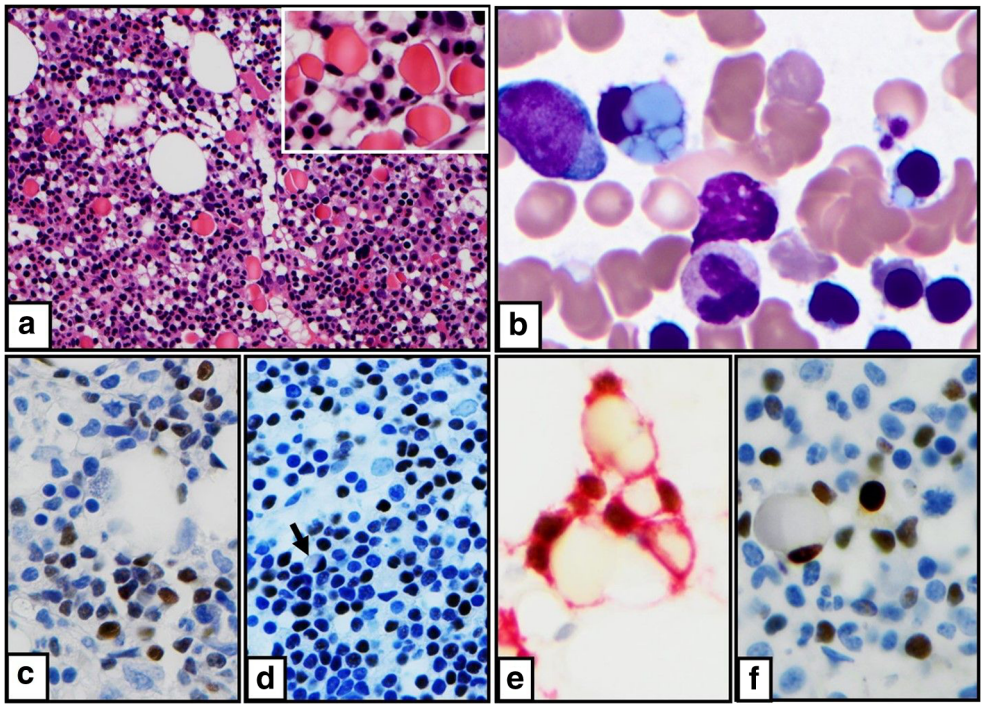

Fig. 1 Lymphoma cells are composed of occasional large round cells with eosinophilic globular cytoplasmic inclusions (**a** × 200 and insert × 1000). Bone marrow aspirate also shows scattered larger cells with similar cytoplasmic globular inclusions (**b** × 1000). LEF-1 immunohistochemical study is positive in both cases: the original biopsy (**c** × 400) and the most recent biopsy with LEF1 positive cells with cytoplasmic globules (arrow) (**d** × 400). The small- and large-sized lymphoma cells are identified and show positivity for CD5/PAX5 dual stain (**e** × 1000) and MUM1 (**f** × 1000)

Compliance with ethical standards

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

Research involving human participants and/or animals This article does not contain any studies with human participants or animals performed by any of the authors.

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