Quiz

Correct answer to the quiz. Check your diagnosis

Case report

Concurrence of chronic lymphocytic leukaemia/small lymphocytic lymphoma and acute myeloid leukaemia in a bone marrow biopsy

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The association of small lymphocytic lymphoma/chronic lymphocytic leukaemia (CLL) with different malignancies has been reported in the literature. Also the occurrence of a second haematological disease has been described, more frequently as a secondary event in patients receiving chemotherapeutic agents. We report a case of CLL with concurrent acute myeloid leukaemia in an untreated patient, with emphasis on the need of a detailed immunomorphological study to identify the coexistence of the two diseases in the same pathological tissue.

Key words: chronic lymphocytic leukaemia, acute myeloid leukaemia.

Introduction

Chronic lymphocytic leukaemia (CLL) can be associated with other oncological diseases, such as lung or skin cancers [1]. The association with other malignant hematological diseases, in particular acute myeloid leukaemia (AML), has been described as a secondary event to chemotherapy treatment or irradiation [2]. Cases of simultaneous, concurrent bone marrow involvement by CLL and AML have only rarely been reported in patients who underwent no previous treatment [3, 4]. A rare case of coexistence of the two diseases in the bone marrow of a patient never treated with cytotoxic agents or radiation therapy is described.

Case presentation

An 86-year-old man came to the attention of the attending physician for fatigue, dyspnea and weakness, with a history of heart failure under treatment, but no previous malignancies or related treatments. The clinical examination excluded the presence of splenomegaly or superficial lymphadenopathy. Laboratory tests revealed modest leukocytosis (12.7×10^9/l) with inversion of the leukocyte formula, thrombocytopenia (86×10^9/l) and a monoclonal IgG(κ) component. Based on these findings, the patient underwent a bone marrow biopsy.

The morphological examination immediately revealed markedly increased cellularity for the patient's age (> 95%), with evidence of multiple lymphoid nodular aggregates, consisting of mostly small elements.

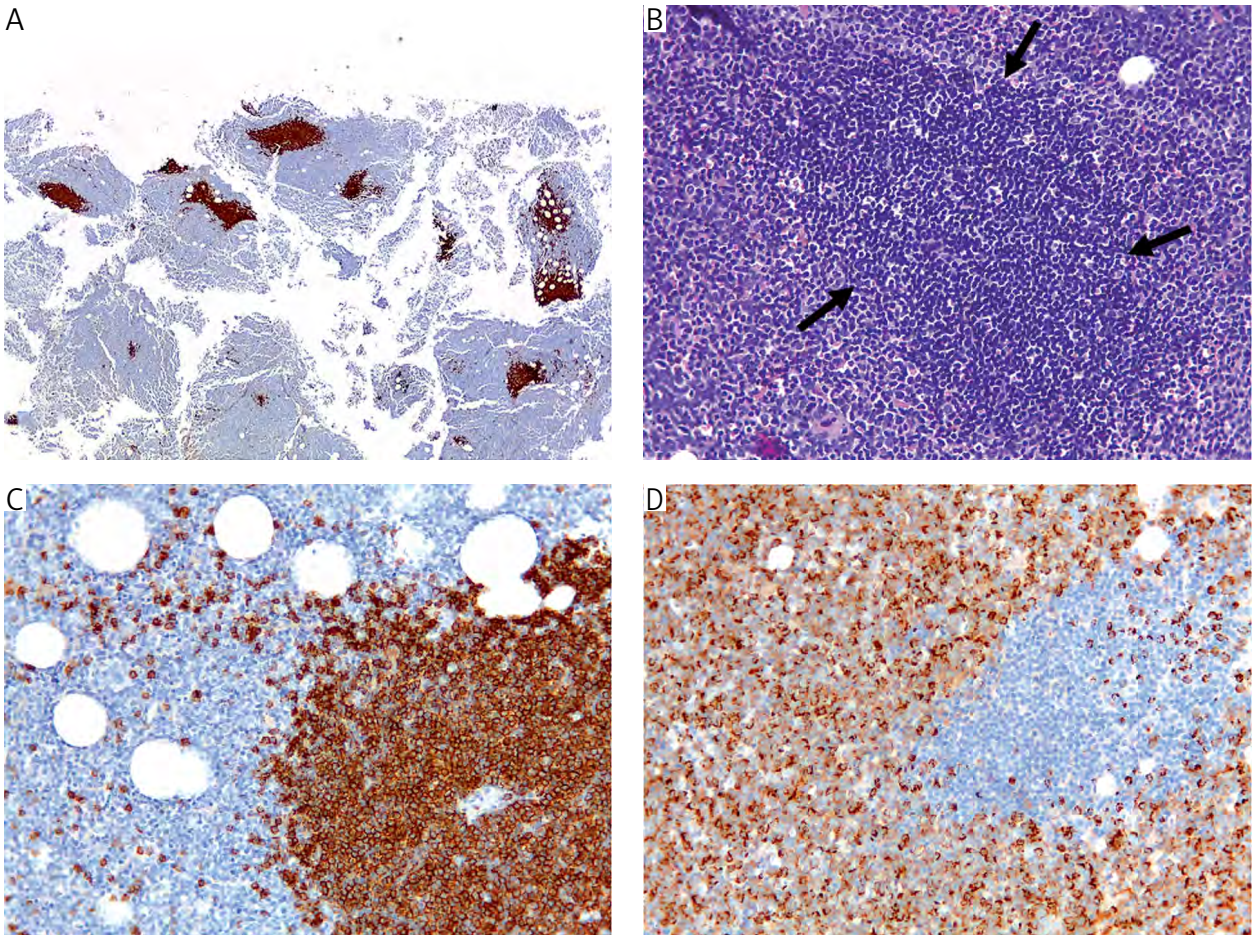

Fig. 1. A routinary first step immunohistochemical study better disclosed the presence of nodular aggregates of PAX5+ (A, magnification 2,5×) B lymphoid cells in the context of bone marrow tissue. The aggregates were composed of small and mature lymphocytes (B, hematoxylin-eosin, magnification 20×, arrows) with a prevalent B immunophenotype, as highlighted by CD20 immunostain (C, magnification 20×). Nodules were surrounded by haematopoietic tissue represented predominantly (about 70% of marrow cellularity) by immature elements (B, hematoxylin-eosin, magnification 20×), with a positive immunostain for myeloperoxidase (MPO) (D, magnification 20×)

A first step immunohistochemical study including glycophorin-C, myeloperoxidase (MPO), CD61, CD34, CD117 (c-kit), PAX5, CD20, CD3 and CD138 was performed. Lymphoid nodules had a prevalent B-cell immunophenotype (Fig. 1A, B), suspected of lymphoproliferative disease (approximately 10% of total cellularity). About 70% of the cellularity was composed of immature elements positive for CD34 and MPO (Fig. 1D), with partial coexpression of CD117 (c-kit). CD138 immunostaining revealed the presence of several plasma cells (about 10% of the total cellularity), isolated or gathered in small aggregates. For a better evaluation of the three cellular components a second step immunohistochemical study was performed.

The lymphoid B cell component showed coexpression of PAX5 (Fig. 1A), CD20 (Fig. 1C), CD79a, CD5 (weak), CD23, bcl2 and CD43 (focal), with negativity of cyclin D1, SOX11, CD10, bcl6 and CD38 and a Ki-67 expression about 5% (where assessable).

The immature blast component showed positivity for CD15, CD43 (focal) and CD68 (KP-1) (focal); Tdt, CD7, CD10 and CD79a were negative.

The plasma cell component (CD138+, CD79a+, CD38+) showed a restriction for the immunoglobulin κ light chain.

On the basis of these findings a diagnosis of AML (to be better evaluated with flow cytofluorimetric and biomolecular/cytogenetic examinations on peripheral blood and bone marrow aspirate) with associated low grade B-cell non-Hodgkin lymphoma with plasma cell differentiation, with immunomorphological features consistent with small lymphocytic lymphoma/CLL (according to the 2017 WHO classification of tumours of haematopoietic and lymphoid tissues [5]) was made.

Follow-up clinical data are not known because unfortunately the patient died few days later of heart failure.

Discussion

The association of CLL with other malignant neoplasms has already been described [1]. Most often these are solid tumors, in particular lung and skin cancers [1]. The association of CCL with AML has already been reported, with AML appearing more often as an event secondary to the treatment of CLL with chemotherapy agents [2]. The simultaneous presence of both neoplasms as distinct unrelated neoplastic entities has rarely been described [3, 4].

Our case shows an uncommon concurrence of CLL and AML in a patient who underwent bone marrow biopsy for thrombocytopenia with an immunoglobulin monoclonal component. The death of the elderly patient due to heart failure did not allow the bone marrow to be studied from a cytofluorimetric, biomolecular and cytogenetic point of view. However, the case remains very interesting and implies some considerations.

The simultaneous presence of the two neoplasms in a patient not previously treated with chemotherapy agents or radiation would seem to suggest a distinct oncogenetic event for the two entities. Some authors have proposed an important role of immunosuppression [6]. Others have speculated that the simultaneous development of CLL and AML may be due to a common stem cell defect, leukemogenic factors or genetic susceptibility [7]. The presence of different cytogenetic and biomolecular alterations has been demonstrated in some cases [8], showing that they are separate neoplastic events. Further studies will be necessary to understand the oncological pathogenesis of these rare cases.

Another important consideration is from a purely histomorphological point of view. In histopathology, it is crucial to examine the slides keeping in mind the clinical question, without being completely conditioned. This would risk piloting our diagnosis and overlooking other morphological alterations not clinically suggested. This is even more important in haematopathology, especially when examining bone marrow. It is a topographically very peculiar tissue, with an admixture of several cellular components that could obscure the presence of concomitant alterations different from those clinically suspected. For this reason, it is very important to examine the bone marrow with a first step immunohistochemical study that takes into account the morphological aspect of the tissue and the clinical question, but adding to the panel further immunostains that could highlight aspects not appreciable from morphology alone.

In our clinical case of a patient with an immunoglobulin monoclonal component and thrombocytopenia, the morphological evidence of lymphoid nodules immediately attracted our attention, in the hypothesis of a B-cell lymphoproliferative disease with plasma cell differentiation. The typing of the lymphoid infiltrate alone would not have allowed the identification of the leukaemic CD34+ component. In this specific case, the hypercellularity and the immature aspect of the hematopoietic component suggested a concomitant haematopoietic disease, but very often, in more nuanced pictures, there is no morphological immediacy and a risk of overlooking the presence of further histological alterations. It is advisable to examine the bone marrow to carry out a first immunohistochemical panel giving clearer information on all cellular components of the tissue. Simple CD34 immunostaining in a bone marrow biopsy examined in the suspicion of a lymphoproliferative disease or a plasma cell neoplasm can highlight an associated myelodysplastic syndrome or, even, an AML, as in our case. Similarly, in cases examined in the suspicion of myelodysplasia or myeloproliferative disease, the addition of lymphoid and plasma cell markers (CD20, CD3 and CD138 sufficient as a first approach) can better highlight the presence of atypical cell infiltrates concurrent with the haematopoietic disease.

The author declares no conflict of interest.

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