lymphomagenesis,^{9,10} especially for nasal-type NK/T-cell lymphoma and PTLDs. Based on the distinct patterns of EBV latency programs: type I (EBER+/LMP1-/EBNA2-), type II (EBER+/LMP1+/EBNA2-) and type III (EBER+/LMP1+/EBNA2+),¹¹ the tumour cells of NK/T-cell lymphoma and PTLT are consistent with type I and type III latency patterns, respectively.⁶ In this regard, in addition to its tumourigenetic role, the expression of EBV latency program may also play a role in the differential diagnosis of NK/T-cell lymphoma (LMP1-/EBNA2-) versus PTLT (LMP1+/EBNA2+) in our case.

Conflicts of interest and sources of funding: The authors state that there are no conflicts of interest to disclose.

**Shu-Hsien Wang¹, L. Jeffrey Medeiros²,
Tsai-Yun Chen³, Kung-Chao Chang^{1,4,5}**

¹Department of Pathology, National Cheng Kung University Hospital, National Cheng Kung University, Tainan, Taiwan; ²Department of Hematopathology, The University of Texas, Texas, USA; ³Division of Hematology and Oncology, Department of Internal Medicine, National Cheng Kung University Hospital, National Cheng Kung University, Tainan, Taiwan; ⁴Department of Pathology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan; ⁵Department of Pathology, Kaohsiung Medical University, Kaohsiung, Taiwan

Contact Dr Kung-Chao Chang.

E-mail: changkc@mail.ncku.edu.tw

1. Swerdlow SH, Campo E, Harris NL, *et al.* WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. (Rev 4th ed.) Lyon: IARC, 2017.
2. Yamaguchi M, Oguchi M, Suzuki R. Extranodal NK/T-cell lymphoma: updates in biology and management strategies. *Best Pract Res Clin Haematol* 2018; 31: 315–21.
3. Tse E, Kwong YL. NK/T-cell lymphomas. *Best Pract Res Clin Haematol* 2019; 32: 253–61.
4. Xiong J, Cui BW, Wang N, *et al.* Genomic and transcriptomic characterization of natural killer T cell lymphoma. *Cancer Cell* 2020; 37: 403–19.
5. Huang WT, Chang KC, Huang GC, *et al.* Bone marrow that is positive for Epstein-Barr virus encoded RNA-1 by in situ hybridization is related with a poor prognosis in patients with extranodal natural killer/T-cell lymphoma, nasal type. *Haematologica* 2005; 90: 1063–9.
6. Roschewski M, Wilson WH. EBV-associated lymphomas in adults. *Best Pract Res Clin Haematol* 2012; 25: 75–89.
7. Al Hamed R, Bazarbachi AH, Mohty M. Epstein-Barr virus-related post-transplant lymphoproliferative disease (EBV-PTLD) in the setting of allogeneic stem cell transplantation: a comprehensive review from pathogenesis to forthcoming treatment modalities. *Bone Marrow Transplant* 2020; 55: 25–39.
8. Lindsay J, Yong MK, Greenwood M, *et al.* Epstein-Barr virus related post-transplant lymphoproliferative disorder prevention strategies in allogeneic hematopoietic stem cell transplantation. *Rev Med Virol* 2020; 30: e2108.
9. Jones JF, Shurin S, Abramowsky C, *et al.* T-cell lymphomas containing Epstein-Barr viral DNA in patients with chronic Epstein-Barr virus infections. *N Engl J Med* 1988; 318: 733–41.
10. Su JJ, Hsieh HC, Lin KH, *et al.* Aggressive peripheral T-cell lymphomas containing Epstein-Barr viral DNA: a clinicopathologic and molecular analysis. *Blood* 1991; 77: 799–808.
11. Chen YP, Jones D, Chen TY, *et al.* Epstein-Barr virus present in T cells or B cells shows differential effects on hemophagocytic symptoms associated with outcome in T-cell lymphomas. *Leuk Lymphoma* 2014; 55: 2038–47.

Unique nested formation in a case of large cell transformation of follicular lymphoma mimicking adenocarcinoma

To the Editor,

Follicular lymphoma (FL) is the archetypal indolent lymphoma and the second most common type of non-Hodgkin lymphoma. Histological transformation to an aggressive lymphoma occurs at a rate of 1–2% per year, is associated with accelerated clinical progression and alters the therapeutic paradigm.^{1,2} Transformation causes a loss of follicular architecture with the accumulation of large cells, with features most frequently resembling diffuse large B-cell lymphoma (DLBCL). We report a case of large cell transformation of FL in which nests or foci of cohesive clustering large cells in the bone marrow gave rise to a distinct pseudo-acinar architecture; this initially caused diagnostic confusion as it raised the possibility of metastatic carcinoma infiltrating the marrow.

A 78-year-old man with a history of AL (light chain) amyloidosis and FL Stage II, the latter condition being treated 4 years earlier with radiotherapy only, presented with fatigue, symptomatic splenomegaly and pancytopenia. Positron emission tomography scan confirmed splenomegaly and showed nodal involvement on both sides of the diaphragm with intense fluorodeoxyglucose avidity in the spine and proximal appendicular skeleton suggestive of bone marrow involvement. Core biopsy of a supraclavicular lymph node showed morphological features of low-grade FL only, the limited diagnostic material being insufficient for immunohistochemical studies.

A bone marrow biopsy was performed. The aspirate was aparticle with no specific diagnostic features. The trephine biopsy was markedly hypercellular, with normal haematopoietic tissue being effaced by sheets of small lymphocytes throughout the marrow. Additionally, foci of cohesive clusters of larger cells resembling acini were observed (Fig. 1) with an appearance reminiscent of carcinoma. By immunohistochemistry, the larger cells were negative for AE1/3 and CD30, and had a germinal centre B-cell phenotype, with CD45+, CD20+, CD10+, bcl2+ and bcl6+ (Fig. 2A–E). Immunostaining with CD31 and CD34 for endothelial cells and D2-40 for lymphatics showed that these clusters of cells were not confined within blood or lymphatic vessels. Overall the Ki-67

Fig. 1 Nests or foci of cohesive clustering large cells resembling acini or metastatic carcinoma in the bone marrow (bone marrow trephine, H&E).

Fig. 2 Pseudoacini positive on immunostaining for (A) CD45, (B) CD20, (C) CD10, (D) bcl2 and (E) bcl6. (F) Ki-67 staining is higher in the clusters of large cells than in the background smaller lymphocytes (bone marrow trephine).

index was low, but staining generally corresponded to the clusters of large cells (Fig. 2F). The background small lymphocytes had an immunophenotype consistent with FL, these cells being CD20+, CD5–, CD10+ and bcl2+. An excisional lymph node biopsy was subsequently performed, confirming a diagnosis of DLBCL, germinal centre type, on a background of FL. The patient proceeded to receive chemo-immunotherapy and obtained a complete metabolic remission.

Lymphomas can display unusual cohesive growth patterns. In the case of anaplastic large cell lymphoma,³ the striking intrasinusoidal infiltration and perivascular homing of the lymphoma cells may be explained by the expression of clusterin.⁴ Likewise, the formation of rosettes in a manner akin to neuroepithelial and neuroendocrine tumours^{5–7} has been described in both B- and T-cell lymphomas at nodal and extra-nodal sites.^{8–11} The acellular fibrillary material that produces such rosettes' central lumen is believed to result from the long interdigitating cytoplasmic processes of lymphoma cells with microvilli or from adjacent histiocytes.⁷

Herein, we report a unique manifestation of tumour architecture leading to the formation of discrete large cell aggregates on a background of FL, separate from vascular sinuses and without rosette formation. This peculiar motif is rare; while it has been described in a case of DLBCL affecting a lymph node,¹² it has not been reported in the bone marrow. In our case, this feature was observed only in the bone marrow and not in the lymph node, even though large cell transformation was present at both sites. The histogenesis of our case is uncertain. Conceivably, the architecture depicted here may be secondary to surface glycoproteins mediating cell-to-cell adhesion amongst the larger cells. Alternatively, the nests of larger cells may represent the initial seeds of large cell transformation which, given time, may have proliferated to infiltrate the marrow diffusely.

Lymphoma histology can be protean, and our case illustrates a unique histological manifestation of DLBCL.

Without the benefit of the patient's past clinical history and immunohistochemistry, this case may have been misdiagnosed as metastatic carcinoma. Our case is intended to serve as a cautious lesson on the mutable nature of lymphoma histology and the potential for diagnostic confusion.

Conflicts of interest and sources of funding: The authors state that there are no conflicts of interest or sources of funding to disclose.

Matthew J. Rees¹, Chris Hogan¹, Tineke Fancourt², Wai Khoon Ho¹

¹Department of Laboratory Haematology, Austin Health, Melbourne, Vic, Australia; ²Department of Anatomical Pathology, Austin Health, Melbourne, Vic, Australia

Contact Dr Matthew James Rees.

E-mail: Matthew.Rees@austin.org.au

1. Wagner-Johnston ND, Link BK, Byrtek M, *et al.* Outcomes of transformed follicular lymphoma in the modern era: a report from the National LymphoCare Study (NLCS). *Blood* 2015; 126: 851–7.
2. Smith S. Transformed lymphoma: what should I do now? *Hematology* 2020; 2020: 306–11.
3. Montes-Mojarro IA, Steinhilber J, Bonzheim I, *et al.* The pathological spectrum of systemic anaplastic large cell lymphoma (ALCL). *Cancers (Basel)* 2018; 10: 107.
4. Jaffe ES. Anaplastic large cell lymphoma: the shifting sands of diagnostic hematopathology. *Mod Pathol* 2001; 14: 219–28.
5. Frizzera G, Gajl-Peczalska K, Sibley RK, *et al.* Rosette formation in malignant lymphoma. *Am J Pathol* 1985; 119: 351–6.
6. Alakeel F, DePalma L. Follicular lymphoma with rosette formation with an exclusive diffuse pattern. *Virchows Arch* 2017; 470: 231–3.
7. Koo CH, Shin SS, Bracho F, *et al.* Rosette-forming non-Hodgkin's lymphomas. *Histopathology* 1996; 29: 557–63.
8. Rekhi B, Gulia A. Rosette forming" primary high-grade B-cell lymphoma, presenting as a scapular mass, masquerading Ewing sarcoma: a rare case with diagnostic implications. *Indian J Pathol Microbiol* 2021; 64: 617–9.
9. Sioutos N, Kadin ME. Perivascular ki-1 + lesions. *Int J Hematol* 1992; 55: 275–9.
10. Goteri G, Costagliola A, Tasseti A, *et al.* Diffuse large B-cell lymphoma with Homer-Wright rosettes, sinusoidal growth pattern, and CD30 expression: a possible overlap between microvillous lymphomas and sinusoidal CD30-positive large B-cell lymphomas. *Pathol Res Pract* 2009; 205: 279–82.
11. Lai R, Medeiros LJ, Dabbagh L, *et al.* Sinusoidal CD30-positive large B-cell lymphoma: a morphologic mimic of anaplastic large cell lymphoma. *Mod Pathol* 2000; 13: 223–8.
12. Mok Y, Goh GH, Wang S. Unusual cohesive growth pattern of diffuse large B-cell lymphoma mimicking metastatic carcinoma. *Br J Haematol* 2017; 176: 850.

DOI: <https://doi.org/10.1016/j.pathol.2021.10.013>

Validation of *EGFR* mutation testing on cytological smears of lung cancer using the Idylla platform

To the Editor,

Patients with stage IV lung cancer have a poor prognosis with only 19% of patients surviving 12 months in Australia.¹ However, for patients with tumours containing specific molecular alterations (such as activating mutations in *EGFR*,