CORRESPONDENCE

A CD5+ Anaplastic DLBCL with Reed–Sternberg-Like Cells: A Diagnostic Pitfall

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Received: 12 September 2017 / Accepted: 2 January 2018 / Published online: 10 January 2018
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Dear Sir,

A 26-year-old male presented to hematology services with generalised lymphadenopathy and hepatosplenomegaly. Hemoglobin was 89 gm/L, platelets $195 \times 10^9/L$ and total leukocyte count $10.1 \times 10^9/L$ with 41% circulating abnormal lymphoid cells (Fig. 1a, b) that were negative on cytochemical myeloperoxidase staining. Axillary lymph node biopsy showed effaced nodal architecture with sheets of large atypical lymphoid cells, 2–4 times the size of mature lymphocytes with 1–3 prominent nucleoli (Fig. 1c). Immunohistochemically, the cells showed strong CD20 positivity (Fig. 1d) and were negative for CD5 (clone 4c7,

internal control positive) (Fig. 1e), CD10, CD30, cyclin D1 and SOX11. MUM1/IRF4 and bcl6 were positive in ~ 60 and ~ 15% cells respectively [all primary antibodies from Dako, Glostrup, Denmark]. Based on these, diffuse large B-cell lymphoma (DLBCL), activated B cell type (CD10^{neg}/BCL6⁺/MUM1⁺) was diagnosed.

The staging bone marrow showed 35% large lymphoid cells with indented-to-multilobate nuclei, coarse chromatin, variably prominent nucleoli and moderate amount of pale basophilic cytoplasm. Flow cytometrically, CD19^{bright} cells expressed CD20^{bright}, CD79b^{bright}, heterogeneous CD5^{dim} to ^{bright} (clone UCHT2), CD45^{bright}, CD200^{dim} with bright surface λ -immunoglobulin light chain restriction. CD23, cyclin D1, CD3, CD4, CD7, CD34 and CD8 were negative (Fig. 1f–i) [All fluorescent labelled antibodies from Becton–Dickinson Biosciences, San Jose, USA]. The hypercellular trephine biopsy (Fig. 1j) showed paratrabecular nodules of intermediate-sized lymphoid cells, a few with eosinophilic intranuclear inclusions (Fig. 1k). Several scattered larger Reed–Sternberg (RS)-like cells with vesicular lobulated nuclei and prominent nucleoli were seen (Fig. 1l–o). Immunohistochemically, the lymphoid aggregates showed CD20^{positive} B-cells. The large RS-like cells were uniformly CD45^{positive} (Fig. 1p) and mostly CD20^{positive} (~ 70%) (Fig. 1q) but negative for CD30 (Fig. 1r) and CD15. CD5 immunostaining using a primary antibody with the same clone and manufacturer as on the lymph node (4c7, DakoTM) was positive in the smaller-sized bone marrow cells.

CD5+ DLBCL constitutes ~ 5–10% of all cases of DLBCL [1], and up to 12% cases can show a mixed cellular morphology with irregularly-shaped nuclei [2]. Most are of activated B-cell subtype (ABC), more common in elderly females with extra-nodal involvement, advanced stage at presentation and poor responses to rituximab-

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Fig. 1 Circulating pleomorphic tumour cells with deep nuclear clefts (**a, b**) (May-Grünwald Giemsa). Lymph node showed sheets of abnormal lymphocytes with interspersed large cells (**c**) (H&E). On immunohistochemistry, the cells expressed CD20 (**d**), and were negative for CD5 (**e**). Flow cytometrically, the CD19+ cells gated (**f**) expressed bright CD20 and variable CD38 (**g**), moderate to bright

CD5 without CD23 (**h**) with surface lambda restriction (**i**). The hypercellular bone marrow biopsy (**j**) showed large nodular collections of monomorphic lymphoid cells, some showing nuclear inclusions (**k**). Scattered amidst these were several RS-like cells (H&E) (**l–o**). Immunohistochemically, the RS-like cells were variably positive for CD45 (**p**) and CD20 (**q**) but negative for CD30 (**r**)

containing therapy [1, 2]. CD5+ DLBCL should be differentiated from Richter transformation (RT) in chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) as well as from mantle cell lymphoma (MCL). *BCL6* rearrangements are usually seen in de novo CD5+ DLBCL but not RT. MCL is distinguished from anaplastic DLBCL by *CCND1* overexpression and the characteristic t(11;14) which are absent in CD5+ DLBCL [1, 2].

Discrepancies in the immunophenotypic profiles of non-Hodgkin lymphomas (NHL) across samples obtained from different anatomic sites have been observed in 15–22% cases in different series [3, 4]. CD5 was the most frequently discrepant antigen (04/64 cases, 6.3%) in the larger

series, followed by FMC7 and CD20 [3]. Once technical factors (for e.g. different antibody clones, fixation times/reagents etc.) and interpretational errors are excluded [4], such discordance could be due to mechanisms of disease dissemination (selective advantages to sub-clones), microenvironmental influences or, in treated cases, differential responses to therapy [3].

RS-like cells are described in high-grade as well as some low-grade, B- and T-cell NHL [5] and can pose a diagnostic challenge in small biopsies. The cellular milieu and immunophenotypic markers are clues to resolving such cases, although composite lymphomas and non-classical Hodgkin lymphomas also occur [5]. In our case, since the

intra-nuclear inclusions in the lymphoid cells were seen only in the trephine biopsy, they might represent cytoplasmic invaginations into the cells' nuclei, akin to Dutcher bodies in myeloma, that occurred due to sectioning of cells at different planes in histological preparations.

In conclusion, this morphologically-concordant, immunologically-discordant case illustrates the importance of careful consideration of all diagnostic data by hematopathologists who report staging bone marrow biopsies. Close consultation with the histopathologist reporting the lymph node biopsy is helpful in such cases.

Compliance with Ethical Standards

Conflict of interest The authors have no conflict of interest regarding this article to disclose.

Ethical Approval All procedures performed in this report involving a human participant were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This is a purely observational report and no research procedure was done.

Informed Consent Informed consent was obtained from this patient.

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