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Hematology

Efficacy of Azacitidine–Venetoclax Therapy Combined with Voriconazole Prophylaxis in Blastic Plasmacytoid Dendritic Cell Neoplasm: A Case Report in an Elderly Patient

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Abstract **Case Report**

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare and highly aggressive hematologic malignancy that predominantly affects older adults. Owing to advanced age and multiple comorbidities, intensive chemotherapy is often not feasible, making therapeutic management particularly challenging. We report the case of a 76-year-old man with BPDCN who achieved a rapid and durable response to azacitidine combined with venetoclax despite the concomitant administration of voriconazole for antifungal prophylaxis. Complete remission with incomplete hematologic recovery (CRi) and cytogenetic normalization were achieved after the first treatment cycle. This case highlights the efficacy and favorable tolerability of hypomethylating agent–venetoclax therapy as a valuable therapeutic alternative for elderly patients ineligible for intensive treatment, while emphasizing the importance of appropriate venetoclax dose adjustment in the setting of concomitant CYP3A4 inhibition.

Keywords : Blastic plasmacytoid dendritic cell neoplasm (BPDCN); Azacitidine; Venetoclax; Voriconazole; CD123; Elderly patient; Hematologic malignancy.

INTRODUCTION

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematologic malignancy accounting for less than 1% of all hematologic cancers. It is characterized by the clonal proliferation of precursors of plasmacytoid dendritic cells and commonly involves the skin, bone marrow, lymph nodes, and peripheral blood.

BPDCN is associated with an aggressive clinical course and poor prognosis. Although allogeneic hematopoietic stem cell transplantation remains the only potentially curative treatment, it is rarely feasible in elderly patients because of age-related frailty and comorbidities. Recently, targeted therapeutic strategies, including the BCL-2 inhibitor venetoclax combined with hypomethylating agents such as azacitidine, have emerged as promising alternatives for patients who are not candidates for intensive chemotherapy.

CASE PRESENTATION

A 76-year-old man presented with multiple erythematous-to-violaceous cutaneous lesions involving the trunk and scalp. Skin biopsy together with bone marrow examination, which demonstrated 32% blasts, established the diagnosis of BPDCN. Immunophenotypic analysis revealed the characteristic profile of BPDCN, with expression of CD4, CD56, and CD123 in the absence of myeloid or lymphoid lineage-specific markers. Conventional cytogenetic analysis demonstrated a complex karyotype.

Given the patient's advanced age and ineligibility for intensive chemotherapy, treatment was initiated using 28-day cycles consisting of:

- Azacitidine 75 mg/m²/day on days 1 through 7;
- Venetoclax 100 mg once daily, with dose reduction because of drug-drug interaction;
- Voriconazole 200 mg twice daily as antifungal prophylaxis.

RESULTS

Following the first treatment cycle (day 28), the patient achieved complete remission with incomplete hematologic recovery (CRi), accompanied by complete resolution of cutaneous lesions and normalization of the previously abnormal karyotype. After two treatment cycles, bone marrow blasts had decreased to less than 2%, and multiparametric flow cytometry no longer detected residual BPDCN cells. This deep response was maintained after four treatment cycles, with excellent clinical tolerance and no major infectious complications.

Figure 1: Frontal cutaneous lesions at the time of diagnosis

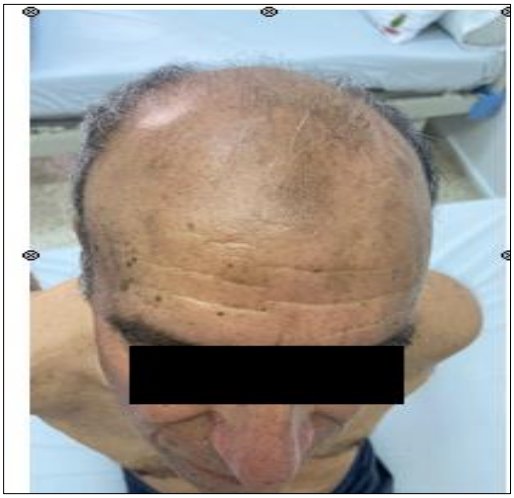

Figure 2: Complete resolution of cutaneous lesions at day 28 following the first cycle of azacitidine–venetoclax therapy

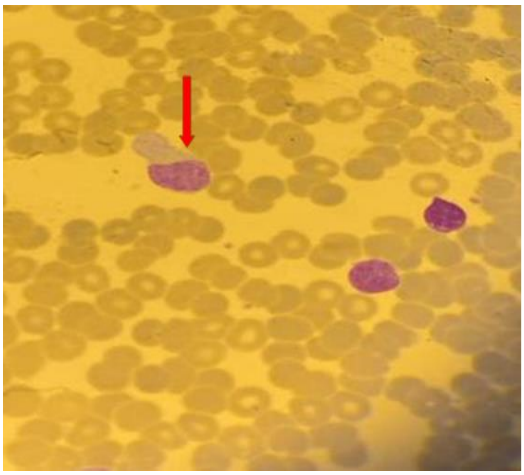

Figure 3: High-power bone marrow smear demonstrating a BPDCN blast cell with a characteristic cytoplasmic projection (arrow)

DISCUSSION

Management of BPDCN in elderly patients remains particularly challenging. Although tagraxofusp, a CD123-targeted therapy, has significantly expanded the therapeutic landscape, its availability remains limited in many countries, and its use may be complicated by severe adverse events, particularly capillary leak syndrome.

The rationale for venetoclax therapy is supported by the marked dependence of BPDCN cells on the anti-apoptotic protein BCL-2. The originality of the present case lies in the successful concomitant administration of voriconazole, a potent CYP3A4 inhibitor known to substantially increase venetoclax exposure. This case demonstrates that careful venetoclax dose reduction to 100 mg daily allowed preservation of therapeutic efficacy while minimizing the risk of excessive hematologic toxicity.

Such individualized therapeutic management is particularly relevant in BPDCN, where evidence is largely derived from small retrospective series and case reports owing to the rarity of the disease and the absence of large prospective randomized trials.

CONCLUSION

The combination of azacitidine and venetoclax represents a promising therapeutic strategy for elderly patients with BPDCN who are not eligible for intensive chemotherapy. This regimen can induce rapid and profound remissions even in the presence of adverse cytogenetic features such as a complex karyotype. Careful dose adjustment of venetoclax in the presence of strong CYP3A4 inhibitors, including azole antifungal agents, is essential to optimize both treatment efficacy and safety. Prospective multicenter studies are warranted to further define the role of this combination in the therapeutic management of BPDCN.

Declaration of Patient Consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying clinical data and images.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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