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CASE REPORT

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Plasma cell myeloma following a prior diagnosis of chronic lymphocytic leukemia/small lymphocytic lymphoma

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Abstract

A 69-year-old man presented with plasma cell myeloma (PCM) 4 years after the treatment of chronic lymphocytic leukemia (CLL). Light chain expressions in the two tumors were different suggesting unrelated cell of origin clonality. Few reports have been added to the literature describing synchronous CLL and PCM in a patient.

KEYWORDS

chronic lymphocytic leukemia, plasma cell myeloma, second cancer

1 | INTRODUCTION

Chronic lymphocytic leukemia (CLL) and plasma cell myeloma (PCM) are common hematologic malignancies and both tend to occur in the older population.[1,2] There are few reports in the literature describing the concurrent or synchronous occurrence of CLL and PCM in the same patient. When two hematologic neoplasms occur concurrently or synchronously, the challenges are to exclude small B cell lymphomas showing plasma cell differentiation and demonstrate the clonal relationship between them.

Using interphase FISH for clonal chromosomal abnormalities and/or immunoglobulin gene rearrangement analysis, an author demonstrated that both arise from a single clone,[3] while another concluded that chronic lymphocytic leukemia and plasma cell myeloma observed in a patient arose from two separate clones.[4]

Herein, we describe a case of a patient with both a recurrence/persistence of CLL and newly diagnosed PCM and emphasize the need to routinely look for clonal plasma cells in cases of chronic lymphoproliferative disorders and clonal B lymphoid cells in cases of plasma cell myeloma.

2 | CASE DESCRIPTION

September 2015: The patient is a 62-year-old asymptomatic male that was first seen in the hematology clinic with an elevated white blood cell count (WBC) of 29.8×10^9/L, absolute lymphocyte count of 24.8×10^9/L, hemoglobin 146 g/L, and platelet 182×10^9/L. There was no associated lymph node enlargement or organomegaly. Flow cytometry showed a Lambda light chain restricted B cell population co-expressing CD5 and CD23, indicating a diagnosis

of chronic lymphocytic leukemia/small lymphocytic lymphoma. CD38 subset of this clonal B cells was less than 5%. Interphase FISH analysis using CLL/SLL-specific probes showed del3q, considered a good prognostic lesion.

August 2016: He developed axillary and cervical lymphadenopathy (painless, 1.5-2 cm each) with WBC 53.2×10^9/L, lymphocyte count 48.3×10^9/L, hemoglobin 143 g/L, platelet 171×10^9/L, and a normal LDH at 173. CT imaging did show multiple enlarged nodes in the axilla right hilar area, mesentery, porta hepatis, and retroperitoneal areas.

05/2017: Repeat Laboratory findings indicated with WBC 139.4×10^9/L, lymphocyte count 131.4×10^9/L, hemoglobin 126 g/L, platelet 152×10^9/L He was treated with fludaribin, cyclophosphamide, and rituximab (FCR). After 6 cycles, laboratory findings showed WBC 2.7×10^9/L, lymphocyte count 0.3×10^9/L, hemoglobin 143 g/L, and platelet 112×10^9/L. By 10/2017, he was in clinical remission.

Between 2017 and 2021, the patient was monitored quarterly and remained in clinical and hematologic remission.

October 2021: He presented with increasing bone pain. Serum protein electrophoresis showed monoclonal free kappa light chains. His free kappa measures 3413 mg/L. His lambda light chain was 19.8 mg/L with a ratio of 172.41. Creatinine of over 300 μmol/L and calcium of 3.32 mmol/L. Serum protein electrophoresis showed a monoclonal kappa light chain paraprotein. A skeletal survey and positron emission tomography (PET) scan showed diffuse bony lytic lesions.

A peripheral blood smear demonstrated lymphocytosis with smudge cells (Figure 1A). Bone marrow biopsy and aspirate showed a relapse/persistence of earlier diagnosed chronic lymphocytic leukemia, with clonal B cells accounting for 60% of all cells. There was no clonal plasma cell population. Concurrent flow cytometry indicated these to be lambda light chain restricted (similar to earlier diagnosed CLL/SLL). Cytogenetics (interphase FISH) showed del11 and del13.

A CT-guided core biopsy from a lytic lesion in the right iliac crest identified a diffuse sheet of kappa light chain restricted CD138 positive plasma cells co-expressing CD56 (Figure 1B–E). The diagnosis of plasma cell myeloma was made and he was started on CyBorD chemotherapy.

September 2022: To date, the patient has had 8 cycles of cyclophosphamide, bortezomib, and dexamethasone (CyBorD) chemotherapy. A review of his most recent blood work shows white blood cell count of 7.9×10^9/L with neutrophils 6.3×10^9/L, hemoglobin 125 g/L, and platelets 116×10^9/L. Clinical chemistries continue to demonstrate normal renal and hepatic function. The most recent serum free light chain shows a continued improvement in his free kappa measuring 309.1 mg/L, free lambda 8.3 mg/L, and an improved ratio of 37.24.

3 | DISCUSSION

Plasma cell myeloma and chronic lymphocytic leukemia share a common cell of origin (B lymphocytes) and may

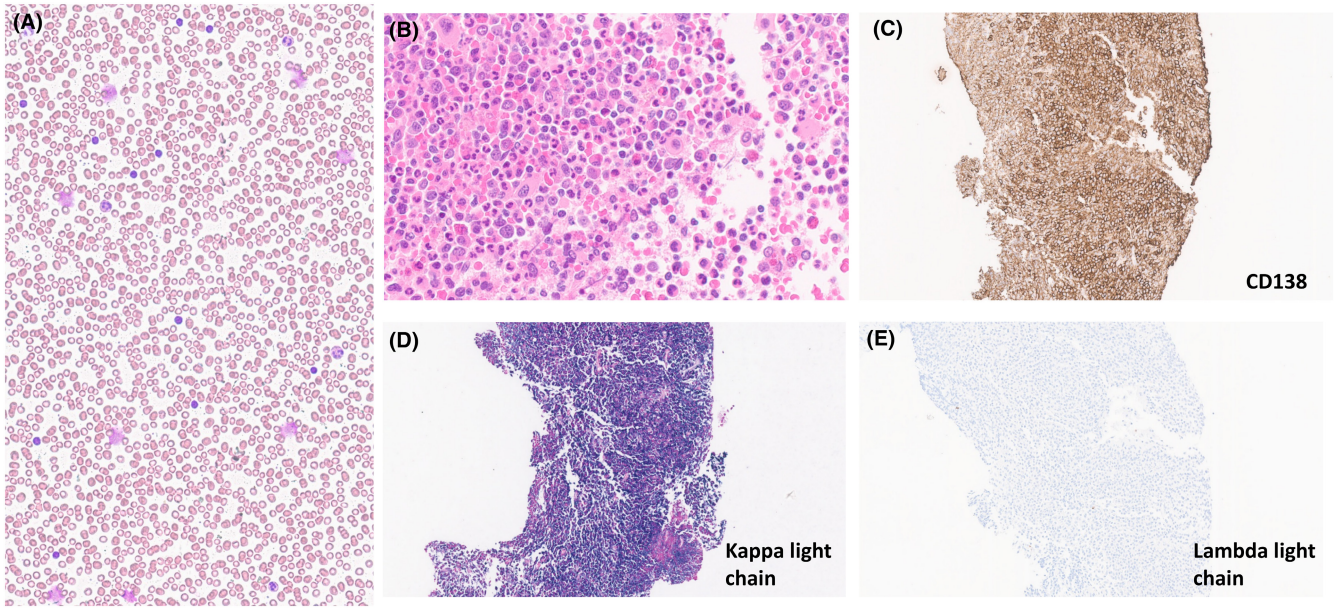

FIGURE 1 Peripheral blood (A) and right iliac crest biopsy were obtained via CT guidance (B–E). (A) Peripheral blood showing absolute lymphocytosis with smudge cells, 20X magnification. B, H&E stained bone marrow biopsy showing diffuse sheets of neoplastic plasma cells, at 20X magnification. (C) Positive IHC staining for CD138. (D) Positive IHC staining for Kappa light chain. (D) Negative IHC staining for lambda light chain.

have overlapping epidemiologic and clinical features. However, the occurrence of both neoplasms in one patient is uncommon.[2–5] Our patient developed plasma cell myeloma 4 years after a prior diagnosis of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).

In patients with both malignancies, the two neoplasms may be clonally unrelated arising independently from the same stem cell or unrelated stem cells.[3,4] Interestingly, the light chain expressions in the two malignancies differ (clonal lambda light chain restriction in the CLL versus kappa light chain restriction in the plasma cell myeloma), suggesting unrelated cell of origin clonality. The question of clonal relationship may further have been answered definitively via genomic analyses, like a comparative genomic hybridization (CGH) assay, of the two populations of cells. This assay was not performed.

The mechanisms that interplay in the development of second cancers in a patient with a prior diagnosis of chronic lymphocytic leukemia/small lymphocytic lymphoma are unclear. Possible explanations include a protumorigenic microenvironment, immune dysfunction, or chemotherapy-related factors.[5,6]

Cytotoxic drugs are implicated in the pathogenesis of therapy associated with acute myeloid leukemia. There is increasing evidence that agents used in the therapy of primary cancers also aid the development of secondary non-Hodgkin lymphomas. Exposure to chemotherapy (like fludarabin, a purine analog, used in the treatment of this patient) results in single- and double-stranded breaks and inter-strand cross-links in host DNA. These genomic lesions may interact and may overwhelm normal repair mechanisms to increase the risk of aberrant recombination events and malignant transformation.[7–10]

We add to the limited medical literature on co-occurrence of two age-related hematologic malignancies (CLL and plasma cell myeloma) and highlight that both neoplasms in one patient could make the diagnosis, management, and assessment for clinical outcomes challenging. It is unknown if certain cytogenetic lesions of CLL/SLL predispose one to the development of a secondary malignancy.

4 | TAKE AWAY LESSON

Following the diagnosis of CLL, the development of second cancer can be a chance event. The roles of genetic lesions, therapy, and immune dysfunction are unclear. We emphasize the need to look for clonal plasma cells in cases of chronic lymphoproliferative disorders and clonal B lymphoid cells in cases of PCM.

AUTHOR CONTRIBUTIONS

MNL, KG, and OFI wrote and edited the manuscript.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

CONSENT

The patient's written informed consent has been obtained for publication of this case report, in accordance with this journal's policy.

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REFERENCES

1. Swerdlow SH, Campo E, Harris NL, et al. *WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues (Revised 4th Edition)*. Lyon; 2017.
2. Tynski Z, Hirama I, Rossetti JM. The synchronicity of chronic lymphocytic leukemia and multiple myeloma in a bone marrow biopsy with therapy discussion. *Diagn Pathol Open*. 2018;3(1):1-5.
3. Saltman DL, Ross JA, Banks RE, Ross FM, Ford AM, Mackie MJ. Molecular evidence for a single clonal origin in biphenotypic concomitant chronic lymphocytic leukemia and multiple myeloma. *Blood*. 1989;74(6):2062-2065.
4. Novak PM, Mattson JC, Crisan D, Chen J, Poulik MD, Decker D. Separate clones in concomitant multiple myeloma and a second B-cell neoplasm demonstrated by molecular and immunophenotypic analysis. *Eur J Haematol*. 1995;54(4):254-261.
5. Dholaria B, Agarwal A, Roy V, et al. Outcomes of patients with combined chronic lymphocytic leukemia and multiple myeloma. Abstract #89635. Presented at the ASH Meeting on Hematologic Malignancies, September 16-17, 2016; Chicago, IL.
6. Alley CL, Wang E, Dunphy CH, et al. Diagnostic and clinical considerations in concomitant bone marrow involvement by plasma cell myeloma and chronic lymphocytic leukemia/monoclonal B-cell lymphocytosis: a series of 15 cases and review of literature. *Arch Pathol Lab Med*. 2013;137(4):503-517.
7. Kaufmann H, Ackermann J, Nösslinger T, et al. Absence of clonal chromosomal relationship between concomitant B-CLL and multiple myeloma—a report on two cases. *Ann Hematol*. 2001;80(8):474-478.
8. Beiggi S, Johnston JB, Seftel MD, et al. Increased risk of second malignancies in chronic lymphocytic leukemia patients

as compared with follicular lymphoma patients: a Canadian population-based study. *Br J Cancer*. 2013;109(5):1287-1290.
9. Tarella C, Passera R, Magni M, et al. Risk factors for the development of secondary malignancy after high-dose chemotherapy and autograft, with or without rituximab: a 20-year retrospective follow-up study in patients with lymphoma. *J Clin Oncol*. 2011;29(7):814-824.
10. Krishnan B, Morgan GJ. Non-Hodgkin lymphoma secondary to cancer chemotherapy. *Cancer Epidemiol Biomarkers Prev*. 2007;16(3):377-380.

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