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Case Reports

Blinatumomab-induced remission of refractory immune thrombocytopenia in pediatric acute lymphoblastic leukemia: a case report

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Data sharing statement

The data used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Disclosures

No conflicts of interest to disclose.

Contributions

YA and HZ wrote the manuscript; YF, JF and DZ designed the study; YH, SK and YZ performed treatments; QZ and CH collected and analyzed data; XW and YF collected data on clinical follow-up. All authors approved the final version of the manuscript.

Immune thrombocytopenia (ITP) is characterized by isolated thrombocytopenia, which predisposes patients to an elevated risk of hemorrhage. This condition is associated with autoimmune mechanisms, in which the host's immune system erroneously targets and eradicates its own platelets.[1] ITP represents an uncommon complication in pediatric patients with acute lymphoblastic leukemia (ALL). The incidence of ITP in children with ALL is not thoroughly documented, but it has been acknowledged as a potential secondary complication. The pathogenesis of ITP in these patients may involve immune dysregulation precipitated by the leukemia itself or by therapeutic interventions (e.g., chemotherapy), which can modulate immune function and consequently induce ITP.[2] Furthermore, the manifestation of ITP in pediatric ALL patients may reflect a more intricate underlying immune dysfunction, potentially complicating treatment protocols and prognosis.[3] Although most affected patients respond to standard therapeutic modalities including corticosteroids, intravenous immunoglobulin (IVIG), thrombopoietin receptor agonists and rituximab, some patients develop treatment-refractory ITP, which represents a substantial clinical challenge.

Blinatumomab is a pioneering bispecific T-cell engager (BiTE) antibody engineered to target cluster of differentiation (CD)19 on B cells and CD3 on T cells. This innovative therapeutic strategy is designed to redirect endogenous T cells to recognize and eradicate malignant B cells, which are characteristic of specific leukemia and lymphoma subtypes. The mechanism of action comprises simultaneous binding of blinatumomab to CD19, a surface protein expressed on B cells, and CD3, a constituent of the T-cell receptor complex. This bridging facilitates the activation and proliferation of T cells, enabling them to attack cancerous B cells.[4] Nevertheless, the potential

utility of blinatumomab extends beyond oncology, particularly within the domain of autoimmune diseases. Subklewe et al. reported blinatumomab demonstrated therapeutic efficacy in severe systemic sclerosis.[5] Blinatumomab's distinctive capacity to engage T cells independently of major histocompatibility complex (MHC) class I presentation or costimulation suggests that blinatumomab could modulate immune responses in autoimmune conditions characterized by pathogenic B cells.[6]

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Medical Ethical Committee of Shunde Women and Children's Hospital of Guangdong Medical University (Approval No. LW-2025-014). Written informed consent was obtained from the the patient's legal guardians for the publication of any potentially identifiable images or data included in this article.

A 5-year-old girl received a diagnosis of B-ALL after presenting with fever, pallor and abdominal pain. Initial laboratory assessments at a local hospital indicated a white blood cell count of 3.95×10^9/L, a hemoglobin level of 95 g/L, and a platelet count of 131×10^9/L. A subsequent bone marrow smear confirmed a diagnosis of ALL. Flow cytometric analysis of the bone marrow demonstrated that 97.21% of immature blasts expressed CD10 and CD19. Four days later, she began induction chemotherapy following the SCCLG-ALL-2016 protocol. After continued treatment under a standard pediatric ALL regimen, the patient achieved complete morphological and molecular remission (Figure 1). During the course of reinduction therapy, the patient experienced chemotherapy-induced myelosuppression. Notably, while hemoglobin and white blood cell counts demonstrated progressive recovery, platelet counts continued to decline. This persistent thrombocytopenia prompted clinical concern. We attempted various therapeutic

interventions to increase the patient's platelet count, which resulted in partial recovery; however, the levels remained well below the normal range. During maintenance therapy, the patient developed isolated thrombocytopenia without concurrent anemia or neutropenia (Figure 2). Bone marrow aspiration revealed no evidence of leukemic relapse or myelosuppression. Human Immunodeficiency Virus, hepatitis B virus, cytomegalovirus, parvovirus B19, and circovirus yielded negative results, thereby excluding common infection-related causes of acquired thrombocytopenia.[7] Furthermore, imaging showed no splenomegaly. Nevertheless, platelet counts continued to demonstrate intermittent decline (Figure 2). Bone marrow re-evaluation revealed 45 megakaryocytes per low-power field, including 12 platelet-producing megakaryocytes. Platelet production was low, and platelets were rarely observed. The patient's platelet count substantially decreased after oral administration of mercaptopurine. We reduced the dose of mercaptopurine to one-quarter, but the patient's platelet count still failed to recover. Treatment with oral prednisone and hetrombopag provided minimal improvement. On 28 December 2023, testing for anti-platelet antibodies was positive [platelet antibody PAIgG (+)]. Flow cytometry demonstrated increased CD19 and CD20 expression on peripheral B cells (Figure 3A). Based on clinical, hematologic and immunologic findings, a diagnosis of secondary ITP was established.

Although the patient received standard therapy—including high-dose corticosteroids, IVIG, hetrombopag, eltrombopag, and sirolimus—her thrombocytopenia remained refractory. Platelet transfusions provided only transient benefit, and she developed mild mucocutaneous bleeding. Maintenance chemotherapy was discontinued. Considering the refractory thrombocytopenia and suspicion of immune-related etiology, she underwent a 28-day continuous intravenous infusion of blinatumomab (Figure 1). The treatment was well tolerated, without neurological or

cytokine-related adverse effects. The platelet count began to rise by day 4 of blinatumomab treatment, reaching 124×10^9/L by day 14; it stabilized within the normal range by day 28 (Figure 2). Follow-up bone marrow examination after blinatumomab treatment detected 280 megakaryocytes per low-power field. Among them, 100 were classified as mature megakaryocytes, and platelet-producing megakaryocytes constituted 44.7%. Platelets were scattered and easily observed. Post-treatment flow cytometry revealed pronounced depletion of circulating CD19+ B cells (Figure 3B), and anti-platelet antibodies became undetectable. The patient remained in complete leukemia remission, and no recurrence of thrombocytopenia was observed during one and half year of follow-up.

In the setting of ALL treatment, immune dysregulation may arise secondary to chemotherapy or related therapeutic strategies, thus precipitating ITP. Although rare, the emergence of ITP after treatment for ALL has been reported.[2] Similar autoimmune complications, including hemolysis and thrombocytopenia, have been reported in chronic lymphocytic leukemia following fludarabine- or cyclophosphamide-based regimens.[8] Most secondary ITP cases respond to conventional therapies. However, when ITP occurs in the context of an underlying hematologic malignancy, standard therapeutic approaches often show limited efficacy. This therapeutic limitation underscores the need for alternative strategies that can simultaneously address both the malignant clone and the autoimmune mechanism of platelet destruction.[9]

The application of immunotherapy in refractory ITP has emerged as an important therapeutic approach. Rituximab, a CD20-targeting monoclonal antibody, is established in ITP management, has been a cornerstone in the management of ITP due to its capacity to deplete B cells. Although rituximab induces treatment-free remission in over 50% of patients, responses are often transient,

and resistance frequently develops.[10] There are two underlying mechanisms contributing to this phenomenon: First, CD20 expression begins at the pre-B cell stage, is lost at the plasmablast stage, and is absent in plasma cells.[11] Second, in autoimmune diseases, because plasmablasts and long-lived memory plasma cells may play a key role, targeting CD20 alone may not fully block autoantibody production.[12] Thus, rituximab primarily eliminates mature B cells but spares plasmablasts and long-lived plasma cells, thereby limiting its efficacy in sustaining long-term remission of ITP. These findings highlight the need to investigate alternative treatments or combination approaches for better clinical outcomes. Additionally, the prolonged immunosuppressive effects of rituximab may be undesirable in pediatric oncology populations. Emerging B-cell-directed therapies, including anti-CD19 and anti-CD38 monoclonal antibodies, are currently under investigation and may represent promising alternatives capable of overcoming resistance mechanisms and improving clinical outcomes in refractory ITP.[13] In addition, Chimeric antigen receptor T-cell (CAR-T) therapy has also recently been reported to show therapeutic efficacy in refractory ITP. Li et al. reported the first successful use of CAR-T therapy as treatment for refractory ITP secondary to systemic lupus erythematosus. [14]

Blinatumomab effectively treats ITP secondary to compensatory B-cell hyperplasia after B-ALL chemotherapy, while preventing relapse and correcting B-cell-driven immune dysregulation. Blinatumomab targets CD19, which is expressed across the entire spectrum of B-cell development from the pro-B cell stage to plasmablasts, thereby achieving a more comprehensive and profound depletion of B cells.[11] Consequently, blinatumomab effectively reduces autoreactive B-cell populations across multiple developmental stages, including those contributing to autoantibody production. The sustained remission observed in this patient may be related to the profound B-cell

depletion induced by blinatumomab; however, current evidence is insufficient to determine whether this effect extends to broader ITP populations. Additionally, blinatumomab's ability to engage T cells in a non-MHC-restricted manner is a key advantage, which enables T cell activation without requiring a stimulus from professional antigen-presenting cells.[5] This rapid mechanism renders blinatumomab particularly effective in clinical scenarios that demand prompt intervention. Most importantly, blinatumomab was not only advantageous in addressing the patient's ITP but also demonstrated potent antitumor activity. This dual benefit provided the primary rationale for selecting blinatumomab as the subsequent immunotherapeutic approach in this case. Also, blinatumomab—characterized by its short half-life and reversible immunologic activity—may offer a safer therapeutic option in selected cases.

Adverse effects of blinatumomab, including cytokine release syndrome, neurotoxicity, neutropenia and hypogammaglobulinemia, should be carefully monitored.[15] In our case, only mild hypogammaglobulinemia occurred without severe infections or neurological complications, indicating that blinatumomab can be safely used with appropriate monitoring. Cases of ITP after ALL therapy have been reported, mostly responding to IVIG.[2] However, our patient did not respond to standard ITP treatments but achieved complete remission after blinatumomab administration. This case demonstrates blinatumomab's potential to reverse refractory ITP caused by ALL therapy. Given its strong immunomodulatory effects and high cost, blinatumomab should not be used routinely for ITP but may serve as a rescue option in exceptional or treatment-refractory cases, especially those with concomitant hematologic malignancy.

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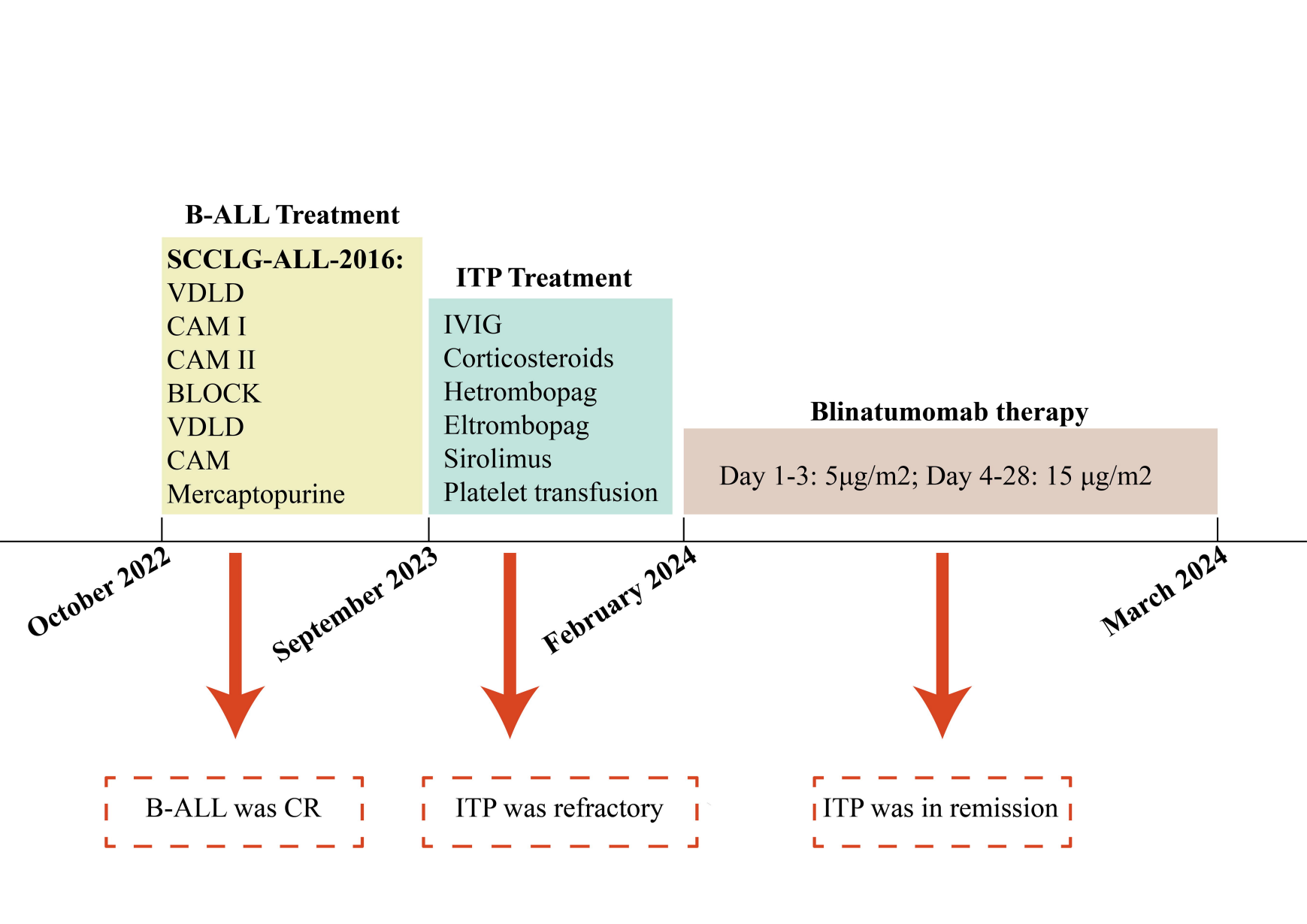
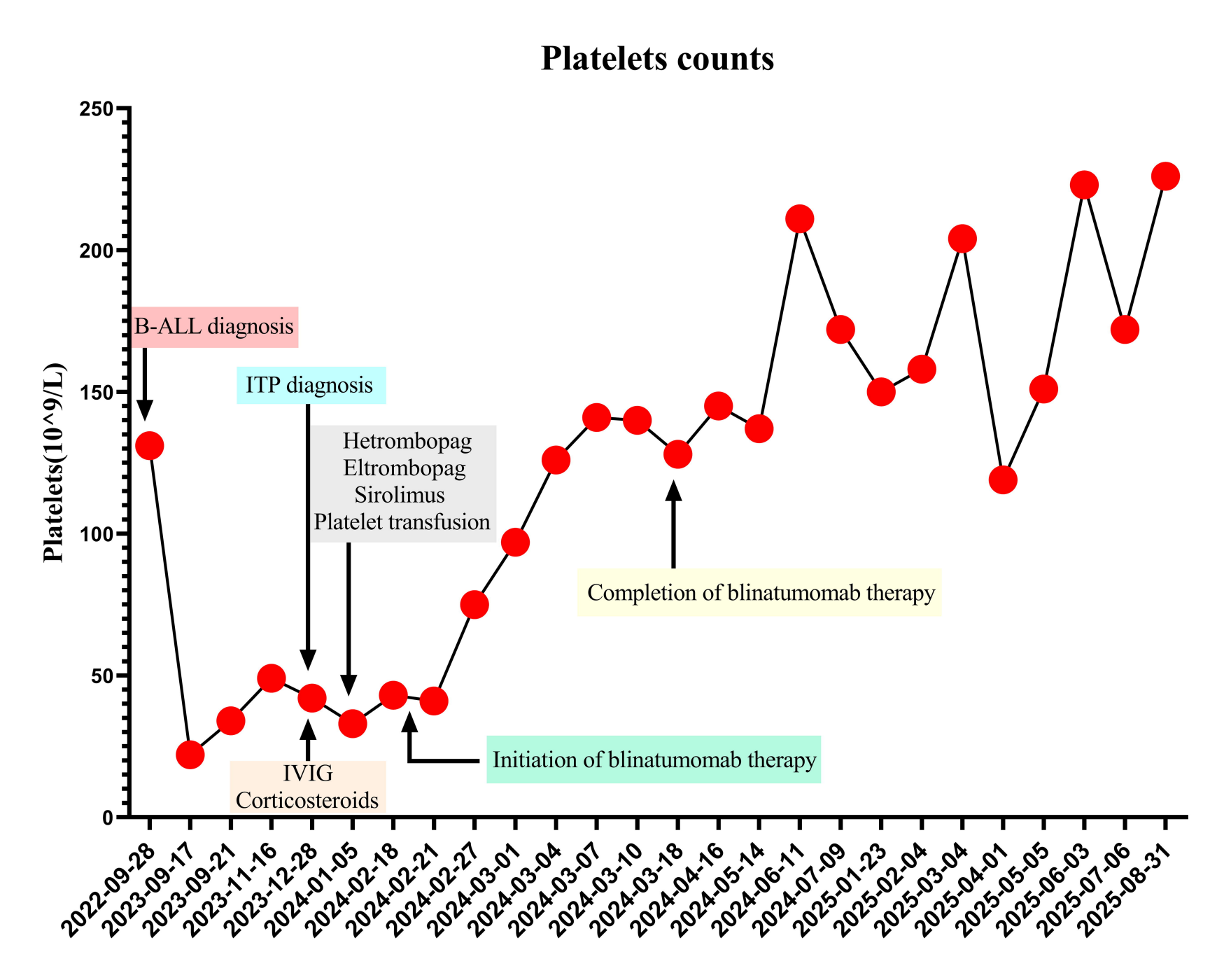
Figure legend

Figure 1. Timeline for Treatment. The patient was diagnosed with B-ALL in October 2022 and achieved complete remission after standard SCCLG-ALL-2016 chemotherapy. In September 2023, ITP was diagnosed and found to be refractory to multiple lines of treatment, including IVIG, corticosteroids, thrombopoietin receptor agonists, sirolimus, and platelet transfusion. Blinatumomab therapy was initiated in February 2024, resulting in ITP remission by March 2024. Note: the SCCLG-ALL-2016 protocol is registered with the Chinese Clinical Trial Registry (Chi-CTR; https://www.chictr.org.cn/; number ChiCTR2000030357). B-ALL: B-cell acute lymphoblastic leukaemia; ITP:immune thrombocytopenia; IVIG: intravenous immunoglobulin.

Figure 2. Platelet counts and major treatments during the clinical course. Longitudinal platelet counts are shown from B-ALL diagnosis through the development of ITP and subsequent therapies. Key interventions—including corticosteroids, IVIG, thrombopoietin receptor agonists, sirolimus, platelet transfusion, and blinatumomab—are annotated. The initiation and completion of blinatumomab therapy are highlighted. Note: the X-axis reflects a clinical timeline with non-uniform intervals. Equal spacing is used to illustrate the sequence of treatments and platelet responses rather than exact chronological distances. B-ALL: B-cell acute lymphoblastic leukaemia; ITP:immune thrombocytopenia; IVIG: intravenous immunoglobulin.

Figure 3. Alterations in T-Cell and B-Cell Counts During ITP Diagnosis and Blinatumomab Treatment. (A) Flow cytometry at ITP diagnosis showed T cells (CD3+) 33.33%, B cells (CD19+) 60.29%, and B cells (CD20+) 58.50%, indicating an elevated B-cell proportion. (B) After blinatumomab treatment, flow cytometry revealed a marked increase in T cells and a significant reduction in B cells. ITP: immune thrombocytopenia.


B-ALL Treatment
SCCLG-ALL-2016:
VDLD
CAM I
CAM II
BLOCK
VDLD
CAM
Mercaptopurine
ITP Treatment
IVIG
Corticosteroids
Hetrombopag
Eltrombopag
Sirolimus
Platelet transfusion
Blinatumomab therapy
Day 1-3: 5μg/m2; Day 4-28: 15 μg/m2
October 2022
September 2023
February 2024
March 2024
B-ALL was CR
ITP was refractory
ITP was in remission


Platelets counts
Platelets(10^9/L)
250
200
150
100
50
0
B-ALL diagnosis
ITP diagnosis
Hetrombopag
Eltrombopag
Sirolimus
Platelet transfusion
Completion of blinatumomab therapy
IVIG
Corticosteroids
Initiation of blinatumomab therapy
2022-09-28
2023-09-17
2023-09-21
2023-11-16
2023-12-28
2024-01-05
2024-02-18
2024-02-21
2024-02-27
2024-03-01
2024-03-04
2024-03-07
2024-03-10
2024-03-18
2024-04-16
2024-05-14
2024-06-11
2024-07-09
2025-01-23
2025-02-04
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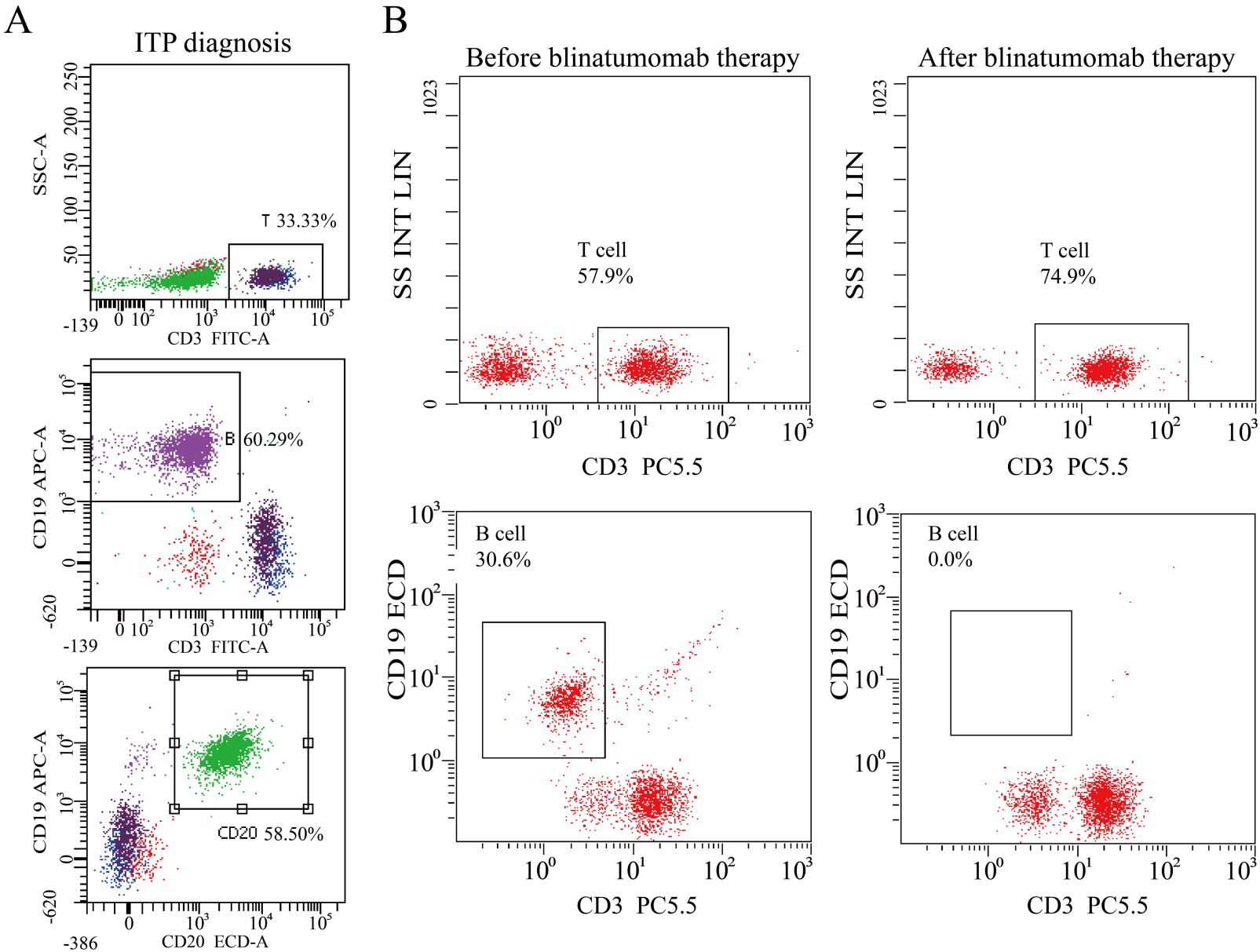
2025-04-01
2025-05-05
2025-06-03
2025-07-06
2025-08-31


A
ITP diagnosis
SSC-A
T 33.33%
CD3 FITC-A
CD19 APC-A
B 60.29%
CD3 FITC-A
CD19 APC-A
CD20 58.50%
CD20 ECD-A
B
Before blinatumomab therapy
After blinatumomab therapy
SS INT LIN
T cell
57.9%
CD3 PC5.5
T cell
74.9%
CD3 PC5.5
CD19 ECD
B cell
30.6%
CD3 PC5.5
B cell
0.0%
CD3 PC5.5