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CASE REPORT

Secondary B-Cell Acute Lymphoblastic Leukemia Following Multiple Myeloma Treatment

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ABSTRACT

Background: **Secondary B-cell acute lymphoblastic leukemia (B-ALL) following multiple myeloma (MM) is rare.**
Methods and Results: **Our case presents a patient with non-secretory MM, using bortezomib-based induction, autologous transplantation, and sequential Lenalidomide maintenance treatment and persistent complete remission (CR) for about 5 years. Then the patient got secondary B-ALL.**
Conclusions: **Autologous stem cell transplant with bortezomib therapy has achieved CR of patients with MM, but also has an increased risk of secondary B-ALL.**
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KEYWORDS

multiple myeloma, secondary B-cell acute lymphoblastic leukemia, bortezomib, autologous stem cell transplant

CASE REPORT

In February 2020, the patient developed unexplained chest pain. PET-CT revealed multiple osteolytic lesions in the axial and appendicular bones with heterogeneously increased FDG metabolism, suggestive of myeloma. Bilateral rib pathological fractures were noted. Pulmonary CT confirmed extensive bony abnormalities consistent with multiple myeloma (MM). WBC 5.13 x 10^9/L, HB 134 g/L, PLT 411 x 10^9/L, IgG 6.42 g/L, IgA 0.69 g/L, IgM 0.39 g/L, IgE 12.70 g/L. Serum free light chains (sFLC): κ 796.00 mg/dL, λ 280.00 mg/dL (κ/λ ratio 2.84:1, normal 0.26 - 1.65). Urine free light chains (uFLC): κ 1.85 mg/dL, λ 5.00 mg/dL (κ/λ ratio 0.37:1). Immunofixation electrophoresis is negative. Bone marrow (BM) aspirate smear revealed 68.5% plasma cells (Figure 1). BM Flow cytometry (FLC) showed abnormal plasma cells 40.39%, positive for CD138, CD45-dim, CD38, CD81, and cKappa; negative for CD28, CD19, CD27, CD117, CD20, CD56, CD200, and cLambda. BM pathology confirmed plasma cell myeloma. Cytogenetic analysis revealed a normal karyotype (46, XX[24]). Fluorescence in situ hybridization (FISH)

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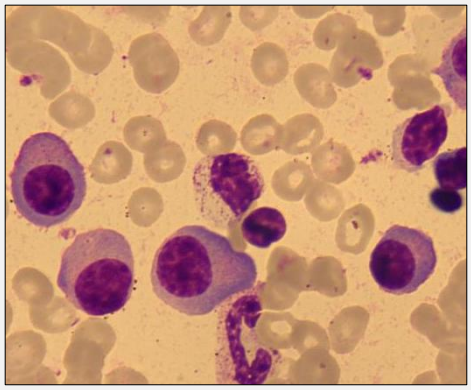

Figure 1. Wright-Giemsa staining of plasma cells.

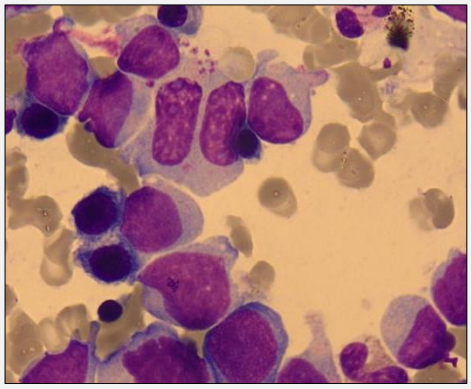

Figure 2. Wright-Giemsa staining of B lymphoblasts.

result is IGH-CCND1 fusion gene (t(11;14)) detected in 3% of cells. Non-secretory multiple myeloma (NSMM), Durie-Salmon (DS) stage IIIA, International Staging System (ISS) stage II was diagnosed. On March 11, 2020 she received 4 courses of BD regimen chemotherapy (bortezomib was injected subcutaneously on day 1 and 15, pamidronate was administered intravenously once a month to consolidate bone), and achieved complete remission (CR). On September 2, 2020, autologous hematopoietic stem cells were transfused. On December 14, 2020, the patient entered maintenance therapy and the evaluation of the condition was CR.

On May 10, 2023, the patient was readmitted for the 54th time with a BM profile showing 4.5% plasma cells. BM FLC showed 0.88% abnormal plasma cells. The treatment was adjusted to 25 mg of lenalidomide capsules orally once daily for 21 days. On September 4, 2024, the patient was admitted for the 58th time. The disease was still assessed as CR, and pomalidomide continued to be treated with oral monotherapy.

On April 3, 2025, the patient was readmitted, BM aspirate smear with 3% plasma cells and 40% immature lymphocytes (Figure 2). BM FLC analysis revealed approximately 18.98% immature B lymphocytes, positive for cTDT, cCD79a, CD19, CD34, CD38, HLA-DR, CD33, CD10(part), and CD45(dim); negative for cMPO, cIgM, CD9, CD117, CD5, CD20, CD13, CD14, CD11b, CD15, CD16, CD3, CD4, CD8, CD7, CD5, CD64, CD36, and CD56; 0.24% normal plasma cells. Cytogenetic test showed normal female karyotype

46,XX[15]. FISH testing for BCR::ABL1, TCF3/PBX1, TEV6/AML1, MLL, MYC, IGH were negative. NGS results showed that: DNMT3A R882H mutation positive (17%, TierI), KDM6A N1149Kfs*11 mutation positive (3%, TierII), STAT6 R652k (2%, TierII), XPO1 V808F (1, TierII), GNA13 I149V mutation positive. Secondary B-ALL was diagnosed.

DISCUSSION

MM patients have a high incidence (0.7% to 25%) of secondary leukemia, which is 100 to 200 times higher than the incidence of leukemia in the normal population.

Patients with MM have a risk of developing second hematological malignancies, particularly MDS and AML [1]. ALL related treatment accounts for only approximately 12%. B-ALL is a rare second primary malignancy (SPM) in patients with MM. Therapy-related myeloid neoplasia (t-MN) after cytotoxic chemotherapy for MM has been described for about 40 years [2]. Before autologous stem cell transplant (ASCT), the use of alkylating agents, such as oral melphalan and high-dose melphalan, thought to contribute to the development of myeloid malignancies in patients with MM [3]. The use of lenalidomide is common for patients with MM, especially during maintenance treatment after autologous stem cell transplant (ASCT). Maintenance therapy with lenalidomide has an increased risk of second primary malignancies (SPMs) [4]. However, whether lenalidomide is associated with a significant risk of secondary hematologic malignancies in the absence of high-dose melphalan has been questioned [5]. Patients develop B-ALL during lenalidomide maintenance treatment for MM is rare.

This case highlights successful long-term control of non-secretory MM using bortezomib-based induction, ASCT, and sequential immunomodulatory maintenance. Lenalidomide maintenance treatment may have an increased risk of secondary B-ALL.

Ethical Approval:

All procedures performed in studies involving human participants 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.

Declaration of Interest:

None of the authors have a conflict of interest to disclose.

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