Case Report

Small clonal B-cell population in the bone marrow as a possible tool in the diagnosis of occult primary parotid lymphoma

Pequeña población de células B monoclonales en medula ósea como posible herramienta diagnóstica en el linfoma oculto primario de parótida

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Introduction

The small clonal B-cells populations (SCBP) have been studied widely in peripheral blood. These have been detected with an estimated frequency between 3.5% and 14.0% in healthy subjects older than 40 years and they are known as monoclonal B-cell lymphocytosis (MBL). Its finding in peripheral blood is largely incidental, sometimes linked to some nonspecific clinical conditions and in a minority of cases it confers an increased risk for the development of B-cell neoplasms. Nevertheless, the clinical significance of detecting an SCBP in bone marrow as a primary finding is largely uncertain at this time. Its evaluation in bone marrow has been mainly used for lymphoma staging or to monitor response to treatment. But, the role as a useful diagnostic tool and in the clinical management of patients with occult lymphoma is not known. We present an unusual case of SCBP detection of 1% in bone marrow by using a high sensitivity flow cytometry approach, during the evaluation of thrombocytopenia, which led to the diagnosis of a rare parotid follicular lymphoma associated with Warthin tumor which could not be found otherwise. The overall aim was to describe the possible association of SCBP with occult lymphomas.

Case description

An 82-years old Hispanic woman with a past medical history significant for pulmonary thromboembolism on oral anticoagulation, rheumatoid arthritis on treatment with hydroxychloroquine, and hypertension developed a new onset thrombocytopenia, with a platelet count of 52 x 10^9/L during a routine assessment. She denied any symptoms and her physical exam was unremarkable. Complete blood count showed a hemoglobin of 14.6 g/dL; and a white blood cells count, 5.9 x 10^9/L with 71% segmented neutrophils, 17% lymphocytes (absolute lymphocyte count: 1.0 x 10^9/L), 11% monocytes, and 1% eosinophil. Her international normalized ratio was in a therapeutic range. Her initial thrombocytopenia evaluation based on the current guidelines did not reveal the presence of an alternative diagnosis. Infectious disease testing including human immunodeficiency virus (HIV) was negative. Hence, given her age, a bone marrow biopsy was performed.

Immunophenotypic studies of bone marrow cells, using 8-color flow cytometry approach (FACSCanto II flow cytometer (BD) and Infinicyt software program (Cytognos, V1.4)) detected 1% of Lambda-restricted B-cells CD45+, CD20+, CD10+, BCL2++, CD5- (Fig. 1A-F), FMC7+, CD38dim, CD200- and CD5 - (Fig. 1F). BM biopsy revealed a 1% paratrabecular small cleaved lymphocyte infiltrate. Immunohistochemical staining demonstrated CD20 (Fig. 1G-H), BCL2 and CD10 expression in tumor cells.

Assessment with positron emission tomography/computed tomography (PET/CT) showed two mass-like foci over right parotid (Fig. 2A-B) and left maxillary (Fig. 2C-D) Parotid excisional biopsy multiparameter flow cytometry revealed a 42% of lambda-restricted B-cells, with low forward scatter and SSC, CD20+, CD10+, BCL2+ (Fig. 2E), CD38-, CD19+, and CD45+; consistent with a diagnosis of follicular lymphoma. Examinations of the histological sections confirmed a low-grade follicular lymphoma, with a 5% proliferation rate measured by Ki-67 (Fig. 2F-I). Translocation t (14; 18) (q32; q21) was detected in parotid lymphoma (Fig. 2J) as well as bone marrow biopsy, by using fluorescence in situ hybridization (IgH/ BCL2 dual color dual fusion translocation probes Vysis-Abbott).

The coexistence of a Warthin tumor composed of cystic spaces lined by papillary bilyeral oncocytic epithelium was also observed (Fig. 2L-M). Pathologic examination of maxillary biopsy showed an oncocytic papilloma, constituted by a fibrovascular stroma lined by multiple layers of columnar cells with oncocytic features (Fig. 2N).

The final diagnosis was a parotid primary follicular lymphoma coexisting with Warthin tumor involving the bone marrow in a small extent and oncocytic papilloma located in the maxillary sinus. Given her age, performance status and intermediate risk FLIPI (2 points) she was treated with Rituximab monotherapy, having received four cycles at the last clinical follow-up with improvement on her platelet count up to 165 x 10^9/L.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.
29% of patients developed non-Hodgkin lymphoma in up to 40 months of follow up. Three patients were classified under the CD5-/CD10+ immunophenotype; from them, one developed non-Hodgkin lymphoma. Likewise, in the same study there were some limited associations with diffuse large B-cell lymphoma, hairy cell leukemia, splenic B-cell marginal zone lymphoma, and Waldenström macroglobulinemia. In our case, it led to the diagnosis of a rare parotid follicular lymphoma associated with Warthin tumor, an unusual coexistence, with 23 previous cases reported.

Herein we were able to establish an association of SCBP in bone marrow with a glandular based lymphoma. The finding of this type of population of cells prompted further workup that ultimately led to the final diagnosis. It is unclear the clinical significance of these clones and it still can be a serendipitous association; however they proved to be successful detecting varies forms of non-Hodgkin lymphoma, as pointed out in our case. Interestingly, in the previous report by Chen et al., what initially prompted further analysis in the majority of cases was cytopenias. Similarly, the thrombocytopenia was the initially detected abnormality in this case. There is insufficient evidence to use these clone cells in BM as a potential screening tool for lymphomas or to consider them a real premalignant condition. Further prospective studies may prove useful to confirm the clinical utility of this particular finding.

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