immunophenotypically indistinguishable. To our knowledge, this is the first example of HGBCL-NOS with concurrent expression of CD5 and cyclin D1, strongly mimicking BVMCL. In this setting, only the absence of the *CCND1* gene rearrangement evaluated with both dual fusion and break-apart FISH probes excluded BVMCL and allowed us to classify the neoplasm as HGBCL-NOS.

Unlike DH/TH lymphomas, HGBL-NOS do not carry the gene rearrangements for *c-MYC* and *BCL2* and/or *BCL6*. Moreover, the genetic landscape of HGBL-NOS is not well understood, and few cases carry translocation involving chromosome 8q24 (*MYC*) alone, also called SHL.⁸ Our case harboured a single *c-MYC* rearrangement despite morphological and phenotypic criteria for BL being excluded. This last cytogenetic finding in addition to blastoid morphology, permitted us to place this aggressive lymphoma into the category of HGBCL-NOS despite its own unusual phenotype.

The group of lymphoproliferative disorders such as HGBCL-NOS are recognised as aggressive neoplasms with poor prognosis and short overall survival.¹ Usually, single-hit HGBCL-NOS has a similarly poor prognosis as that of DH/TH lymphomas.⁹ In fact, *MYC* rearrangements predict poor survival in HGBCLs, and as in BL, *MYC* rearrangement could be the driver in HGBCL-NOS. However, very few studies have focused on the prognostic relevance of *MYC* rearrangement in HGBCL-NOS without *BCL2* and/or *BCL6* translocations. Therefore, this issue is an area of controversy.⁹ To date, the impact of CD5 as a prognostic factor in HGBCL-NOS is unknown. Likewise, as to the negative prognostic significance of the presence of CD5 in DLBCL, it might be possible to speculate that the expression CD5 may also serve as an indicator of biological aggressiveness in HGBCL-NOS. Furthermore, we do not have any insight regarding the prognostic role of cyclin D1, keeping in mind that to date there are no published data on the prevalence of cyclin D1 expression in HGBCL-NOS.

In conclusion, this is the first report of HGBCL-NOS with *MYC* rearrangement and concurrent overexpression of CD5 and cyclin D1. Therefore, the present case suggests that occasionally HGBCL-NOS can closely mimic BVMCL both morphologically and phenotypically. Their distinction is especially important clinically, as these two aggressive diseases have quite different treatment strategies. Therefore, a careful molecular work-up for all high-grade B-cell lymphomas with blastoid features is of paramount importance to provide the right diagnosis.

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Concomitant diagnosis of chronic myeloid leukaemia and myeloma

To the Editor,

G-banding for karyotype analysis has been part of routine pathological practice since the 1970s, playing a critical role in improving our understanding of the genetic causes of malignancies. Whilst newer methods, such as fluorescent *in situ* hybridisation (FISH) testing and sequencing technologies have evolved and now play a critical role in diagnosis and management of patients, karyotypic analysis remains an important tool in our diagnostic armament. We present a case which demonstrates the ongoing role that karyotype analysis continues to play and which led to a therapeutic change in management.

A 57-year-old male teacher was referred with an incidental finding of a raised lambda light chains of 597.0 mg/L (reference range 5.7–26.0 mg/L) detected during routine blood testing screening for diabetic nephropathy. His kappa light chains were 9.7 mg/L (reference range 3.3–19.4 mg/L) with a ratio of 0.016 (reference range 0.26–1.65). His past medical history included type 2 diabetes mellitus, hypertension, and benign prostate hypertrophy. He was asymptomatic and examination revealed no lymphadenopathy and no hepatosplenomegaly. He had a normal full blood examination, renal function, and calcium level. Computed tomography (CT) skeletal survey and magnetic resonance imaging (MRI) spine revealed no myelomatous bone disease. He underwent bone marrow aspirate and trephine which demonstrated a

Fig. 1 (A) H&E stain of bone marrow trephine demonstrating normal trilineage haematopoiesis and normal megakaryocyte morphology. (B) CD138 immunohistochemistry stain (brown cells) of bone marrow aspirate and trephine showing clumps of plasma cells comprising 30% of total cellularity.

normocellular marrow with normal trilineage haematopoiesis (Fig. 1A), normal megakaryocyte morphology and an excess of plasma cells (30% on trephine Fig. 1B) consistent with a diagnosis of smouldering plasma cell myeloma.

Cytogenetic analysis of his bone marrow aspirate revealed a highly unexpected finding of a Philadelphia chromosome (translocation 9;22) (Fig. 2A), confirmed on FISH testing, which was not seen within the plasma cell compartment when assessed using plasma cell bead selection or intracellular immunoglobulin staining (Fig. 2B). FISH analysis identified trisomy 1q and an IgH (chromosome 14q32) rearrangement with an unknown partner within the plasma cell compartment but no evidence of a Philadelphia chromosome (Fig. 2C).

As a consequence of these unexpected results, a BCR-ABL was performed and confirmed an e14a2 (b3a2) transcript (7.707%) consistent with a concomitant diagnosis of chronic myeloid leukaemia (CML) in chronic phase with a low SOKAL score. Therefore, the patient was diagnosed with both smouldering plasma cell myeloma and CML from the same bone marrow biopsy. As the patient had no myeloma defining events, the patient was commenced on imatinib and had achieved a molecular response (BCR-ABL 0.44%) at 3 months.

Plasma cell myeloma is a cancer of plasma cells.¹ Patients with multiple myeloma requiring therapy are usually treated with combinations of corticosteroids, proteasome inhibitors (e.g., bortezomib) and immunomodulatory imide drugs (IMiDs) (e.g., lenalidomide). Since 2020 when 'triplet' therapy was approved via the Australian PBS, fit patients have been most commonly treated with the combination of lenalidomide, bortezomib and dexamethasone (RVD). Despite their widespread use in patients with myeloma, the mechanism of action of the IMiDs remained unclear for many years. IMiDs appear to induce a multitude of changes including having anti-angiogenesis properties, cytokine modulation and causing T cell activation.² Recent studies have also demonstrated that IMiDs lead to direct myeloma cell death by causing increased degradation of the transcription factors Ikaros (IKZF1) and Aiolos (IKZF3) via Cereblon-CRL4 ubiquitin ligase.^{3,4} The loss of Ikaros and Aiolos leads to downstream transcriptional alterations ultimately leading to myeloma cell death.

CML is a myeloproliferative neoplasm, characterised by the presence of the Philadelphia (Ph) chromosome formed as a result of a reciprocal translocation between chromosome 9 and 22 t(9;22)(q34;q11.2). This results in the formation of *BCR-ABL* fusion gene and production of BCR-ABL fusion protein.¹ Treatment of CML has been revolutionised by the discovery of tyrosine kinase inhibitors (TKI) with exceptionally high response rates.⁵ A major predictor of poor long-term survival in patients with CML is the progression to advanced stages such as accelerated phase or blast crisis either at diagnosis or during therapy.⁵ The pathophysiology of advanced stages of CML is incompletely understood, however, it is commonly

Fig. 2 (A) G-band karyotype demonstrating a translocation 9;22 (arrows). (B) FISH testing with *BCR-ABL* fusion probes (green and red) demonstrating a fusion of *BCR-ABL* indicated by red and green signal adjointed. (C) FISH testing using *BCR-ABL* fusion probe with intracellular immunoglobulin staining (blue) demonstrating a lack of *BCR-ABL* fusion in plasma cells (green and red signals distant).

associated with additional cytogenetic abnormalities and mutations within *BCR-ABL*.⁶ Further studies have also demonstrated that disruption to Ikaros can play a critical role in progression of CML to advanced stages.⁷

A diagnosis of myeloma and CML in the same patient is a rare event, only reported in a small number of case studies.^{2,3,5} The postulated aetiologies of synchronous or metachronous diagnosis of two different haematological malignancies includes a common haematological progenitor stem cell, environmental exposure to carcinogens, presence of pre-existing plasma cell myeloma, treatment of one haematology malignancy predisposing to the second diagnosis and genetic or epigenetic changes associated with myeloma predisposing to other malignancies.^{8–10} Simultaneous diagnosis of myeloma and CML is even rarer and raises a therapeutic conundrum. IMiDs form the backbone of myeloma therapy and are known to cause Ikaros suppression, particularly in myeloma cells; however, Ikaros suppression has been demonstrated to be a potential cause of progression to advanced stages in CML. Whether lenalidomide is safe to use in patients with synchronous CML and myeloma remains unclear. Whilst the risk remains theoretical, due to the paucity of patients diagnosed with concurrent myeloma and CML, there is almost no real-world data to guide therapy. In our case, given the patient did not imminently need myeloma-directed therapy, we elected to control the CML clone with a TKI with the aim of maximal suppression, to allow adequate myeloma therapy if and when he requires it.

This case demonstrates the ongoing critical role that karyotype analysis plays in the diagnosis of haematological malignancies. The incidental finding of CML has real-world therapeutic ramifications for our patient and highlights the ongoing importance of maintaining karyotype analysis, even with the expansion of more sensitive techniques such as FISH and genome sequencing.

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***Enterococcus cecorum* infective endocarditis in a patient with chronic myeloid leukaemia and cirrhosis**

To the Editor,

Enterococcus cecorum is a rare infection in humans, predominantly occurring in immunocompromised patients. We report the second known case of infective endocarditis caused by *E. cecorum* in a patient with chronic myeloid leukemia (CML).

A 70-year-old man presented to the Emergency Department with a 2-week history of dyspnoea, fatigue and intermittent fevers. He had a background history of CML diagnosed in 2003, which was initially in a sustained molecular remission on imatinib. In 2019, after developing an imatinib resistance mutation, therapy was changed to dasatinib 100 mg daily. Other medical background included alcohol-induced hepatic cirrhosis with associated portal hypertension. He underwent an endoscopy for upper gastrointestinal bleeding 4 months prior to presentation with findings of portal hypertensive gastropathy. The patient's only zoonotic exposure was his pet dog.

The peripheral blood count was unremarkable and a chest X-ray demonstrated bilateral moderate sized pleural effusions. Blood cultures were positive for non-motile, Gram-positive cocci in chains growing in both aerobic and anaerobic bottles. The isolate was unambiguously identified as *E. cecorum* on matrix assisted laser desorption-ionisation time of flight (MALDI-TOF) mass spectrometry (Vitek; bioMérieux, France) with a score of 2.2. The patient commenced therapy with intravenous benzylpenicillin and synergistic ceftriaxone. Dasatinib was temporarily ceased. A transoesophageal echocardiogram revealed an 8×8 mm vegetation attached to the right coronary cusp with abscess formation and severe aortic incompetence.

Antimicrobial susceptibility testing was achieved using antibiotic gradient strips and interpreted against European Committee on Antimicrobial Susceptibility Testing (EUCAST) published breakpoints. The isolate demonstrated susceptibility to ampicillin [minimum inhibitory concentration (MIC) 0.38 mg/L], vancomycin (0.75 mg/L), and linezolid (0.75 mg/L). No breakpoint exists for cefotaxime (MIC 0.19 mg/L).