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Case Report

Status Epilepticus as Immune Effector Cell–Associated Neurotoxicity (Icans) During Blinatumomab in High-Risk B-Cell Acute Lymphoblastic Leukemia

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Abstract

Blinatumomab, a CD19 × CD3 bispecific T-cell engager, improves outcomes in Relapsed/Refractory (R/R) and Measurable Residual Disease (MRD) positive B-Cell Acute Lymphoblastic Leukemia (B-ALL) but can trigger neurologic toxicities, including Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS). We report a 19-year-old male with high-risk B-ALL who developed grade IV ICANS presenting as status epilepticus within 18 hours of blinatumomab initiation. Seizure control required benzodiazepines, airway protection, and high-dose corticosteroids. Neuroimaging and Cerebrospinal Fluid (CSF) studies excluded structural, leukemic, or infectious etiologies. After resolution, blinatumomab was re-introduced at a reduced dose with careful escalation, without recurrence, and the patient proceeded to Allogeneic Hematopoietic Stem-Cell Transplantation (allo-HSCT) in MRD-negative remission. This case underscores the need for early neurologic monitoring and rapid, steroid-based management of severe ICANS during blinatumomab therapy.

Keywords: blinatumomab; B-ALL; ICANS; Status epilepticus; Neurotoxicity; CRS; Allo-HSCT

Introduction

Adult and Adolescent/Young Adult (AYA) outcomes in B-ALL have improved with pediatric-inspired regimens, MRD-guided therapy, and targeted immunotherapies [1-3]. Blinatumomab links cytotoxic T cells (CD3) to CD19-positive leukemia cells, forming cytolytic synapses and promoting apoptosis/lysis [4]. In the phase 3 Tower trial, blinatumomab prolonged overall survival versus chemotherapy in R/R B-ALL, leading to regulatory approval; efficacy in MRD-positive disease was shown in a separate study that supported expanded approval [5,6].

Neurologic Adverse Events (AEs) with blinatumomab range from tremor and confusion to seizures and encephalopathy, reflected in trial reports and product labelling [5,7-10]. ICANS provides a unified clinical framework for neurotoxicity grading and management across immune-effector platforms [8]. Although seizures occur in a minority of patients, status epilepticus is rare and can be life-threatening, requiring immediate recognition and intervention [7-10,12].

Case Presentation

Baseline disease and genetics. A 19-year-old male (June 2022) had BCR-ABL1–negative, CD19/CD20-positive B-ALL. Cytogenetics showed a hypotriploid karyotype (62-65), 9p deletion, and loss of Y. FISH demonstrated a triploid/near-triploid population with gains of ABL1 (9q34), BCR (22q11.2), KMT2A/MLL (11q23), PBX1 (1q23), and TCF3 (19p13.3).

Front-line therapy and relapse. The patient received a pediatric-inspired AYA protocol (AYA-15), achieving complete remission with MRD negativity by flow cytometry. During maintenance (cycle 7), he developed febrile neutropenia with circulating blasts, consistent with relapse. One cycle of inotuzumab ozogamicin rendered the marrow MRD-negative.

Blinatumomab initiation and acute deterioration. For bridging to allow-HSCT, continuous-infusion blinatumomab 28 μg/day was started. Approximately 18 hours later, he developed low-grade fever compatible with grade 1 Cytokine-Release Syndrome (CRS), followed by abrupt neurologic decline to grade IV ICANS with five generalized tonic–clonic seizures (~2 min each) over several hours. Blinatumomab was immediately interrupted. Lorazepam 0.5 mg terminated the first event transiently; recurrent seizures required three doses of midazolam 2 mg with only partial control. Ongoing seizure activity for ~5 hours met criteria for status epilepticus.

Diagnostic work-up. Non-contrast head CT and brain MRI showed no acute lesions. CSF was negative for blasts; bacterial/viral/fungal testing was negative. Laboratory evaluation excluded significant metabolic derangements. Findings supported severe ICANS-related seizures rather than CNS leukemia or infection.

Management and ICU course. The patient was intubated for airway protection. High-dose corticosteroids were given (dexamethasone 8 mg bolus → 20 mg bolus → 20 mg every 6 hours), with a brief interval of methylprednisolone before returning to dexamethasone. Neurologic status improved gradually; seizures resolved and he was extubated after ~1 week. Examination returned to baseline.

Re-challenge and outcome. Blinatumomab was re-introduced at 9 μg/day with slow escalation under close monitoring; no recurrent neurotoxicity occurred. He proceeded to allo-HSCT in MRD-negative

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remission and remains in remission at last follow-up.

Discussion

Incidence, timing, and clinical spectrum

Across studies and labelling, neurologic AEs occur in a meaningful subset of blinatumomab-treated patients, with variability in incidence estimates owing to differences in ascertainment and grading [5,7-10]. Seizures are uncommon but well-described, and critically for clinical practice can occur early, including within the first 24-48 hours of infusion, as seen here [9,10]. ICANS offers a standardized lexicon for severity grading, integrating features such as depressed level of consciousness, seizures, motor findings, and neurocognitive changes [8].

Pathophysiology

Blinatumomab rapidly activates T cells, leading to cytokine release and downstream endothelial activation. While mechanistic data are more mature in CAR-T literature, similar pathways endothelial injury and transient Blood Brain Barrier (BBB) dysfunction are implicated in Bite-related neurotoxicity [11,12]. Endothelial/BBB perturbation allows cytokines and immune cells to access the CNS, producing excitotoxicity and seizure propensity in susceptible patients [11,12]. Patient-level factors (e.g., prior CNS disease, high disease burden, infection, metabolic disturbances) may amplify risk, although consistent predictors remain limited [7-10,12].

Differential diagnosis and evaluation

ICANS is a diagnosis of exclusion. Acute imaging (non-contrast CT to exclude hemorrhage; MRI for parenchymal or inflammatory lesions) and CSF analysis to rule out leukemic infiltration or infection are essential, alongside metabolic panels and medication review. Our patient's negative MRI/CSF strengthened the attribution to ICANS.

Management principles

Management aligns with ASTCT-informed algorithms adapted to blinatumomab [8-10]:

1. Immediate drug interruption for grade ≥ 3 neurotoxicity;
2. Seizure control with benzodiazepines ± escalation to additional antiseizure medications if needed;
3. High-dose corticosteroids (e.g., dexamethasone 10-20 mg IV q6h) for grade ≥ 3 ICANS;
4. Airway protection/ICU care for refractory seizures or depressed consciousness;
5. Treat co-existing CRS (e.g., tocilizumab) when present recognizing that IL-6 blockade is not a primary treatment for isolated neurotoxicity [8-10].

Our patient's course rapid steroid initiation plus airway protection mirrors these steps and likely contributed to full neurologic recovery.

Seizure prophylaxis

Routine primary seizure prophylaxis is not universally recommended for blinatumomab; many centers reserve it for patients with prior seizures, CNS pathology, or other risk factors, given low absolute seizure risk and drug-drug interaction considerations [9-12]. Our institutional practice is concordant [13,14].

Re-Challenge after severe ICANS

Evidence is limited but suggests that cautious re-challenge after complete resolution and steroid taper can be considered if the benefit-risk profile is favourable (e.g., to achieve/maintain MRD-negative status prior to allo-HSCT). Strategies include dose reduction, slower escalation, inpatient monitoring, and low threshold for interruption if symptoms recur [9,10]. Our successful re-introduction at 9 μg/day without recurrence supports the feasibility of individualized re-challenge.

Clinical implications

This case emphasizes: (i) the need for intensive neurologic observation during initiation (first 24-48 h), (ii) rapid, protocolized escalation for seizures/status epilepticus, and (iii) disciplined evaluation to exclude alternative etiologies. For transplant-intent pathways, timely control of ICANS permits continuation toward potentially curative allo-HSCT [15-18].

Limitations

Single-patient observations limit generalizability; serum cytokines or neuroimaging biomarkers of endothelial activation were not obtained [19,20]. Nonetheless, the temporal association, exclusion of competing diagnoses, and steroid responsiveness make ICANS highly likely.

Patient perspective

The patient and family were counselled about suspected immune-mediated mechanisms, acute risks, and the rationale for cautious re-exposure and transplant. They agreed with the plan to proceed to curative-intent allo-HSCT after recovery.

Learning Points

1. Severe ICANS from blinatumomab can present within 24-48 hours of infusion; continuous early neurologic monitoring is advisable [9,10].
2. For grade ≥ 3 neurotoxicity, stop infusion, manage seizures immediately, and start high-dose corticosteroids; exclude structural, leukemic, and infectious causes [8-10].
3. Re-challenge may be feasible after full recovery using reduced starting dose and slow escalation with close monitoring [9,10].

References

1. Stock W, Luger SM, Advani AS, Yin J, Harvey RC, Mullighan CG, et al. A pediatric regimen for older adolescents and young adults with acute lymphoblastic leukemia: CALGB 10403. Blood. 2019;133:1548-59.
2. Berry DA, Zhou S, Higley H, Mukundan L, Fu S, Reaman GH, et al. Association of MRD with outcomes in pediatric and adult ALL: meta-analysis. JAMA Oncol. 2017;3(7):e170580.
3. Maury S, Chevret S, Thomas X, Heim D, Leguay T, Huguet F, et al. Rituximab in B-lineage adult ALL. N Engl J Med. 2016;375(11):1044-53.
4. Newman MJ, Benani DJ. A review of blinatumomab, a novel immunotherapy. J Oncol Pharm Pract. 2016;22(4):639-45.
5. Kantarjian H, Stein A, Gökbuget N, Fielding AK, Schuh AC, Ribera JM, et al. Blinatumomab vs chemotherapy for Advanced Acute Lymphoblastic Leukemia. N Engl J Med. 2017;376(9):836-47.
6. Gökbuget N, Dombret H, Bonifacio M, Reichle A, Graux C, Faul C, et al. Blinatumomab in MRD-positive B-ALL (adults). Blood. 2018;131(14):1522-31.
7. Topp MS, Gökbuget N, Stein AS, Zugmaier G, O'Brien S, Bargou RC, et al. Safety and activity of blinatumomab in adult R/R B-precursor ALL: phase 2. Lancet Oncol. 2015;16(1):57-66.
8. Lee DW, Santomasso BD, Locke FL, Ghobadi A, Turtle CJ, Brudno JN, et al. ASTCT

consensus grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. Biol Blood Marrow Transplant. 2019;25(4):625-38.

9. U.S. Prescribing Information: BLINCYTO® (blinatumomab). 2024.
10. EMA Product Information: BLINCYTO®. 2025.
11. Gust J, Hay KA, Hanafi L-A, Li D, Myerson D, Gonzalez-Cuyar LF, et al. Endothelial activation and BBB disruption in neurotoxicity after CD19 CAR-T. Cancer Discov. 2017;7(12):1404-19.
12. Śliwa-Tytko P, Kaczmarska A, Lejman M, Zawitkowska J. Neurotoxicity in ALL chemotherapy and immunotherapy (review). Int J Mol Sci. 2022;23(10):5515.
13. Santomasso BD, Park JH, Salloum D, Riviere I, Flynn J, Mead E, et al. Clinical and biological correlates of neurotoxicity in cellular therapies. Nat Rev Clin Oncol. 2021;18(8):759-71.
14. Locatelli F, Zugmaier G, Mergen N, Bader P, Jeha S, Schlegel PG, et al. Blinatumomab in pediatric R/R B-ALL: RIALTO final analysis. Blood Adv. 2022;6(3):1004-14.
15. Goebeler ME, Knop S, Viardot A. Blinatumomab in R/R non-Hodgkin lymphoma: phase 1 (safety signals incl. neurotox). J Clin Oncol. 2016;34:1104-11.
16. Brudno JN, Kochenderfer JN. Toxicities of CAR-T and other T-cell therapies. Nat Rev Clin Oncol. 2016;127(26):3321-30.
17. Rubin DB, Danish HH, Ali AB. Neurologic toxicities associated in cellular immunotherapy. Neurology. 2019;92:542-554.
18. Neelapu SS, Tummala S, Kebriaei P, Wierda W, Locke FL, Lin Y, et al. Toxicity management after chimeric antigen receptor T cell therapy: one size does not fit 'ALL'. Nat Rev Clin Oncol. 2018;15(4):47-62.
19. Zhang B, Li X, Yin T, Qin D, Chen Y, Ma O, et al. Neurotoxicity of Tumor Immunotherapy: The Emergence of Clinical Attention. J Onclo. 2022: 4259205.
20. Amgen. Blinatumomab (BLINCYTO®) HCP materials risk mitigation and monitoring (access for clinicians). 2025.