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Progressive Multifocal Leukoencephalopathy Following CAR T-Cell Therapy and Bispecific Antibody Therapy in Adults with Hematologic Malignancies: A Systematic Review

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Abstract

Background

Progressive multifocal leukoencephalopathy (PML) is a rare, often fatal demyelinating CNS disease caused by JC virus reactivation under profound cellular immunosuppression. PML has increasingly been reported in hematologic malignancy patients treated with CAR T-cell therapy and T-cell-redirecting bispecific antibodies.

Methods

The systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 guidelines. A systematic search of the electronic databases PubMed, Science Direct and Google Scholar were done from database inception to August 25, 2026, using the key words "Progressive Multifocal Leukoencephalopathy", "CAR T cell therapy", "Bispecific Antibody". Studies which reported cases in adult population were eligible. A narrative synthesis was done from the included studies.

Results

18 studies were included in the review. Four pharmacovigilance studies FAERS data put CD19-CAR-T-associated PML incidence at 0.9 per 1,000 recipients; FAERS disproportionality analysis flagged a significant epcoritamab-specific signal. A French multisource study (registry/FPVD/VigiBase) identified 14 bispecific-associated PML cases in myeloma, with a markedly elevated reporting odds ratio versus other myeloma therapies. Median time to onset ranged 2–22 months post-treatment. Out of 2 retrospective studies one reported a case of PML after CART cell therapy, and one reported a case of five patients with multiple myeloma treated with Bispecific antibodies. Case reports reported 13 cases with 9/13 (69.23%) females, with mean age of 63.92 years. Among the 9 cases, the mean time of survival after CAR-T therapy or bispecific antibody treatment was 11.57 months. The common clinical manifestations included weaknesses of the limbs, cognitive disability and visual disturbances. MRI findings included multifocal non enhancing white matter lesions.

Conclusion

PML is a rare but serious brain infection that can happen after CAR T-cell and bispecific antibody treatments for blood cancers, because these therapies weaken the immune system.

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