Annals of Hematology (2019) 98:1507–1508
https://doi.org/10.1007/s00277-018-3545-9

LETTER TO THE EDITOR

Uncommon lymphoplasmacytic lymphoma with IgA paraproteinemia: a challenging clinical diagnosis solved by MYD88 mutation analysis

Giovanni Martino[1] · Andrea Marra[1] · Stefano Ascani[2] · Paolo Sportoletti[1]

Received: 21 September 2018 / Accepted: 6 November 2018 / Published online: 13 November 2018

Dear Editor,

A 73-year-old man, with a 2-year history of IgA/K monoclonal gammopathy of undetermined significance (MGUS), came to our outpatient clinic because his recent blood examination showed an acute increase of the M-Protein (40,5 g/L), a decrease of hemoglobin level (12,7 g/dL), and platelet count (84.000/mmc). Urinary immunofixation revealed the presence of monoclonal K light chains (68 mg/24 h). No bone pains, fatigue, or recent weight loss were reported. Medical examination revealed no abnormalities with the absence of lymphadenopathies and/or splenomegaly. Giving the high suspicion of a disease progression in smoldering multiple myeloma (SMM), a bone marrow (BM) biopsy was executed.

BM histological examination highlighted a small fraction of mature plasma cells, accounting for 15% of BM cellularity (Fig. 1, red arrowhead, panel a), and an unexpected diffuse interstitial infiltration by a small-sized B lymphocyte population (Fig. 1, black arrowhead, panel a). Both cellular populations were monoclonal for K-light chain (Fig. 1, panel c). IgA immunostaining was performed and turned out positive on both plasma cells and in small lymphocytes (Fig. 1, panel b). Molecular analysis on BM specimen was executed and disclosed L265P point mutation of the MYD88 gene (Fig. 1, panel d), thus establishing an uncommon diagnosis of IgA-secreting lymphoplasmacytic lymphoma (LPL). The patient is in decent clinical condition and is currently undergoing a combination treatment, including bendamustine and rituximab.

IgA-secreting LPL, together with IgG or non-secreting variants, represents a very rare disease, comprising less than 5% of reported LPLs diagnosis. Plasmacytic differentiation is a common feature between indolent B cell lymphomas; hence, in a case of coexisting different lymphocyte populations, heavy-chain immunostaining can help in identifying a common monoclonal origin.

When typical laboratory findings (e.g., IgM M-protein) are lacking, LPL in the bone marrow and lymph node can be a diagnostic challenge and needs to be approached as a diagnosis of exclusion.

The identification of MYD88 L265P mutation serves as a very effective diagnostic biomarker, as it is found positive in more than 90% cases of LPL, despite the variability in histological features or secreted monoclonal proteins [1]. This case report indicates that MYD88 mutation testing is needed to render a WHO diagnosis of LPL in otherwise ambiguous cases.

Giovanni Martino and Andrea Marra are first authors who contributed equally

Stefano Ascani and Paolo Sportoletti are senior authors who contributed equally

✉ Paolo Sportoletti
paolo.sportoletti@unipg.it

[1] Hematology and Clinical Immunology, University of Perugia, Perugia, Italy

[2] Department of Experimental Medicine-Section of Pathologic Anatomy and Histology Medical School, University of Perugia, Perugia, Italy

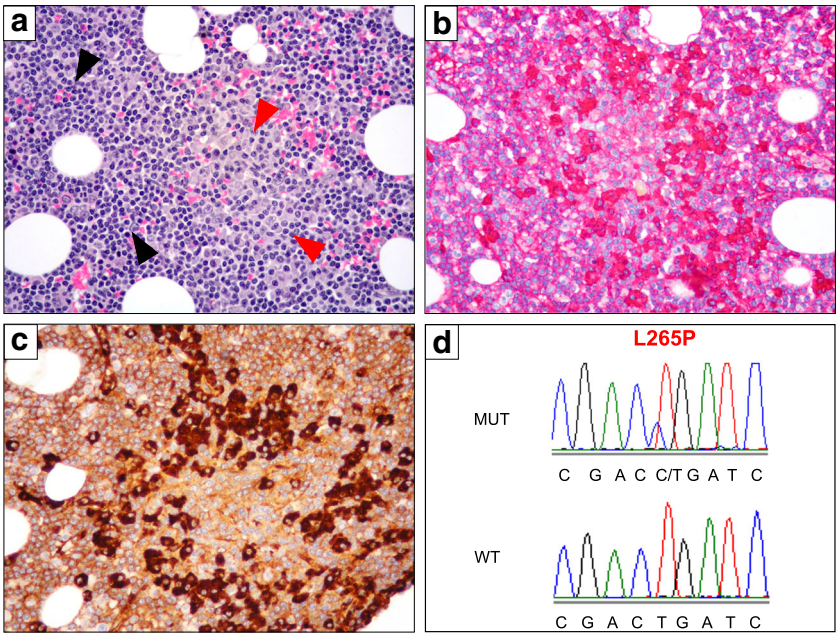

Fig. 1 The presence of a diffuse infiltration by a small-sized B lymphocyte population and scant plasma cells (**a** Hematoxylin eosin; **b** IgA immunostaining; **c** K-light chain immunostaining), mutated for MYD88 gene (**d**)

Author contributions G. M. and A. M. performed the stainings and took the related pictures of the current marrow biopsy, and drafted the text; S. A. reviewed all stainings, supervised G. M. and A. M. in taking pictures, and drafted and edited the text.; P. S. conceived the idea, performed MYD88 gene molecular analysis, and supervised G. M. and A. M. in drafting and editing the text.

Funding Paolo Sportoletti is a recipient of a My First AIRC Grant No. 17442, Associazione Italiana per la Ricerca sul Cancro (AIRC) Foundation and the Scientific Independence of young Researchers (SIR) 2014 Grant No. RBSI14GPBL, Ministero dell'Istruzione, dell'Università e della Ricerca.

Compliance with ethical standards

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

Reference

1. Swerdlow SH, Kuzu I, Dogan A, Dirnhofer S, Chan JKC, Sander B, Ott G, Xerri L, Quintanilla-Martinez L, Campo E (2016) The many faces of small B cell lymphomas with plasmacytic differentiation and the contribution of MYD88 testing. Virchows Arch 468(3):259–275. https://doi.org/10.1007/s00428-015-1858-9