Mantle cell lymphoma with diminished expression of B-cell antigens: an unusual presentation

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DESCRIPTION

A 64-year-old diabetic male presented with generalised weakness for 2 months. On evaluation, he had pallor, generalised lymphadenopathy and mild splenomegaly. Peripheral blood (PB) showed anaemia (haemoglobin 84 g/L), leucocytosis (total leucocyte count 17.1×10^9/L), lymphocytosis (absolute lymphocyte count 5.8×10^9/L) and thrombocytopenia (platelet count 111×10^9/L). Bone marrow (BM) examination revealed predominantly atypical small-sized lymphoid cells (92%) (figure 1A–B) that on multicolour flow cytometry were CD19^{bright}, CD5^{bright}, CD20^{dim}, CD79b^{dim}, CD22^{dim}, IgM^{moderate}, IgD^{moderate}, CD43^{dim}, FMC7^{negative}, CD200^{negative}, CD23^{negative} and surface light chain^{negative} (figure 1C). Diagnosis of chronic lymphocytic leukaemia (CLL) or atypical CLL was initially considered. However, due to subtle atypical features (CD23^{negative}, CD200^{negative}, CD43^{dim}), fluorescence in-situ hybridisation (FISH) testing was advised. FISH revealed *IgH* and *cyclin D1/CCND1* translocation in 90% cells (figure 1D–E). A lymph node biopsy confirmed the diagnosis of SOX-11-negative mantle cell lymphoma (MCL) (figure 2). Renal biopsy for the evaluation for renal dysfunction (serum creatinine 283 µmol/L) revealed diabetic nephropathy as well as infiltration by MCL. He was counselled for chemoimmunotherapy (bendamustine and rituximab); however, he declined treatment and stopped hospital visits due to financial reasons. A telephonic follow-up 11 months after the initial diagnosis revealed that his condition is stable and although he continues to experience fatigue, but is still not on any specific therapy.

Flow cytometry represents an invaluable tool for the diagnosis of mature B-cell neoplasms (MBN) infiltrating PB or BM. In the presence of typical CLL immunophenotype (bright CD5, dim CD20 and surface immunoglobulins), haematopathologists may render a diagnosis of CLL without any further work-up. Unlike CLL, virtually all other CD5+ve MBNs including MCL show bright

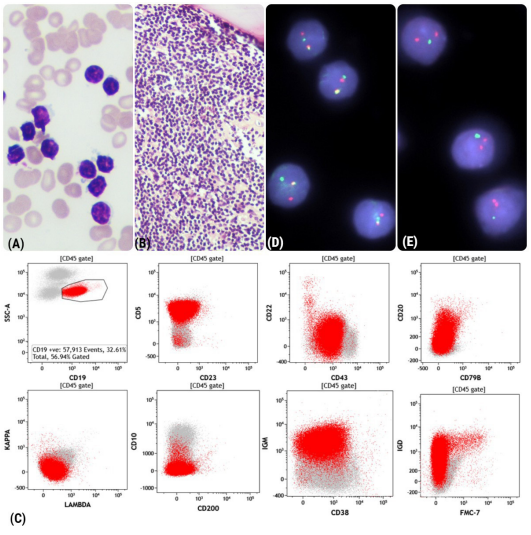

Figure 1 (A, B) Bone marrow aspirate and biopsy show atypical lymphoid cells with variably clumped nuclear chromatin, predominantly regular nuclear contours and scant cytoplasm (May-Grünwald Giemsa stain; ×200 and H&E stain; ×400, respectively). (C) Flow cytometry shows CD5^{bright}, CD20^{dim}, CD79b^{dim}, CD22^{dim}, FMC7^{neg}, surface light chain^{neg}, IgM^{moderate}, IgD^{moderate}, CD200^{neg} immunophenotype; fluorescence in-situ hybridisation (FISH) testing shows positivity for (D) *cyclin D1/CCND1* translocation and (E) *IgH* translocation of one allele with deletion of variable gene segment on the telomeric side of other *IgH* allele (Vysis dual-colour break-apart probes; Abbott, USA). This pattern does not entirely exclude a biallelic *IgH* translocation, even though the second partner is unknown in our case. The cells were also negative for *BCL2* and *BCL6* translocations as well as *TP53* and *ATM* gene deletions (not shown).

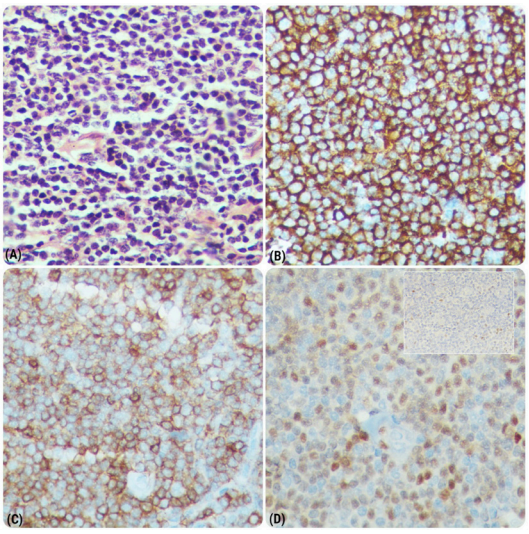

Figure 2 Lymph node biopsy showing (A) diffuse effacement of nodal architecture by sheets of small-sized lymphoid cells (×400). (B–D) Cells express CD20, CD5 and cyclin D1. They were also positive for BCL2 and negative for CD23 (not shown) and SOX-11 (<10% positivity; inset).

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expression of pan–B-cell antigens (CD19, CD20 and CD22).[1] However, variations from typical immunophenotype have been observed, some of which could be misleading and cause diagnostic difficulties. Atypical immunophenotypic features in CLL include CD23 negativity, dim/negative CD5, expression of FMC7 and strong expression of surface immunoglobulins.[2] MCL has been reported to show variations like CD5 and FMC7 negativity, or CD10 and CD23 positivity.[3] Our patient not only was FMC7 negative but also had a dimmer expression of most of the B cell-associated antigens (CD20, CD79b, CD22, surface light chains). This finding was unusual and has not been reported earlier. Absence of SOX-11 expression probably explains the relatively indolent nature of the disease in our patient.[4]

The distinction between the clinically indolent CLL from MCL is important due to the aggressive course of MCL as well as differences in clinical management. Our case highlights the relevance of evaluation for cyclin D1 immunohistochemistry or *CCND1* translocation by FISH, as well as the importance of giving attention to subtle immunophenotypic variations (CD23/CD200 negativity, dim CD43 and moderate IgM/IgD positivity) in patients with a CLL-like immunophenotype, even if morphology is unremarkable. Awareness of these immunophenotypic aberrancies can prevent misdiagnosis and subsequent inappropriate management.

Learning points

- Mantle cell lymphoma (MCL) can mimic chronic lymphocytic leukaemia (CLL) morphologically and immunophenotypically.
- Downregulation of B-cell-associated antigens, though typical of CLL, may also rarely occur in MCL.
- Evaluation for *cyclin D1*/*CCND1* translocation by fluorescence in-situ hybridisation, as well as awareness of subtle immunophenotype variations, can help to distinguish CLL versus MCL, with their clinically contrasting disease courses, survival and management strategies.

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REFERENCES

1 Jain P, Wang M. Mantle cell lymphoma: 2019 update on the diagnosis, pathogenesis, prognostication, and management. *Am J Hematol* 2019;94:710–25.
2 Campo E, Ghia P, Montserrat E, *et al*. Chronic lymphocytic leukemia/small lymphocytic lymphoma. In: Swerdlow S, Campo E, Lee Harris N, *et al*, eds. *WHO classification of tumor of haematopoietic and lymphoid tissues, Revised*. 4th edn. Lyon, France: IARC, 2017.
3 Gao J, Peterson L, Nelson B, *et al*. Immunophenotypic variations in mantle cell lymphoma. *Am J Clin Pathol* 2009;132:699–706.
4 Narurkar R, Alkayem M, Liu D. Sox11 is a biomarker for cyclin D1-negative mantle cell lymphoma. *Biomark Res* 2016;4:6.