Cancer Management and Research

Elevate Series

Open Access Full Text Article

CASE REPORT

Successful Treatment of Diffuse Large B-Cell Lymphoma and Antisynthetase Syndrome with Bispecific Antibody Glofitamab

Chong Wei[1,*], Mei Zhang[2,*], Danqing Zhao[1], Wei Zhang[1], Yan Zhang[2]

[1]Department of Hematology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, People's Republic of China; [2]Department of Hematology, Beijing Longfu Hospital, Beijing, People's Republic of China

*These authors contributed equally to this work

Correspondence: Wei Zhang; Yan Zhang, Email vv1223@vip.sina.com; zhangyan7217@sina.com

Abstract: Glofitamab, a CD20×CD3 T-cell–engaging bispecific monoclonal antibody, has emerged as a promising therapeutic agent for relapsed/refractory B-cell non-Hodgkin lymphoma. The advent of chimeric antigen receptor T-cell therapy and T-cell-engaging bispecific antibodies has also stimulated growing interest in their potential application in autoimmune diseases. Here, we report a case of diffuse large B-cell lymphoma (DLBCL) in a patient with a long-standing history of antisynthetase syndrome (ASyS). The patient achieved complete remission of lymphoma with third-line glofitamab therapy after failure of first-line R-CHOP and second-line polatuzumab vedotin combined with lenalidomide. Remarkably, her ASyS symptoms, which had been refractory to multiple immunosuppressive agents (cyclosporine, methotrexate, hydroxychloroquine) and targeted therapies (tofacitinib, baricitinib), also resolved following glofitamab treatment. This case underscores the potential of glofitamab not only as an effective treatment for refractory DLBCL but also as a novel therapeutic strategy for concomitant autoimmune manifestations, warranting further investigation in the context of autoimmune disorders.

Keywords: diffuse large B-cell lymphoma, T-cell-engaging bispecific antibody, glofitamab, antisynthetase syndrome

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin's lymphoma (NHL) and is associated with poor outcomes in patients who were refractory to or relapsed after first-line R-CHOP therapy. Glofitamab, a CD20×CD3 T-cell-engaging bispecific monoclonal antibody, has emerged as a promising therapeutic option for adult patients with relapsed or refractory B-cell NHL, particularly those who have received at least two prior lines of systemic therapy.

Antisynthetase syndrome (ASyS) is a distinct clinical entity within the spectrum of idiopathic inflammatory myopathies (IIM) and is considered a protective factor against hematological malignancies, rendering the coexistence of DLBCL and ASyS exceptionally rare. However, this comorbidity presents unique therapeutic challenges due to potential bidirectional influences between the two diseases. On the one hand, the immunosuppressive agents required to manage ASyS, such as glucocorticoids, calcineurin inhibitors, or JAK inhibitors, may impair anti-lymphoma immune responses and reduce the efficacy of lymphoma-directed therapies. On the other hand, cytotoxic or immunomodulatory agents used to treat DLBCL may exacerbate or unmask autoimmune manifestations. Furthermore, the risk of treatment-related infections is increased due to overlapping immunosuppressive mechanisms.

The advent of chimeric antigen receptor T (CAR-T) cell therapy and T-cell-engaging bispecific antibodies has stimulated interest in their potential application beyond hematologic malignancies, including autoimmune diseases (AID). Several case reports have demonstrated the successful use of CD19 CAR-T cell therapy in refractory AID, such as rheumatoid arthritis, systemic lupus erythematosus (SLE), and ASyS. However, to date, there have been no published reports describing the use of glofitamab in patients with autoimmune diseases. Here, we report a case of DLBCL in a patient with a long-standing history of ASyS. The patient achieved complete remission (CR) of lymphoma

Received: 22 April 2025
Accepted: 23 August 2025
Published: 27 August 2025

with third-line glofitamab therapy after failing multiple prior treatments. Remarkably, her ASyS symptoms, which had been refractory to numerous immunosuppressive and targeted agents, also resolved after glofitamab therapy.

Case Presentation

A 46-year-old female presented with a 14-year history of recurrent rashes and myalgia, and a one-month history of a pulmonary mass. In 2009, she developed violaceous rashes on her anterior chest and rough, thickened skin on her palms, accompanied by bilateral knee joint pain. Laboratory tests revealed elevated muscle enzymes, with creatine kinase (CK) levels at 330 IU/L. She was diagnosed with connective tissue disease and responded to glucocorticoid treatment. In 2018, her rash worsened, accompanied by recurrent fever, muscle soreness, and lower limb weakness. Electromyography indicated myogenic damage, while a muscle biopsy revealed degeneration, necrosis, and regeneration of muscle fibers, along with focal perivascular lymphocyte infiltration, consistent with inflammatory myopathy. Chest computed tomography (CT) revealed interstitial lung disease. Antibody screening showed a positive antinuclear antibody (ANA) titer of 1:0000 with a cytoplasmic granular pattern, anti-Ro-52 (++), and anti-Jo-1 (+++), leading to a diagnosis of ASyS. Between 2019 and 2023, she was treated with glucocorticoids, various immunosuppressants (cyclosporine, methotrexate, hydroxychloroquine), and targeted therapies (tofacitinib, baricitinib) without significant improvement.

In February 2023, a follow-up chest CT revealed two soft tissue masses adjacent to the pleura, one in the middle lobe and one in the lower lobe of the right lung (Figure 1A–D). CT-guided lung biopsy confirmed DLBCL, non-germinal center type. PET/CT showed increased metabolic activity in a subpleural mass in the right lower lobe (2.6×3.9 cm, SUVmax 15.14), another subpleural mass in the right middle lobe (5.3×3.4 cm, SUVmax 7.3), bilateral axillary lymph

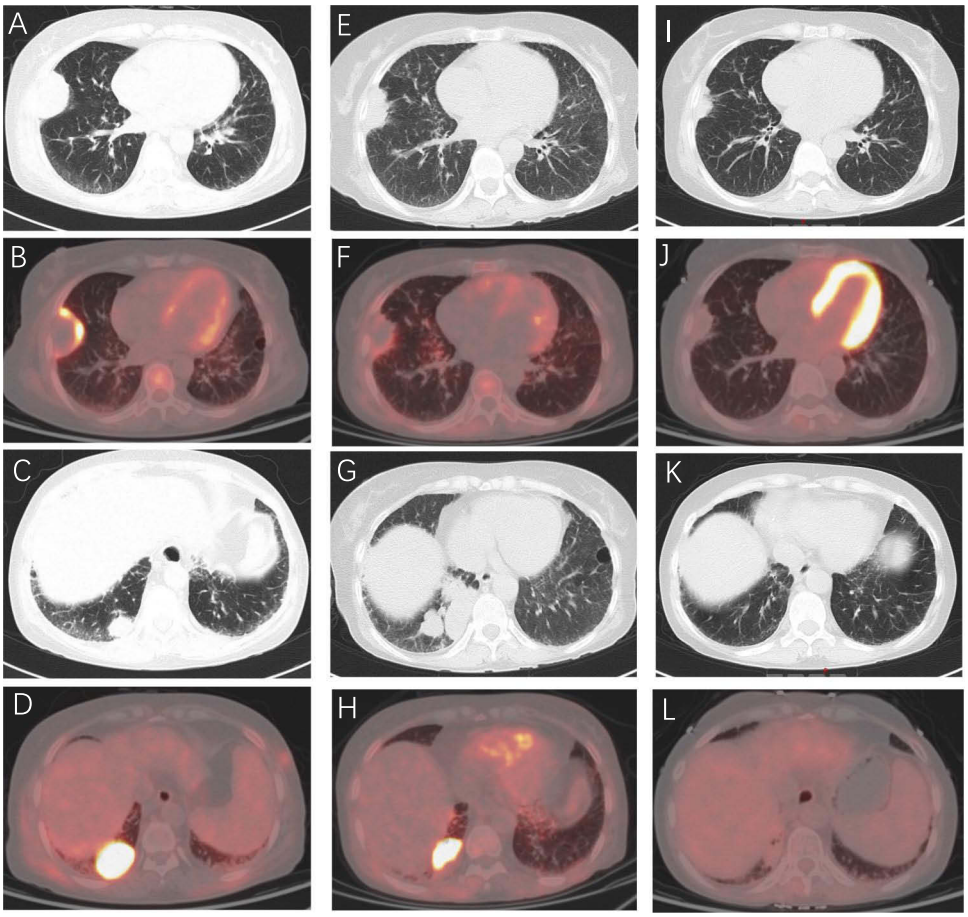

Figure 1 Computed tomography (CT) and positron emission computed tomography (PET) of this patient. (**A**–**C**) CT finding of the pulmonary lesions of on Feb 2023; (**B**–**D**) PET showing increased metabolic activity of the pulmonary lesions of on Feb 2023; (**E**–**H**) The pulmonary lesions on CT scan and PET/CT after 8 cycles of R-CHOP therapy; (**I**–**L**) Significant reduction of the pulmonary lesions with decreased metabolic activity after 4 cycles of glofitamab therapy.

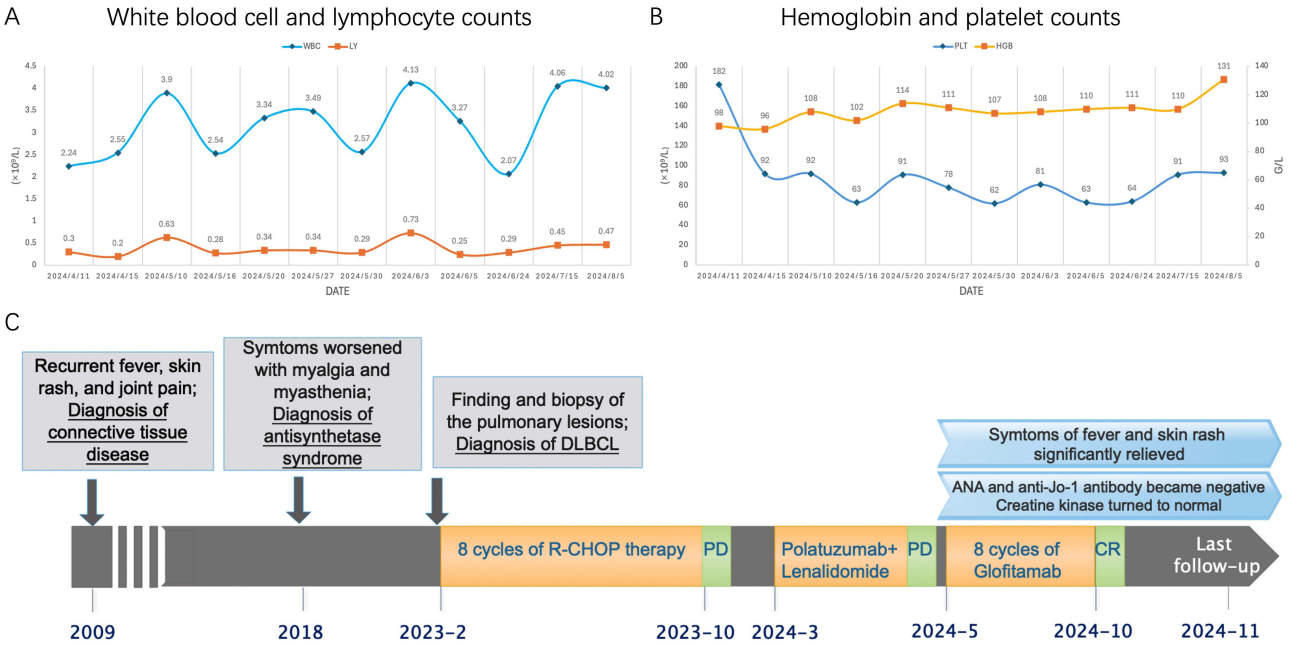

Figure 2 A timeline illustrating the clinical course and treatment of this case. (**A**) Changes of the white blood cell counts and lymphocyte counts during glofitamab treatment; (**B**) Changes of the hemoglobin and platelet counts during glofitamab treatment. (**C**) A timeline illustrating the clinical course and treatment of this case.

nodes (0.5–1.1 cm, SUVmax 4.1), and multiple subcutaneous nodules. The patient was diagnosed with DLBCL, Ann Arbor stage IV, with an International Prognostic Index score of 4. She received eight cycles of R-CHOP (rituximab combined with cyclophosphamide, doxorubicin, vincristine, and, prednisone) therapy as first-line treatment. End-of-treatment PET/CT showed a slight reduction in the size and metabolic activity of the right middle lobe mass, but increased metabolic activity in the right lower lobe mass, indicating disease progression (Figure 1E–H). A repeat biopsy of the right lung mass reconfirmed the diagnosis of DLBCL. During this time, she continued to experience recurrent fever, rashes, and muscle weakness.

The patient was subsequently treated with second-line polatuzumab vedotin combined with lenalidomide, but no remission was achieved. Third-line therapy with the CD20×CD3 bispecific antibody glofitamab was initiated. After four cycles, follow-up PET/CT revealed decreased metabolic activity and reduced size of the right middle and lower lobe masses (SUVmax 1.8), indicating complete metabolic remission (Figure 1I–L). During glofitamab treatment, the patient experienced grade 1 cytokine release syndrome (CRS), grade 2 leukopenia, and grade 2 thrombocytopenia, with no serious infections. In addition to the successful lymphoma treatment, the patient showed significant improvement in fever and rashes. As of October 2024, she has completed eight cycles of glofitamab, with lymphoma remaining in sustained CR. Following treatment, the patient experienced significant improvement in her dermatomyositis symptoms. Objective indicators of ASyS also improved, including normalization of CK levels and conversion to negative ANA and anti-Jo-1 antibody status. Figures 2A and B depict the dynamic changes in white blood cell count, hemoglobin, and platelet levels during glofitamab treatment. Figure 2C presents a timeline summarizing the patient's clinical course.

Discussion

Glofitamab is a CD20×CD3 T-cell-engaging bispecific monoclonal antibody under development for the treatment of B-cell NHLs.[1] In a Phase II trial evaluating glofitamab in patients with relapsed or refractory DLBCL who had received at least two prior lines of therapy, encouraging results were reported, with a CR rate of 39% and a 12-month progression-free survival rate of 37%.[2] Glofitamab has also demonstrated efficacy in patients with DLBCL relapsing after CAR-T cell therapy, inducing the expansion of residual CAR-T cells.[3] In this case, the patient, who was primarily refractory to R-CHOP therapy and did not respond to polatuzumab vedotin combined with lenalidomide, received glofitamab as third-line treatment and achieved CR.

https://doi.org/10.2147/CMAR.S536049

The patient's medical history included a prior diagnosis of ASyS, preceding the onset of lymphoma. ASyS is a distinct entity within the spectrum of IIM.[4] Patients with IIM are recognized to have an increased risk of malignancy, with symptoms often preceding tumor onset. However, within the IIM spectrum, ASyS has been reported as a protective factor against hematological malignancies.[5] In this patient, typical dermatomyositis symptoms began 14 years before the lymphoma diagnosis. Given the delayed onset of lymphoma and the relatively low malignancy risk associated with ASyS, ASyS was not considered a paraneoplastic syndrome in this case. Interestingly, the patient's ASyS symptoms resolved following glofitamab treatment, coinciding with the lymphoma response. Prior treatment for ASyS with various immunosuppressive agents, JAK inhibitors, and rituximab yielded unsatisfactory results. Unexpectedly, her ASyS symptoms responded well to glofitamab, with ANA and anti-Jo-1 antibodies becoming negative.

With the advent of CAR-T cell therapy, which has shown promising outcomes in B-cell NHLs, researchers have explored its potential application in AID, including rheumatoid arthritis, SLE, and multiple sclerosis. Emerging evidence suggests that CD19 CAR-T cell therapy may effectively manage refractory AID. Preliminary studies have indicated that CD19 CAR-T cell therapy is a safe and effective therapeutic option in SLE.[6,7] Case reports have also described successful use of CD19 CAR-T cell therapy in refractory ASyS.[8] Similar to CAR-T cell therapy, T-cell–engaging bispecific antibodies recruit T cells to mediate B-cell cytotoxicity, presenting a potential alternative strategy for treating refractory AID. Schreiber et al recently reported the effective use of a BCMA-targeting bispecific T-cell–engaging antibody in a patient with treatment-refractory LRP4-positive myasthenia gravis.[9] To the best of our knowledge, this is the first report of successful ASyS treatment with a CD20×CD3 T-cell–engaging bispecific antibody, glofitamab.

T-cell engagers (TCEs) may offer certain advantages over CAR-T cell therapy in AID treatment. First, TCEs enable precise dosing and treatment duration, offering greater control compared to CAR-T cell therapy. Additionally, TCE therapy does not require lymphodepletion before infusion, potentially lowering the risk of infection. Furthermore, TCEs do not require the lag time associated with leukapheresis and CAR-T cell engineering, allowing for more rapid treatment initiation. These features suggest that TCEs may address some limitations of CAR-T cell therapy in AID management. However, the concurrent use of immunosuppressants, such as mycophenolate mofetil, may impair T-cell function and reduce the efficacy of both CAR-T cell and TCE therapies.[10] To mitigate this, withholding immunosuppressants for a period to allow T-cell recovery may be considered in both treatment approaches.[11]

While this case highlights the potential immunomodulatory effects of T-cell-engaging bispecific antibodies, the use of TCEs in AIDs also raises important considerations regarding the balance between efficacy and safety. Several risks must be considered. First, TCEs can induce CRS and immune effector cell–associated neurotoxicity syndrome, which may be particularly hazardous in patients with underlying systemic inflammation or end-organ dysfunction. Second, excessive or prolonged B-cell depletion may increase susceptibility to infections and impair vaccine responses. Careful patient selection, vigilant monitoring, and a deeper understanding of the immune contexture in AIDs are therefore essential when considering TCEs in this setting.

In conclusion, this single-case observation raises the possibility that T-cell–engaging therapies may offer benefit in refractory autoimmune diseases (AIDs), particularly in immunologically complex settings. However, given the inherent limitations of an isolated case, no definitive conclusions can be drawn. Ultimately, prospective clinical studies will be essential to evaluate the safety, efficacy, and broader applicability of TCEs in patients with AID.

Data Sharing Statement

Data supporting the findings of this study are available upon reasonable request from either of the corresponding authors, Dr. Yan Zhang or Dr. Wei Zhang.

Ethics and Consent

The patient had given written informed consent for the publication of any potentially identifiable images or data included in this article. Institutional approval from Peking Union Medical College Hospital review board was not required to publish the case details.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Bacac M, Colombetti S, Herter S, et al. CD20-TCB with obinutuzumab pretreatment as next-generation treatment of hematologic malignancies. *Clin Cancer Res*. 2018;24(19):4785–4797. doi:10.1158/1078-0432.CCR-18-0455
2. Dickinson MJ, Carlo-Stella C, Morschhauser F, et al. Glofitamab for relapsed or refractory diffuse large B-cell lymphoma. *N Engl J Med*. 2022;387(24):2220–2231. doi:10.1056/NEJMoa2206913
3. Rentsch V, Seipel K, Banz Y, et al. Glofitamab treatment in relapsed or refractory DLBCL after CAR T-cell therapy. *Cancers*. 2022;14(10):2516. doi:10.3390/cancers14102516
4. Tiniakou E, Mammen AL. Idiopathic inflammatory myopathies and malignancy: a comprehensive review. *Clin Rev Allergy Immunol*. 2017;52(1):20–33. doi:10.1007/s12016-015-8511-x
5. Mammen AL. Paraneoplastic myopathies. *Handb Clin Neurol*. 2024;200:327–332.
6. Mackensen A, Müller F, Mougiakakos D, et al. Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus. *Nat Med*. 2022;28(10):2124–2132. doi:10.1038/s41591-022-02017-5
7. Li M, Zhang Y, Jiang N, et al. Anti-CD19 CAR T cells in refractory immune thrombocytopenia of SLE. *N Engl J Med*. 2024;391(4):376–378. doi:10.1056/NEJMc2403743
8. Müller F, Boeltz S, Knitza J, et al. CD19-targeted CAR T cells in refractory antisynthetase syndrome. *Lancet*. 2023;401(10379):815–818. doi:10.1016/S0140-6736(23)00023-5
9. Schreiber S, Al-Dubai M, Vielhaber S, et al. Effective use of BCMA-targeting bispecific T cell-engaging antibody in treatment-refractory LRP4+ myasthenia gravis. *Mol Ther*. 2025;S1525-0016(25):00480.
10. Nakamura M, Ogawa N, Shalabi A, et al. Positive effect on T-cell regulatory apoptosis by mycophenolate mofetil. *Clin Transplant*. 2001;15(Suppl 6):36–40. doi:10.1034/j.1399-0012.2001.00006.x
11. Mamlouk O, Nair R, Iyer SP, et al. Safety of CAR T-cell therapy in kidney transplant recipients. *Blood*. 2021;137(18):2558–2562. doi:10.1182/blood.2020008759