RESEARCH LETTER

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TO THE EDITOR:

Successful eltrombopag discontinuation in paraneoplastic immune thrombocytopenia: a case report

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Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by a low platelet count. Although often idiopathic, ITP can be secondary to conditions including systemic autoimmune diseases, chronic infections, drugs, and malignancies. The association of ITP with lymphoproliferative malignancies is well established in the scientific literature, whereas its occurrence in patients with nonhematologic solid tumors is less frequently reported.[1,2]

Here, we present the case of a patient whose ITP diagnosis preceded symptomatic cancer recurrence and in whom the start of breast cancer treatment led to a significant improvement in her platelet count, allowing discontinuation of ITP-directed therapy.

A woman aged 67 years presented to our center in March 2022 with spontaneous bleeding (petechiae and bruising). Laboratory tests showed severe isolated thrombocytopenia (platelet count of 13×10^9/L), with normal hemoglobin and white blood cell counts. She had a history of breast cancer radically treated in 2003 with surgery, chemotherapy, and radiotherapy, with years of negative follow-up. There was no evidence of past hematological toxicity in her medical records, and the patient previously had normal platelet counts. Her personal and family history was negative for bleeding disorders and hematological malignancies.

A peripheral blood smear showed normal blood cell morphology, without dysplastic features or circulating blasts. Liver and renal test results were normal, and there were no signs of hemolysis or coagulopathy. Infectious causes of thrombocytopenia, including chronic hepatitis B virus, hepatitis C virus, HIV, and *Helicobacter pylori* infection, were excluded. She had no clinical signs or symptoms of an underlying autoimmune disease, including joint pains or arthritis, photosensitivity, oral ulcers, skin rashes, no history of unexplained lymphadenopathies or hepatosplenomegaly, and no recent exposure to medications known to cause thrombocytopenia. Bone marrow aspirate and biopsy specimens showed normal trilineage hematopoiesis, normal cellularity, no increase in blasts, and no evidence of a lymphoproliferative disorder (supplemental Table 1).

Based on the negative results of the initial diagnostic workup, a diagnosis of primary ITP was made. The patient was initially treated with corticosteroids, which led to temporary improvement in her platelet counts. However, severe thrombocytopenia relapsed over time, requiring the introduction of the thrombopoietin receptor agonist (TPO-RA) eltrombopag in November 2022, with a starting dose of 50 mg daily. During treatment with eltrombopag, the patient required several dose adjustments because of fluctuations in her platelet count (Figure 1).

During follow-up, the patient developed left axillary tenderness, which prompted further investigation. Imaging revealed suspicious axillary lymph nodes, and a biopsy led to the diagnosis of recurrent luminal B breast cancer in her left breast at the beginning of 2024. She was started on targeted treatment with letrozole and ribociclib in March 2024.

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Data are available from the corresponding author, Bianca Clerici (bianca.clerici@unimi.it), on request.

The full-text version of this article contains a data supplement.

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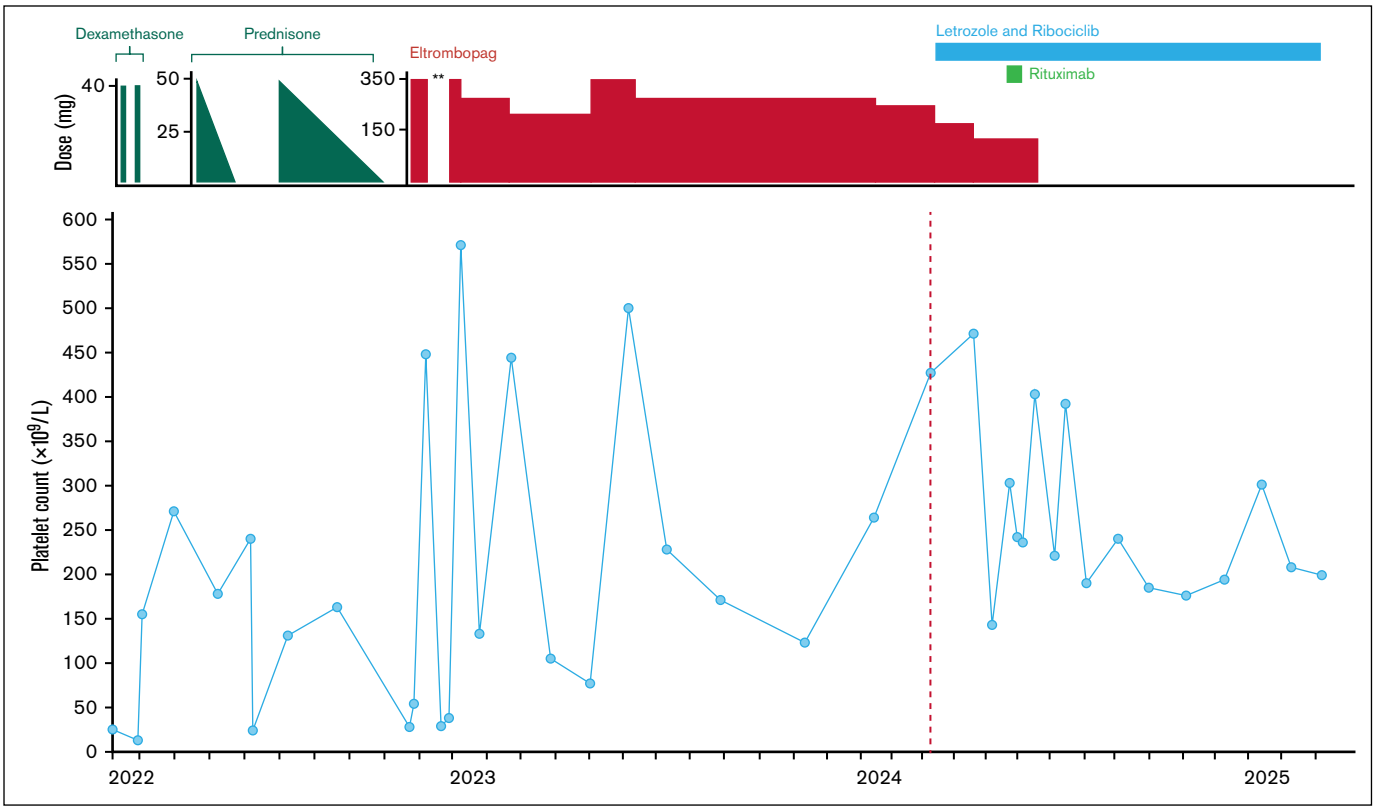

Figure 1. Platelet counts and treatment timeline. The dashed red vertical line indicates initiation of oncologic therapy for breast cancer recurrence and separates the period before and after the start of cancer-directed treatment. Corticosteroid dosing is expressed in milligrams per day, whereas eltrombopag dosing is in milligrams per week. Eltrombopag was temporarily interrupted shortly after its introduction because of thrombocytosis. This is indicated in the graph by asterisks, each representing 1 week without treatment.

During staging of the breast cancer recurrence, a positron emission tomography–computed tomography (PET-CT) scan confirmed focal glucose uptake in her left axillary and retropectoral regions. Moreover, it showed increased metabolic activity located at the splenic flexure of the colon and adjacent regional lymph nodes (Figure 2). A subsequent biopsy specimen of the colonic mucosa revealed a mature B-cell lymphoid neoplasia with a low proliferation index. Notably, the patient had not developed any new cytopenias, nor did she complain of B symptoms. Several treatment options were discussed with the patient. Radiotherapy was deemed unsuitable because of the disease extent; therefore, the patient chose rituximab monotherapy in May 2024 at a dose of 375 mg/m^2 weekly for 4 weeks.

Since the start of treatment for breast cancer back in March 2024, we observed a steady improvement in the patient's platelet counts, with fewer fluctuations (Figure 1). This allowed us, for the first time, to consider a gradual tapering of eltrombopag, started in March 2024. With consideration of the stability of the platelet counts over time, eltrombopag was discontinued in June 2024 after careful evaluation of the balance between the risk of drug-induced thrombocytopenia posed by ribociclib and the thrombotic risk posed by the underlying active malignancy and continued TPO-RA treatment. Over the following months, the patient checked her blood counts monthly, with platelets remaining steadily above 100 × 10^9/L, with no need to resume ITP-directed therapy or discontinue ribociclib because of incident thrombocytopenia. At her most recent follow-up in December 2025, more than a year since the discontinuation of eltrombopag, the patient continued to exhibit a complete sustained response off treatment (SROT).

In summary, we have presented the case of a patient whose ITP diagnosis preceded the symptomatic recurrence of breast cancer by 2 years, with the additional unexpected discovery of a low-grade lymphoproliferative disorder, further complicating the interpretation of this clinical scenario.

The paraneoplastic nature of ITP is well recognized, especially in association with lymphoproliferative disorders.[2,3] However, its association with solid tumors remains less clearly defined, although documented in several case series and reviews.[1,2,4-11] A critical analysis of 68 cases revealed that paraneoplastic ITP can occur in association with various solid tumors, with lung and breast being the most frequently involved types.[11] ITP can accompany, precede, or follow the diagnosis of the concomitant malignancy, posing challenges in the identification of a definitive causal link.[11,12] This variable temporal relationship, however, highlights the complex interplay between tumor biology and immune dysregulation. Moreover, ITP secondary to malignancy is often characterized by suboptimal responses to first-line therapies; our group has previously found an overall response rate of ~50% to corticosteroids alone or combined with IV immunoglobulin in patients with paraneoplastic ITP.[1]

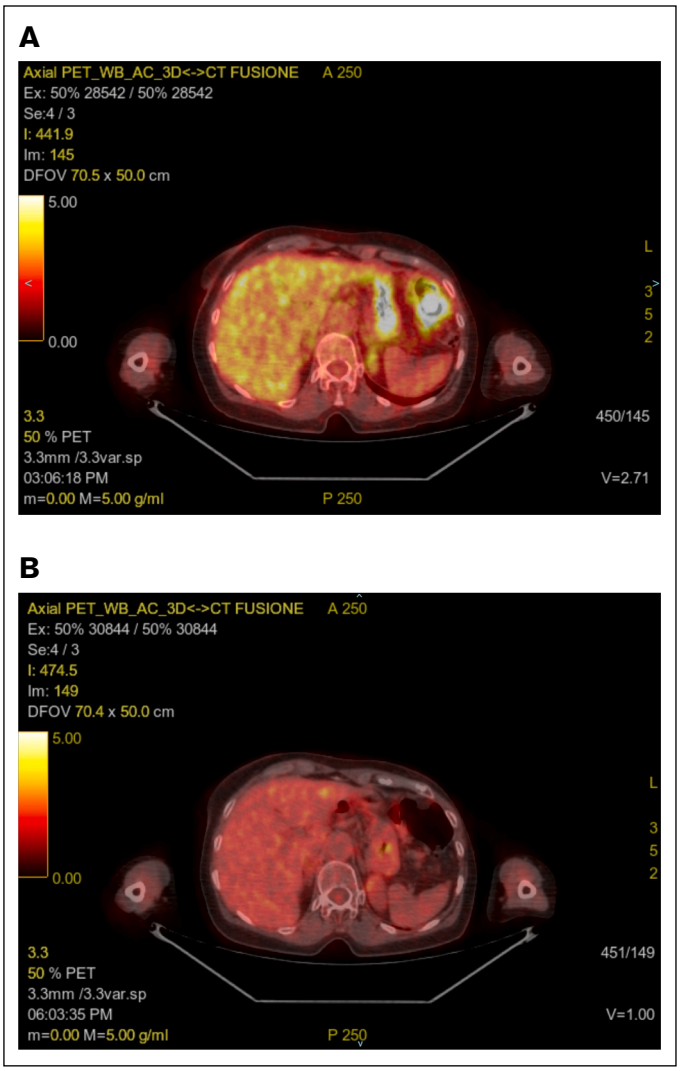

Figure 2. PET-CT scan before and after treatment of marginal zone lymphoma. (A) The PET-CT scan from February 2024, demonstrating increased metabolic activity at the splenic flexure of the colon and adjacent regional lymph nodes. Rituximab was infused over 4 weeks, starting in May 2024. (B) The posttreatment PET-CT scan from December 2024, demonstrating a marked reduction in the size and metabolic activity of the lesion located at the splenic flexure of the colon, with a complete normalization of the lymph node metabolic uptake, consistent with treatment response.

In our patient, ITP was diagnosed 2 years before the symptomatic recurrence of breast cancer. However, we hypothesize that the breast cancer was already present, although in a subclinical form, at the time of ITP onset. The existence of a pathophysiological link between breast cancer and ITP is further supported by the patient's clinical course. In fact, the initiation of breast cancer–directed therapy was followed by a significant and sustained improvement in her platelet counts, evident before her rituximab infusions, which allowed, for the first time, tapering of eltrombopag with the goal of discontinuation. The later administration of rituximab for the treatment of her indolent marginal zone lymphoma may have further helped the achievement of SROT.

The coexistence of ITP and multiple malignancies in this patient could raise the suspicion of an underlying immune deficit. However, the patient did not have a history of recurrent or severe infections or unexplained lymphadenopathies before her lymphoma and did not present with organomegaly or other immune-mediated disorders. The timing of the patient's platelet count stabilization, occurring directly after the start of breast cancer treatment and before the administration of rituximab, supports the hypothesis that breast cancer was the principal driver of ITP. This is consistent with several reports in the literature, describing significant improvements in ITP management immediately after the initiation of cancer-directed therapy.[1,9,11,13,14] However, it is also possible that the patient may have achieved SROT after reconstitution of the platelet mass after years of TPO-RA use,[15,16] and rituximab may have played an additional role in reestablishing immune tolerance.

This case underscores the importance of considering a broad spectrum of conditions as potential triggers of ITP, with particular attention to hematologic neoplasms and, albeit less frequently recognized, solid tumors. Early identification and appropriate treatment of the underlying malignancy are pivotal not only for the patient's overall well-being and survival but also for the achievement of ITP control, likely by reducing the driving immunogenic stimulus and thereby restoring immune tolerance.

This study was conducted in accordance with the Declaration of Helsinki.

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