Navigating Frontline and Salvage Therapeutics in Blastic Plasmacytoid Dendritic Cell Neoplasm:

Manzoor Khan MBBS, FCPS[1], Syed Shahmeer Raza MD, MBBS, MPhil, DipPH[1], Ferdaws Abu Jalal MD, MPhil[2], David Waldron MD[2], Maria Losa Maroto MD[2], Abid Nawaz Khan Adil MD3,4

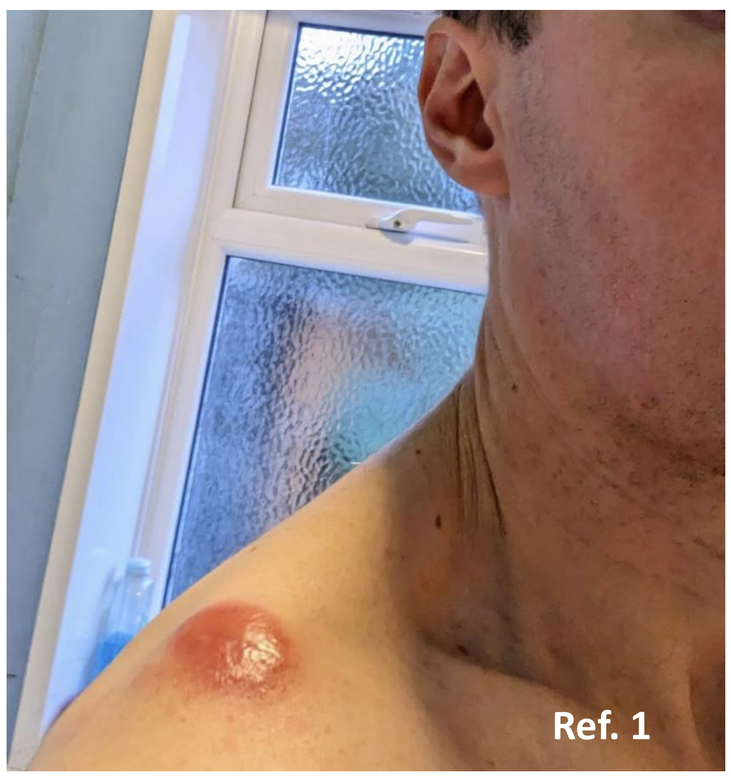
[1]Queen Elizabeth Hospital, Birmingham, United Kingdom. [2]The Wright Center for Graduate Medical Education, Scranton, PA, USA. [3]California Health Sciences University, Clovis, CA, USA. [4]Internist-Fresno Heart & Surgical Hospital, Fresno, CA, USA

Background

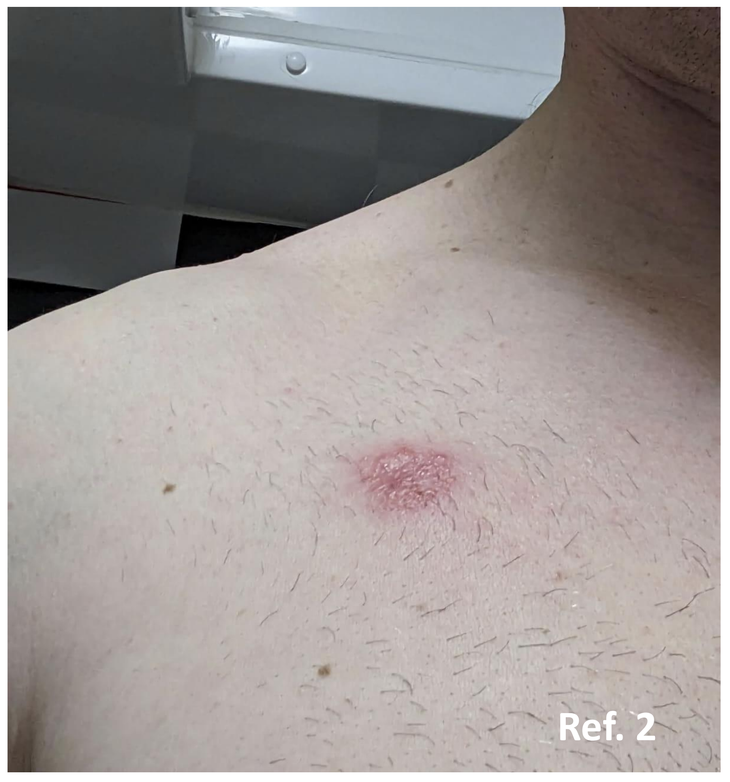
Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare, aggressive hematologic malignancy frequently presenting with cutaneous involvement. Tagraxofusp, a CD123-directed therapy, offers promising response rates but is frequently limited by capillary leak syndrome (CLS). Prompt transition to cytotoxic chemotherapy and allogeneic stem cell transplantation can be critical in achieving durable remission.

Case Presentation

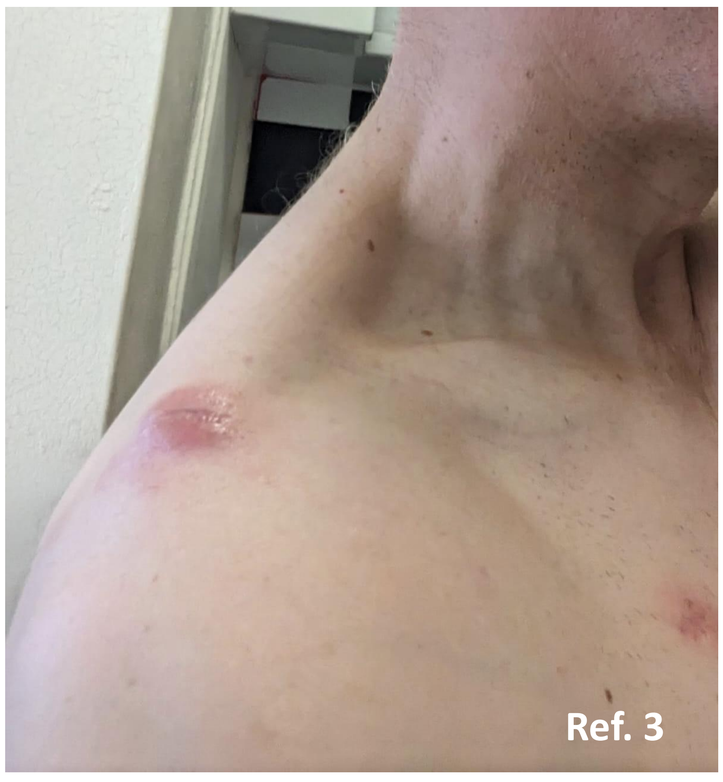
We report a 45-year-old male with no prior comorbidities who presented with a 6-month history of violaceous, pruritic skin lesions on the trunk, shoulder, and lower extremities. Skin biopsy confirmed BPDCN based on blastoid morphology and immunophenotypic expression of CD4, CD56, and CD123. Staging investigations, including PET-CT and CSF analysis, revealed no systemic involvement. Tagraxofusp was initiated with resolution of cutaneous lesions after two cycles. However, treatment was discontinued due to development of grade 2 CLS, necessitating hospitalization. Disease progression with new cutaneous lesions confirmed by repeat biopsy occurred shortly after treatment cessation. Salvage therapy with hyper-CVAD (arm B) and CNS prophylaxis achieved deep molecular remission after four cycles. The patient experienced infectious complications and steroid-induced psychosis, which required psychiatric intervention. Subsequently, he underwent reduced intensity conditioning and allogeneic stem cell transplantation from a matched unrelated donor. At 10-month follow-up, he remains in complete remission with full donor chimerism and no evidence of graft-versus-host disease.



Ref. 1: Pre Treatment



Ref. 2: After one cycle of Tagraxofusp



Ref. 3: After two cycle of Tagraxofusp

Conclusion

This case highlights the diagnostic, therapeutic, and supportive care complexities associated with BPDCN. While tagraxofusp remains a valuable frontline agent, its use is constrained by potentially severe toxicities such as CLS. Hyper-CVAD offers an effective salvage approach, particularly in younger patients, and transplant remains the cornerstone of curative-intent therapy. Early referral for transplant evaluation should be prioritized, especially when treatment-limiting toxicity occurs. BPDCN management demands early diagnosis, multidisciplinary coordination, and prompt escalation to intensive therapy. This case underscores the therapeutic promise and pitfalls of tagraxofusp and reinforces the curative potential of allogeneic transplantation in eligible patients.