

A Dual Response to CD20xCD3 Bispecific Therapy: Remission of Relapsed Diffuse Large B-cell Lymphoma and Improvement in Immune Thrombocytopenia

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Abstract

Immune thrombocytopenia (ITP) is an autoimmune cytopenia that may occur in association with lymphoproliferative disorders. In such cases, treatment of the underlying malignancy may influence platelet recovery. CD20xCD3 bispecific antibodies have become important options for relapsed or refractory diffuse large B-cell lymphoma (DLBCL), but their effect on coexisting autoimmune cytopenias is not well defined. We report the case of an 81-year-old woman with relapsed DLBCL arising from an underlying marginal zone lymphoma and longstanding ITP. She achieved complete metabolic remission with initial rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone (R-CHOP) and again with polatuzumab vedotin, bendamustine, and rituximab (Pola-BR) after the first relapse, but her thrombocytopenia persisted. Following a second relapse, she was treated with epcoritamab, a CD20xCD3 bispecific T-cell engager. Her course was complicated by steroid-induced hyperglycemia, grade 1 cytokine release syndrome, and adrenal insufficiency, but she achieved complete metabolic remission on follow-up positron emission tomography. Her platelet counts also markedly improved, increased to 142 K/mcL (140-450 K/mcL) from a chronically thrombocytopenic baseline. This case highlights the possibility that bispecific therapy may simultaneously control relapsed DLBCL and secondary ITP through depletion of pathogenic CD20-expression B cells, as well as exhaustion and redirection of T-cells. Further study is needed to determine whether this represents a reproducible therapeutic effect.

Categories: Hematology, Internal Medicine, Oncology

Keywords: bispecific t-cell engager, diffuse large b cell lymphoma (dlbcl), epcoritamab, immune thrombocytopenia (itp), non-hodgkin's lymphomas

Introduction

Immune thrombocytopenia (ITP) is an acquired autoimmune disorder characterized by immune-mediated platelet destruction and impaired platelet production. It was once thought to be mainly antibody-driven. However, it is now understood to involve broader immune dysregulation, including autoreactive B cells, plasma cells, Fc-mediated platelet clearance, and T-cell abnormalities. In adults, treatment is guided by bleeding risk and platelet count. Corticosteroids remain standard initial therapy, with subsequent options including thrombopoietin receptor agonists, rituximab, and splenectomy. Rituximab is especially relevant in ITP because CD20-directed B-cell depletion can reduce autoantibody production and disrupt the immune pathways that sustain disease. Long-term remission remains limited in many patients, however [1].

Autoimmune cytopenias can occur in association with lymphoproliferative disorders, including non-Hodgkin lymphomas. They may appear before, during, or after the diagnosis of malignancy. In these cases, treatment of the underlying lymphoma is often central, as improvement in blood counts may parallel lymphoma response [2]. This is especially relevant in diffuse large B-cell lymphoma (DLBCL), where salvage treatment may also affect the immune mechanisms driving concurrent cytopenias.

In recent years, CD20xCD3 bispecific antibodies have expanded the treatment options for relapsed or refractory DLBCL. Epcoritamab is a subcutaneous CD20xCD3 bispecific antibody that redirects endogenous T cells toward CD20-expressing B cells. In heavily pretreated large B-cell lymphoma, it has shown an overall response rate of 63.1% and a complete response rate of 40.1% per the EPCORE NHL-1 trial. Cytokine release syndrome is the most common adverse event and is typically mitigated through step-up dosing [3]. Other CD20xCD3 bispecific antibodies, including glofitamab, have also shown meaningful activity in relapsed or refractory DLBCL, further supporting the role of this drug class in B-cell malignancies [4].

Given that these agents deplete CD20-expressing B cells while simultaneously engaging cytotoxic T-cell activity, they have generated interest beyond lymphoma treatment. This includes possible use in antibody-mediated autoimmune disease [5]. However, evidence for their use in ITP remains limited, and any beneficial effect on thrombocytopenia in this setting is currently viewed as hypothesis-generating rather

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than established. We present a case of relapsed DLBCL with coexisting ITP in which treatment with epcoritamab was associated with complete metabolic remission of lymphoma and concurrent improvement in chronic thrombocytopenia.

Case Presentation

An 81-year-old woman with a medical history notable for nonischemic heart failure with reduced ejection fraction, nonobstructive coronary artery disease, valvular heart disease, sick sinus syndrome status post permanent pacemaker placement, hypertension, hyperlipidemia, type 2 diabetes mellitus, chronic kidney disease stage 3, hypothyroidism, gastroesophageal reflux disease, and chronic back pain related to a T12 compression fracture initially presented with progressive left upper quadrant abdominal pain and back pain. Imaging revealed retroperitoneal, precaval, and mediastinal lymphadenopathy, including a bulky peripancreatic soft tissue mass concerning for lymphoproliferative disease. Biopsy of the retroperitoneal mass demonstrated a small B-cell lymphoma. Subsequent staging with bone marrow biopsy and excisional supraclavicular lymph node biopsy confirmed DLBCL, likely arising from an underlying marginal zone lymphoma. She was treated with rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone (R-CHOP) and achieved a complete metabolic response on end-of-treatment positron emission tomography (PET).

During surveillance, she was found to have persistent thrombocytopenia. Platelet autoantibody testing was positive for antibodies against GPIIb/IIIa, GPIa/IIa, and GPIb/IX, supporting a diagnosis of ITP. Given the mild nature of her thrombocytopenia at that time, she was managed conservatively without ITP-directed therapy. Although it was noted that her platelet counts were steroid-responsive.

She later developed recurrent abdominal and back pain, and repeat imaging demonstrated new thoracoabdominal lymphadenopathy, splenic lesions, and multifocal osseous involvement concerning for relapsed lymphoma. PET-CT confirmed multifocal metabolically active disease involving nodal, splenic, gastrointestinal, and skeletal sites (Figure 1), and a repeat lymph node biopsy confirmed recurrent DLBCL. She was treated with polatuzumab vedotin, bendamustine, and rituximab (Pola-BR), with follow-up PET imaging demonstrating a second complete metabolic response. Despite remission of her lymphoma, thrombocytopenia persisted, with platelet counts remaining chronically below 50 K/mcL (140–450 K/mcL).

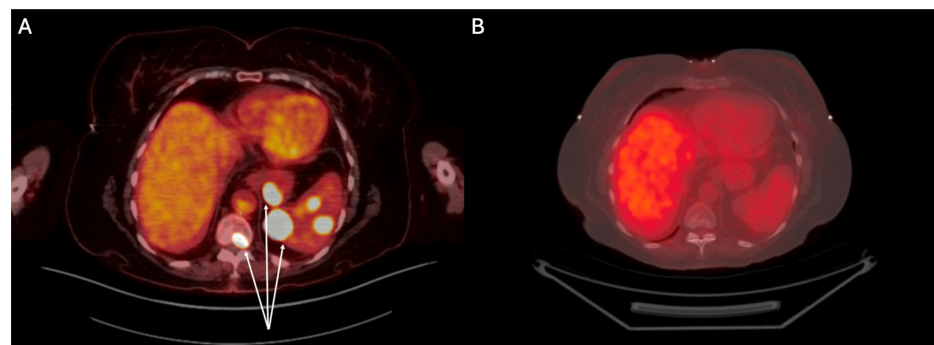


FIGURE 1: A) Positron emission tomography-computed tomography (PET-CT) depicting increased FDG uptake within the proximal stomach, spleen, and bone; B) Post-treatment PET-CT depicting resolution of FDG uptake, indicating metabolic response

She subsequently experienced a second relapse with progressive multifocal lymphadenopathy and extranodal involvement of the lung and kidney (Figure 2). Excisional lymph node biopsy again confirmed recurrent DLBCL, and she was started on epcoritamab. Her treatment course was complicated by steroid-induced hyperglycemia, grade 1 cytokine release syndrome, and iatrogenic adrenal insufficiency requiring hydrocortisone replacement. Nonetheless, she achieved a complete metabolic response on follow-up PET-CT, with resolution of previously identified lymphadenopathy and no new sites of disease.

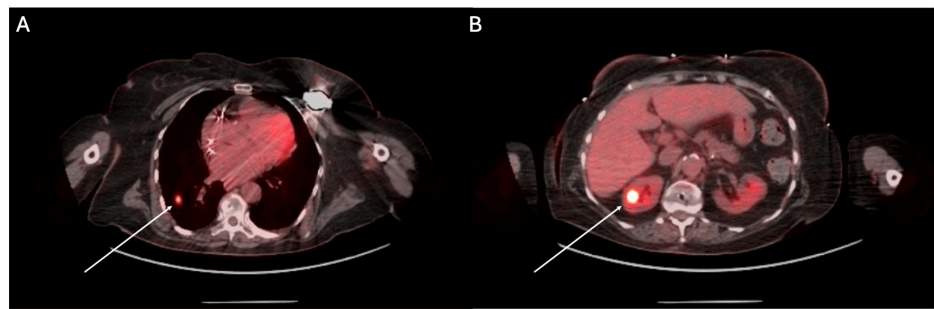


FIGURE 2: Positron emission tomography-computed tomography (PET-CT) depicting extra nodal FDG uptake in the right lower lobe of the lung (A) and right kidney (B)

Notably, her platelet count improved during treatment with epcoritamab. Prior to bispecific therapy, she had longstanding thrombocytopenia attributed to ITP, with platelet counts often in the mild to moderate thrombocytopenic range. During treatment, her platelet count rose progressively and reached 142 K/mcL (140–450 K/mcL), representing a clear improvement from her prior baseline. The concurrent improvement in thrombocytopenia and remission of relapsed DLBCL suggests that CD20-directed bispecific therapy may have provided simultaneous control of both disease processes through depletion of pathogenic CD20-expressing B cells.

Discussion

This case highlights a clinically important overlap between B-cell malignancy and autoimmune cytopenia. Secondary ITP in the setting of lymphoma can be difficult to diagnose and manage. Thrombocytopenia in these patients may reflect marrow involvement, treatment effect, splenic sequestration, or immune-mediated destruction. Prior literature suggests that when ITP occurs in association with non-Hodgkin lymphoma, platelet recovery often depends on successful treatment of the underlying malignancy rather than ITP-directed therapy alone [6]. The present case is notable because the patient's thrombocytopenia persisted despite prior lymphoma-directed treatment and only improved substantially after initiation of epcoritamab.

One possible explanation is that epcoritamab produced an effect similar to anti-CD20 monoclonal antibody therapy alone. Rituximab has long been used in ITP because depletion of CD20-positive B cells can reduce autoreactive B-cell populations, decrease autoantibody production, and alter downstream immune activation. However, rituximab responses in ITP are often incomplete or not durable, likely because long-lived plasma cells and broader immune dysregulation may persist despite conventional B-cell depletion [1]. In our patient, epcoritamab may have produced a deeper elimination of pathogenic CD20-expressing B-cell populations by recruiting endogenous T cells to directly eliminate target cells. This resulted in both lymphoma control and improvement in thrombocytopenia.

ITP is increasingly recognized as a disorder involving not only pathogenic autoantibodies, but also T-cell immune dysregulation, including abnormal helper T-cell activity, impaired regulatory T-cell function, and cytotoxic T-cell-mediated platelet destruction [7]. By redirecting endogenous T cells towards CD20-expressing B cells, CD20xCD3 bispecific antibodies may alter the immune network that sustains ITP. This dual effect of bispecific antibodies on pathogenic B-cell populations and T-cell exhaustion and redirection may help explain why platelet recovery occurred after epcoritamab despite persistent thrombocytopenia following prior lymphoma-directed therapies.

This interpretation is consistent with growing interest in CD20xCD3 bispecific antibodies as immune-modifying agents outside of oncology. Recent reviews have noted that bispecific antibodies capable of potent B-cell depletion may have theoretical and translational relevance in other autoantibody-mediated diseases [8]. However, published evidence in ITP remains limited, and current data is insufficient to regard these agents as established ITP therapy.

From a practical standpoint, this case is most relevant in patients with refractory or relapsed B-cell lymphoma and concomitant autoimmune thrombocytopenia, where a single therapy may affect both disease processes. Whether CD20xCD3 bispecific antibodies could eventually have a role in refractory ITP outside the setting of lymphoma remains unknown. This case suggests that improvement in concurrent autoimmune cytopenias may be an underrecognized effect of bispecific therapy and deserves further study.

Conclusions

We report a case of relapsed DLBCL with coexisting ITP in which treatment with epcoritamab was associated with both complete metabolic remission of lymphoma and marked improvement in chronic thrombocytopenia. Given the established role of CD20-directed B-cell depletion in ITP and the emerging activity of CD20xCD3 bispecific antibodies in relapsed or refractory DLBCL, this case is clinically noteworthy. Although current evidence is insufficient to support bispecific antibodies as treatment for ITP outside selected circumstances, this case suggests that these agents may provide simultaneous control of B-cell lymphoma and secondary autoimmune cytopenia in selected patients and warrants further investigation.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Ravjot K. Virdi, Taha Alrifai

Acquisition, analysis, or interpretation of data: Ravjot K. Virdi, Taha Alrifai

Drafting of the manuscript: Ravjot K. Virdi, Taha Alrifai

Critical review of the manuscript for important intellectual content: Ravjot K. Virdi, Taha Alrifai

Supervision: Taha Alrifai

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Advocate Aurora Health Institutional Review Board issued approval N/A. Institutional Review Board approval was not required for this retrospective case report, as it describes a single patient case and does not constitute human subjects research. All identifying patient information has been removed to ensure confidentiality. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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