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, 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 chemioimmunotherapy (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
expression of pan–B-cell antigens (CD19, CD20 and CD22). 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. MCL has been reported to show variations like CD5 and FMC7 negativity, or CD10 and CD23 positivity. 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.

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.

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