Unveiling the Enigma: Plasma Cell Leukaemia Presenting with Flower-like Cells, Mimicking Adult T-cell Leukaemia – A Rare Diagnostic Conundrum

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Received May 8, 2024; Accepted August 27, 2025.

Key words: Plasma cell – Plasma cell leukaemia – Leukaemia/lymphoma adult T-cell

Abstract: Peripheral plasma cell leukaemia (PCL) is a rare hematologic malignancy that can pose diagnostic challenges due to its resemblance to other conditions such as adult T-cell leukaemia/lymphoma (ATLL) or dissemination lymphoma in peripheral blood. We present a case report of a 40-year-old male with symptoms of fatigue, irregular heartbeat, weight loss, and bone pain, whose peripheral blood examination revealed hyperleukocytosis with atypical lymphoid cells exhibiting flower-shaped nuclei, reminiscent of adult T-cell leukaemia/lymphoma. Further investigations including bone marrow aspiration and biopsy confirmed the diagnosis of primary PCL. Immunophenotyping revealed expression of plasma cell antigens CD38 and CD138. This case underscores the importance of recognizing morphological variants and employing comprehensive immunophenotypic analysis for accurate diagnosis of PCL, especially when atypical nuclear features mimic other hematologic malignancies.

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https://doi.org/10.14712/23362936.2025.25

Prague Medical Report / Vol. 126 (2025) No. 3, p. 159–161

Introduction

Peripheral clonal plasma cells with a count greater than 2×10^9/l are considered to be indicative of plasma cell leukaemia (PCL), an uncommon condition that can develop independently of or as part of plasma cell myeloma (García-Sanz et al., 1999). Plasma cell leukaemia with abnormal plasma cells and nuclear characteristics in the form of flower-like cells has been reported previously. Because "flower cells" or clover-leaf lymphocytes are usually described in human T-cell lymphotropic virus type 1 (HTLV-1) induced adult T-cell leukaemia and very infrequently in B-cell lymphoma, these morphological characteristics can create diagnostic challenges and can mimic lymphoma (Singh et al., 2017). We describe a case of primary PCL that mimicked adult T-cell leukaemia or lymphoma and presented with nuclei in the form of flowers. This is a really informative case report about a patient with multiple myeloma who had flower-shaped nuclear characteristics and aberrant plasma cells.

Case report

A 40-year-old man presented with complaints of fatigue, an irregular heartbeat, weight loss, and bone pain for the last three months. There was no medical history for the patient. Family history was also inconclusive. During the physical examination, neither splenomegaly nor lymphadenopathy were found. On routine blood examination, the total blood count showed hyperleukocytosis, with a count of 112×10^9/l, 97% atypical lymphoid cells, haemoglobin 9.2 g/dl, and a platelet count of 150×10^9/l. Viral markers were negative. The serum biochemical test showed elevated levels of beta-2 microglobulin (19.5 mg/l), lactate dehydrogenase (4,328 IU/l), and hypercalcemia (3.93 mmol/l). C-reactive protein was less than 2.8 mg/l. A renal function test showed a mild elevation of serum creatinine, and a liver function test showed moderately elevated transaminase. Peripheral blood smear examination shows medium to large, profoundly basophilic, coarsely clumped chromatin, medium to large size, and occasionally perinuclear clearing of the highly pleomorphic atypical lymphoid cells. Like adult T-cell leukaemia/lymphoma (ATLL) flower cells, the nuclear morphology was highly asymmetrical and frequently polylobulated (Figure 1A). Based on peripheral smear findings, a differential diagnosis of either an ATLL or a PCL was considered. On bone marrow aspiration and biopsy, there was hypercellularity with >90% of the same large atypical cells as seen in the peripheral blood smear (Figure 1B and C). On initial immunophenotyping, both B-cell and T-cell lineage markers were negative, but with an extended panel of markers, the plasma cell antigens CD38 and CD138 were found to be expressed by these atypical cells (Figure 1D). Serum immunofixation revealed the presence of lambda light chains but not heavy chains. Light chains in the urine were not studied. The study's findings on HTLV-1 or 2 infections were unfavourable. Based on these findings, a primary diagnosis of primary plasma cell leukaemia was made.

Discussion

Flower-shaped nuclei, although typically associated with adult T-cell leukaemia/lymphoma, have also

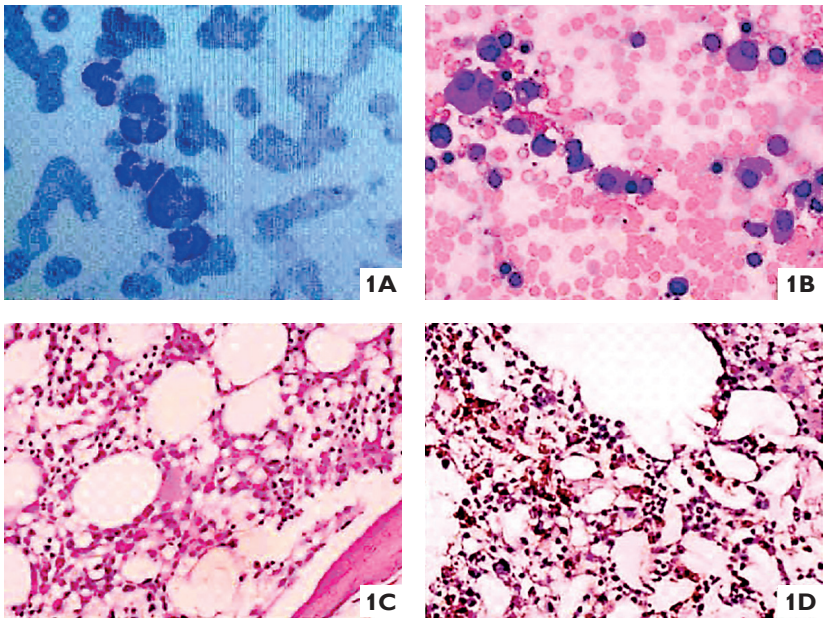

Figure 1: A) Abnormal flower-shaped cells with lobes, numerous nuclear convolutions, and basophilic cytoplasm (arrow), Wright-Giemsa stain, 1000× magnification. B and C) Bone marrow aspiration and biopsy images show many plasma cells with a few binucleated forms, May-Grünwald Giemsa (MGG) stain, and haematoxylin and eosin stain, 100× image. D) Atypical plasma cells show immunopositivity for CD138, 100× image.

been observed as an unusual morphological finding in plasma cell leukaemia. These cases can pose diagnostic challenges due to overlapping features with lymphoid neoplasms. In fact, rare instances of PCL presenting with flower-like nuclei have been misinterpreted as ATLL based on morphology alone have been described in the literature (Shibusawa, 2020; De Miguel Sánchez et al., 2021). Condensed chromatin, on the other hand, may make flower-shaped plasma cells resemble lymphocytes. Whether these cells were flower-like plasma cells or flower-like lymphocytes could have been determined by CD20 or CD138 immunocytochemistry, as reported earlier (Kobayashi et al., 2015; Sall et al., 2021). There have also been reports of a few instances of morphological variants of PCL, such as plasmoblastic or megakaryocytic, mimicking acute leukaemia (Liu et al., 2020). Flow cytometry remains an excellent tool for identifying clonal plasma cells from normal or reactive ones. In PCL, abnormal plasma cells often lack CD19 and CD20 expression while being positive for CD28, CD117, CD56, and CD33. They also have light chain restriction and are clonally positive for either kappa or lambda immunoglobulin, distinguishing them from polyclonal plasma cells. This immunophenotypic profile offers important diagnostic clarity in confusing instances (Flores-Montero et al., 2016). Patients with adult T-cell leukaemia or lymphoma are characterised by the appearance of flower-like lymphocytes in their peripheral blood, however their morphological mimickers can also be seen in PCL as in present case (Dahmoush et al., 2002).

Conclusion

Plasma cell leukaemia indeed presents a diagnostic challenge, especially when encountering unusual features like the presence of flower-like cells, which can lead to confusion with other hematological malignancies such as adult T-cell leukaemia/lymphoma. Immunophenotyping plays a crucial role in accurately diagnosing such cases. Prompt and correct diagnosis is critical in plasma cell leukaemia, as it determines subsequent treatment options such as chemotherapy, targeted therapy, immunomodulatory medications, or stem cell transplantation, depending on disease stage, patient age, and overall health state.

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