RARE INTERSECTIONS: TWO CASES ILLUSTRATING THE IMMUNE COMPLEXITY OF CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) ASSOCIATED WITH PARANEOPLASTIC PEMPHIGUS WITH OCULAR DEVASTATION AND TEMOZOLOMIDE-INDUCED AUTOIMMUNE CYTOPENIAS IN CONCURRENT LYMPHOPROLIFERATIVE DISEASE.

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INTRODUCTION

Chronic lymphocytic leukemia (CLL) creates a uniquely dysregulated immune environment capable of precipitating catastrophic paraneoplastic and treatment-related autoimmune sequelae that extend well beyond conventional hematologic management. We present two cases that together expose critical, underrecognized vulnerabilities at the interface of CLL and immune-mediated end-organ injury, each highlighting distinct but complementary lessons for the hematology and oncology community.

CASE 1

A 60-year-old man with IGHV region-unmutated CLL developed **paraneoplastic pemphigus (PNP)**, a rare autoimmune blistering disorder with a well-established but underappreciated predilection for hematologic malignancies. Despite aggressive multimodal immunosuppression (prednisone, cyclosporine, Upadacitinib, intravenous methylprednisolone, IVIG, and cyclophosphamide) alongside venetoclax-obinutuzumab, he achieved near-complete MRD-negative remission but developed fulminant **corneal melt** with **uveal prolapse** requiring left eye evisceration. Venetoclax was subsequently discontinued due to severe cytopenias, and therapy was transitioned to acalabrutinib to leverage BTK inhibition for both sustained CLL control and its favorable T-cell immunomodulatory properties relevant to PNP pathogenesis.

CASE 2

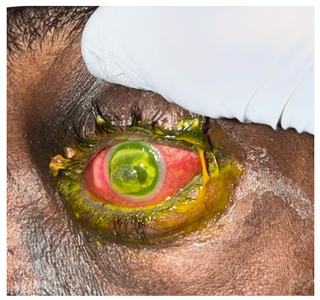
A 75-year-old woman with preexisting Rai stage 0 CLL (del13q) and new T-LGL expansion was diagnosed with IDH-wildtype, MGMT-methylated **glioblastoma** and initiated **temozolomide (TMZ)**-based chemoradiation. She developed severe, **refractory thrombocytopenia** followed by **warm autoimmune hemolytic anemia** requiring three hospitalizations and cessation of TMZ. Despite steroids, IVIG, and avatrombopag, thrombocytopenia persisted. Romiplostim was initiated, with rituximab under consideration for refractory thrombocytopenia. Bone marrow biopsy revealed a stable T-LGL clone and evolving CHIP with rising *RUNX1* VAF, suggesting a complex, multifactorial immune dysregulation landscape.

CONCLUSIONS

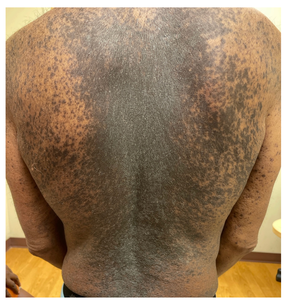
Together, these cases demonstrate that **CLL** is not a passive bystander but an active immunologic substrate that **amplifies the risk of severe paraneoplastic syndromes and unmasks autoimmune toxicity** from therapies such as TMZ. Both cases underscore the necessity of proactive multidisciplinary collaboration between malignant hematology, neuro-oncology, and ophthalmology. **These cases also highlight the emerging therapeutic role of BTK and JAK inhibitors in immune-mediated CLL complications**. These presentations are directly relevant to Society of Hematologic Oncology's mission of advancing care in hematologic malignancies where immune dysregulation drives outcomes.

CLINICAL & IMAGING FINDINGS

CASE 1: Paraneoplastic Pemphigus with Ocular Devastation

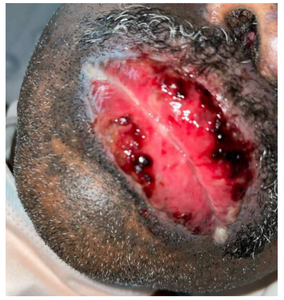


A. Left eye: fulminant corneal melt with uveal prolapse, necessitating evisceration



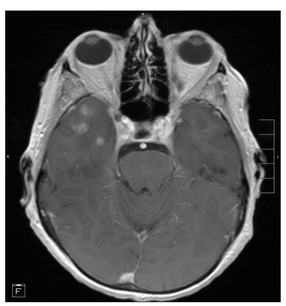
B. Diffuse hyperpigmented patches, sequela of extensive skin involvement

C. Oral mucosal blistering/erosion consistent with paraneoplastic pemphigus

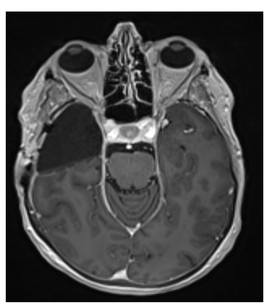


D. Extensive perioral ulcerations associated with paraneoplastic pemphigus

CASE 2: TMZ-Induced Autoimmune Cytopenias



A. MRI brain with skull base tumor involvement (IDH-wildtype, MGMT-methylated GBM)



B. Subsequent right temporal craniotomy

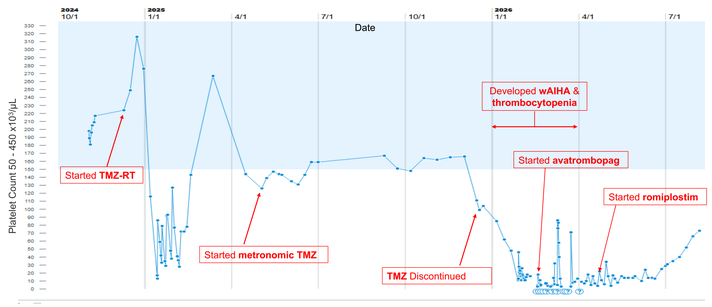


Figure 1: Platelet count trend illustrating severe, refractory thrombocytopenia during and after TMZ-based chemoradiation

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