CASE REPORT

Cerebral Venous Sinus Thrombosis with Hemorrhagic Transformation in a Patient with Immune Thrombocytopenia Treated with Eltrombopag: A Fatal Case Report

Dr. Prathap J[1*], Dr. Jayaprakash Appajigol[2]

[1*] General Medicine Resident (Postgraduate), General Medicine. (Corresponding Author)
Email: Prathapjagadish08@gmail.com

[2] Associate Professor, General Medicine. Email: jayaprakashappajigol@gmail.com

Received: 20th Feb, 2026 | **Revised:** 4th Mar, 2026 | **Accepted:** 25th Mar, 2026 | **Available Online:** 10th Apr, 2026

ABSTRACT

Background: Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by immune-mediated platelet destruction and impaired platelet production. Thrombopoietin receptor agonists (TPO-RAs), including eltrombopag, are increasingly used in refractory ITP to raise platelet counts. Although bleeding is the predominant concern in ITP, paradoxical thrombotic complications, particularly cerebral venous sinus thrombosis (CVST), are rare but potentially fatal adverse events associated with TPO-RA therapy.

Case Presentation: A 63-year-old woman with immune thrombocytopenia who developed cerebral venous sinus thrombosis with hemorrhagic venous infarction following treatment with eltrombopag. She presented with progressive headache, vomiting, focal neurological deficits, and altered sensorium. Neuroimaging revealed extensive cerebral venous thrombosis involving the left cerebral venous system with hemorrhagic transformation, associated subdural hematoma, and significant mass effect. Despite aggressive medical management, including platelet transfusions, corticosteroids, eltrombopag, and intensive care support, her neurological condition deteriorated. Emergency decompressive craniectomy was performed; however, the postoperative course was complicated by diffuse cerebral edema, worsening hemorrhagic venous infarction, and herniation, culminating in a fatal outcome. This case highlights the paradoxical risk of cerebral venous sinus thrombosis associated with eltrombopag therapy in patients with immune thrombocytopenia. Clinicians should maintain a high index of suspicion for thrombotic complications in ITP patients receiving TPO receptor agonists, particularly when new neurological symptoms develop. Early recognition, prompt neuroimaging, and multidisciplinary management are essential to improve outcomes.

Keywords: Immune thrombocytopenia, Eltrombopag, Thrombopoietin receptor agonists, Cerebral venous sinus thrombosis, Hemorrhagic venous infarction, Intracranial hemorrhage, Paradoxical thrombosis.

How to cite this article: Prathap J, Appajigol J. Cerebral Venous Sinus Thrombosis with Hemorrhagic Transformation in a Patient with Immune Thrombocytopenia Treated with Eltrombopag: A Fatal Case Report. Int J Drug Deliv Technol. 2026;16(29s):237-241. DOI: 10.25258/ijddt.16.29s.28

Source of support: Nil.

Conflict of interest: The authors declare no conflict of interest.

CEREBRAL VENOUS SINUS THROMBOSIS WITH HEMORRHAGIC TRANSFORMATION IN A PATIENT WITH IMMUNE THROMBOCYTOPENIA TREATED WITH ELTROMBOPAG: A FATAL CASE REPORT

Introduction

Immune thrombocytopenia (ITP) is an acquired autoimmune disorder characterized by immune-mediated platelet destruction and impaired platelet production, resulting in isolated thrombocytopenia (1). The clinical spectrum of ITP ranges from asymptomatic thrombocytopenia to mucocutaneous bleeding, with intracranial hemorrhage representing the most feared but rare complication (1). Traditionally, bleeding has been considered the dominant clinical concern in ITP; however, accumulating evidence suggests that patients with ITP are paradoxically at increased risk of thrombotic events despite low platelet counts (1).

Thrombopoietin receptor agonists (TPO-RAs), including eltrombopag, have revolutionized the management of chronic and refractory ITP by stimulating megakaryocyte proliferation and increasing platelet production (2). Although these agents are generally well tolerated and effective, thromboembolic complications have emerged as important adverse events. Both arterial and venous thromboses have been reported, including deep vein thrombosis, pulmonary embolism, ischemic stroke, and, rarely, cerebral venous sinus thrombosis (CVST) (3). CVST is an uncommon but potentially fatal condition, accounting for less than 1% of all strokes, and its occurrence in patients with ITP receiving eltrombopag poses significant diagnostic and therapeutic challenges (4).

The pathophysiology underlying thrombosis in ITP, particularly in the setting of TPO-RA therapy, is complex and multifactorial. Proposed mechanisms include excessive platelet production, increased platelet reactivity, release of procoagulant platelet microparticles, endothelial activation, and imbalance between procoagulant and anticoagulant pathways (1). Eltrombopag may further amplify these processes by rapidly increasing platelet counts and altering platelet function, thereby predisposing susceptible individuals to thrombus formation even in the absence of traditional risk factors (5).

CVST associated with eltrombopag is especially challenging to recognize because its clinical presentation headache, vomiting, focal neurological deficits, and altered sensorium can mimic intracranial hemorrhage or other neurological complications commonly associated with severe thrombocytopenia (6). Moreover, venous thrombosis frequently results in hemorrhagic venous infarction, which can obscure the underlying thrombotic etiology on initial imaging and delay definitive diagnosis (7).

Given the increasing use of eltrombopag in ITP, recognition of rare but catastrophic thrombotic complications such as CVST is essential (6). We report a fatal case of cerebral venous sinus thrombosis with hemorrhagic transformation in a patient with immune thrombocytopenia treated with eltrombopag, highlighting the paradoxical thrombotic risk, diagnostic challenges, and therapeutic dilemmas associated with TPO receptor agonist therapy.

CASE PRESENTATION

Patient Information: A 63-year-old female, resident of Karnataka, India, was admitted to a tertiary care teaching hospital with acute neurological symptoms. She was a known case of type 2 diabetes mellitus for the past four years and was on oral hypoglycemic therapy. There was no documented history of hypertension, anticoagulant or antiplatelet use, prior cerebrovascular events, liver disease, renal disease, or known bleeding disorders. There was no history of trauma or head injury preceding the onset of symptoms.

Presenting Complaints: The patient presented with right-sided facial and upper limb numbness associated with blurred vision for four days. She also complained of severe occipital headache for three days, which was continuous, progressively worsening, and non-responsive to analgesics. This was accompanied by intermittent fever, nausea, and multiple episodes of vomiting over the preceding three days. On subsequent presentation, she developed drowsiness and altered sensorium, indicating clinical deterioration.

History of Present Illness: The patient was apparently asymptomatic until four days prior to admission, when she developed numbness over the right side of the face and right upper limb along with blurred vision. The onset was insidious, and symptoms gradually progressed. Three days prior to admission, she developed severe occipital headache described as hammering in nature, which was not relieved by medication. This was associated with fever and repeated episodes of non-projectile vomiting. There was no history of seizures, loss of consciousness, epistaxis, gum bleeding, hematemesis, melena, hematuria, or menorrhagia. There was also no history suggestive of ear or nasal bleed, recent infections, or trauma. Due to worsening neurological symptoms, she was brought to the hospital for evaluation.

Past Medical History: The patient had a history of type 2 diabetes mellitus for four years and was on tablet glimepiride (0.5–1–0–1). There was no history of hypertension, ischemic heart disease, stroke, chronic kidney disease, chronic liver disease, or autoimmune disorders. She had no prior hospital admissions for similar complaints and no known drug allergies.

Personal and Family History: She followed a vegetarian diet. Appetite was reported to be normal, although sleep was reduced during the illness. Bowel and bladder habits were normal. There was no history of tobacco use, alcohol consumption, or substance abuse. Family history was non-contributory, with no known hereditary bleeding or neurological disorders.

Clinical Examination: On examination at admission, the patient was conscious, alert, and oriented. She was moderately nourished and well built. Vital signs were stable, with a blood pressure of 120/70 mmHg and pulse rate of 92 beats per minute. General physical examination revealed pallor, with no icterus, cyanosis, clubbing, lymphadenopathy, or pedal edema.

Neurological examination revealed right-sided

hemiparesis. Plantar response was extensor on the right side and flexor on the left. Pupils were bilaterally equal and reactive to light. There were no signs of meningeal irritation. Cardiovascular examination revealed normal heart sounds with no murmurs. Respiratory examination showed bilateral air entry with no adventitious sounds. Abdominal examination was unremarkable.

Laboratory Investigations: Initial hematological investigations revealed severe thrombocytopenia, with platelet counts as low as 2,000/mm³, showing wide fluctuations during hospitalization. Platelet counts gradually improved following treatment, reaching a maximum of 132,000/mm³. Hemoglobin ranged between 11.1 and 12.6 g/dL. Total leukocyte count showed mild neutrophilic leukocytosis. Peripheral smear demonstrated markedly reduced platelets with normal morphology.

Bone marrow aspiration and trephine biopsy revealed a hypercellular marrow with normoblastic erythropoiesis, increased megakaryocytes with occasional immature forms, and no abnormal or malignant cells. These findings were consistent with immune thrombocytopenic purpura.

Biochemical parameters, including renal function tests, liver enzymes, electrolytes, and coagulation profile (PT/INR and APTT), were within normal limits. HbA1c was 6.9%, indicating suboptimal glycemic control. Viral markers for HIV, hepatitis B, and hepatitis C were non-reactive.

Radiological Findings: Initial non-contrast computed tomography (CT) of the brain revealed an acute-on-chronic subdural hematoma along the left fronto-temporo-parietal convexity, extending along the falx cerebri and bilateral tentorium cerebelli, associated with significant mass effect and midline shift to the right.

Subsequent magnetic resonance imaging (MRI) of the brain with venography demonstrated features consistent with cerebral venous sinus thrombosis, including absence of normal flow void and altered signal intensity involving the left transverse sinus, left sigmoid sinus, and adjacent cortical veins. Associated hemorrhagic venous infarction was noted in the left parieto-temporo-occipital region and left thalamus, characterized by areas of mixed signal intensity with surrounding edema. These findings were accompanied by compression of adjacent brain parenchyma and progressive midline shift.

Repeat CT imaging showed interval progression of hemorrhagic venous infarction with diffuse cerebral edema, effacement of cortical sulci, subfalcine herniation, and worsening mass effect. The radiological appearance was consistent with extensive cerebral venous sinus thrombosis complicated by hemorrhagic transformation and secondary subdural hemorrhage.

Diagnosis: Based on clinical presentation, laboratory findings, bone marrow examination, and neuroimaging, a diagnosis of left fronto-temporo-parietal acute on chronic subdural hematoma with hemorrhagic venous infarction secondary to immune thrombocytopenic purpura in a patient with type 2 diabetes mellitus was established.

Therapeutic Intervention

Medical Management: The patient was initially managed conservatively with aggressive medical therapy. This included multiple platelet transfusions, intravenous corticosteroids, thrombopoietin receptor agonist (eltrombopag), antiepileptic therapy with levetiracetam, osmotherapy with intravenous mannitol, and supportive care. Broad-spectrum intravenous antibiotics were administered. Glycemic control was achieved using insulin therapy. She was monitored closely in a high-dependency unit and later in the intensive care unit.

Surgical Management: Due to progressive neurological deterioration and radiological evidence of worsening mass effect and midline shift, neurosurgical intervention was deemed necessary. The patient underwent left fronto-temporo-parietal decompressive craniectomy with augmentative duroplasty under general anesthesia. The procedure was performed after optimization of platelet counts to the extent possible.

Postoperative Course and Outcome: Postoperatively, the patient was managed in the intensive care unit with ventilatory support, anti-edema measures, antiepileptics, antibiotics, and inotropic support. Despite maximal medical and surgical management, her neurological status continued to deteriorate. Repeat imaging demonstrated diffuse cerebral edema and extensive hemorrhagic venous infarction.

On 10 June 2024, the patient's condition worsened, requiring escalation of inotropic support. On 11 June 2024, she developed profound bradycardia and hypotension, followed by cardiopulmonary arrest. Immediate cardiopulmonary resuscitation was initiated as per advanced cardiac life support guidelines. Despite sustained resuscitative efforts, the patient could not be revived and was declared dead at 6:16 AM on 11 June 2024.

DISCUSSION

Immune thrombocytopenia (ITP) is classically regarded as a bleeding disorder due to immune-mediated platelet destruction and impaired platelet production. However, increasing evidence over the past decade has challenged this traditional view, demonstrating that patients with ITP are paradoxically predisposed to thrombotic events despite thrombocytopenia (1). Both arterial and venous thromboembolic complications have been reported, suggesting that ITP represents a complex disorder of immune dysregulation rather than a purely hemorrhagic condition. The introduction of thrombopoietin receptor agonists (TPO-RAs), such as eltrombopag, has further highlighted this paradox by revealing an increased incidence of thrombosis in certain patient populations (2).

Eltrombopag is an oral, non-peptide TPO receptor

agonist that stimulates megakaryocyte proliferation and differentiation, leading to increased platelet production. It has become an integral component in the management of chronic and refractory ITP, significantly reducing bleeding episodes and transfusion requirements (2). Nevertheless, post-marketing surveillance and clinical studies have identified thromboembolic events as an important adverse effect of TPO-RA therapy. These events include deep vein thrombosis, pulmonary embolism, ischemic stroke, splanchnic vein thrombosis, and, rarely, cerebral venous sinus thrombosis (CVST) (8). Although the overall incidence of CVST remains low, its occurrence is associated with high morbidity and mortality, particularly when diagnosis and treatment are delayed (7).

The pathophysiological mechanisms underlying thrombosis in ITP patients receiving eltrombopag are multifactorial and not fully understood. Several hypotheses have been proposed. First, TPO-RAs may lead to a rapid increase in platelet count, producing a population of younger, larger, and more metabolically active platelets with heightened procoagulant potential (6). These platelets exhibit increased surface expression of activation markers and enhanced aggregation responses. Second, eltrombopag has been shown to increase levels of platelet-derived microparticles, which possess strong procoagulant activity due to their phosphatidylserine-rich surfaces. These microparticles can amplify thrombin generation and contribute significantly to a hypercoagulable state (9).

In addition to platelet-related mechanisms, immune-mediated endothelial dysfunction may play a critical role. Chronic immune activation in ITP leads to endothelial injury, cytokine release, and upregulation of adhesion molecules, all of which promote thrombosis (10). Eltrombopag may exacerbate this prothrombotic milieu by altering the balance between procoagulant and anticoagulant pathways. Furthermore, ITP has been associated with reduced levels of natural anticoagulants and increased circulating inflammatory mediators, creating an environment conducive to thrombus formation even in the presence of low platelet counts (6).

Cerebral venous sinus thrombosis represents a unique and particularly dangerous manifestation of this prothrombotic state. CVST results from thrombosis of the dural venous sinuses and/or cortical veins, leading to impaired venous drainage, increased intracranial pressure, venous congestion, and subsequent venous infarction (4). Unlike arterial strokes, venous infarcts are frequently hemorrhagic due to rupture of congested veins and capillaries (4). In the present case, thrombosis of the left transverse and sigmoid sinuses resulted in extensive hemorrhagic venous infarction involving the parieto-temporo-occipital region and thalamus, compounded by secondary subdural hemorrhage and severe cerebral edema.

The diagnosis of CVST in patients with ITP receiving eltrombopag is particularly challenging. Clinical symptoms such as headache, vomiting, focal neurological deficits, and altered sensorium are nonspecific and may be mistakenly attributed to primary intracranial hemorrhage related to thrombocytopenia (4). In such cases, the presence of hemorrhagic lesions on initial CT imaging can obscure the underlying venous thrombosis, leading to diagnostic delay (11). This case underscores the critical importance of early magnetic resonance imaging with venography in ITP patients on TPO-RAs who develop new or progressive neurological symptoms, regardless of platelet count.

Management of eltrombopag-associated CVST presents significant therapeutic dilemmas. Anticoagulation remains the cornerstone of CVST treatment and is recommended even in the presence of hemorrhagic venous infarction under most circumstances. However, in patients with severe thrombocytopenia and active intracranial bleeding, anticoagulation carries substantial risk and may be contraindicated (6). In the present case, fluctuating platelet counts, extensive hemorrhagic transformation, and worsening mass effect limited the feasibility of anticoagulation. The need to balance prevention of thrombus propagation against the risk of catastrophic bleeding represents one of the most difficult aspects of managing CVST in ITP.

Neurosurgical intervention may be required in cases with life-threatening mass effect, refractory intracranial hypertension, or impending herniation. Decompressive craniectomy has been shown to improve survival in selected patients with malignant CVST; however, outcomes are heavily influenced by the extent of venous infarction, degree of hemorrhage, and underlying systemic conditions (12). In this patient, emergency decompressive craniectomy was performed due to progressive neurological deterioration and radiological evidence of herniation. Despite technically successful surgery, ongoing venous congestion, diffuse cerebral edema, and hemorrhagic progression resulted in a fatal outcome (13).

Advanced age and comorbid conditions may further worsen prognosis. Diabetes mellitus, present in this patient, is associated with endothelial dysfunction, impaired microvascular circulation, and increased susceptibility to infections, all of which can adversely affect neurological recovery and postoperative outcomes (14). Additionally, delayed presentation and the insidious onset of symptoms likely allowed progression of venous thrombosis before definitive diagnosis and intervention(15).

This case highlights several important clinical implications. First, clinicians should recognize that ITP is not solely a bleeding disorder and that thrombotic complications can occur even in the setting of severe thrombocytopenia. Second, eltrombopag and other TPO receptor agonists should be prescribed with careful risk stratification, particularly in elderly patients and those with additional prothrombotic risk

factors. Third, new-onset neurological symptoms in ITP patients receiving TPO-RAs should prompt urgent evaluation for CVST with appropriate neuroimaging, including venography.

Eltrombopag-associated cerebral venous sinus thrombosis represents a rare but devastating complication of ITP treatment. Early recognition, prompt imaging, and individualized multidisciplinary management are essential to improving outcomes (6). Greater awareness of this paradoxical thrombotic risk may facilitate earlier diagnosis and more timely intervention, potentially reducing the high morbidity and mortality associated with this condition (16).

CONCLUSION

Cerebral venous sinus thrombosis represents a rare but catastrophic complication in patients with immune thrombocytopenia treated with thrombopoietin receptor agonists such as eltrombopag. This case underscores the paradoxical thrombotic risk associated with ITP and its therapies, even in the presence of severe thrombocytopenia. Eltrombopag may contribute to a prothrombotic state through enhanced platelet production, increased platelet reactivity, and endothelial dysfunction, predisposing susceptible patients to venous thrombosis. The development of hemorrhagic venous infarction can obscure the underlying diagnosis, delay appropriate management, and significantly worsen prognosis. Clinicians should maintain a high index of suspicion for cerebral venous sinus thrombosis in ITP patients receiving TPO receptor agonists who present with new or progressive neurological symptoms. Early neuroimaging with venography, careful risk–benefit assessment of anticoagulation, and prompt multidisciplinary intervention are essential. Increased awareness of this rare adverse event may facilitate earlier diagnosis and potentially improve clinical outcomes.

BIBLIOGRAPHY

1. Li Q, Rebetz J, Provan D, Porcelijn LL, Kapur R, Hofstede-Van Egmond S, et al. Immune thrombocytopenia. In: Manual of Molecular and Clinical Laboratory Immunology. 9th ed. Washington (DC): American Society for Microbiology; 2024. p. 1105–1112.
2. Ijaz A, Patel P. Thrombopoietin receptor agonists. Platelets. 2024;35:1085–1110.
3. Prandoni P. Venous and arterial thrombosis: two aspects of the same disease? Clin Epidemiol. 2009;1:1–6.
4.Drahansky M, Paridah MT, Moradbak A, Mohamed AZ, Owolabi FA, Asniza M, et al. Cerebral venous sinus thrombosis. Radiographics. 2025;26(1):13.
5. Gerrits AJ, Leven EA, Frelinger AL, Brigstocke SL, Berny-Lang MA, Mitchell WB, et al. Effects of eltrombopag on platelet count and platelet activation in Wiskott-Aldrich syndrome/X-linked thrombocytopenia. Blood. 2015;126(11):1367–1378.
6. Lin IW, Lim KH, Huang YC, Sung MT. Eltrombopag-induced cerebral venous thrombosis: a case report and literature review. Case Rep Hematol. 2025;2025:8955513.
7. Katwal S, Suwal S, Lamichhane S, Bhusal A, Yogi TN. Cerebral venous sinus thrombosis with hemorrhagic infarct: a rare presentation in a risk-defying male patient. Radiol Case Rep. 2024;19(1):153–158.
8. Struyf F, Hardt K, Van Rampelbergh R, Shukarev G, Inamdar A, Ruiz-Guiñazú J, et al. Thrombosis with thrombocytopenia syndrome: a database review of clinical trial and post-marketing experience with Ad26.COV2.S vaccine. Vaccine. 2023;41(37):5351–5359.
9. Gerrits AJ, Leven EA, Frelinger AL, Brigstocke SL, Berny-Lang MA, Mitchell WB, et al. Effects of eltrombopag on platelet count and platelet activation in Wiskott-Aldrich syndrome/X-linked thrombocytopenia. Blood. 2015;126(11):1367–1378.
10. Farhid F, Rezaeeyan H, Habibi R, Kamali Yazdi E, Hamblin MR, Naghinezhad J. When the victim becomes the villain: platelets as drivers of immune dysregulation in immune thrombocytopenia. J Transl Autoimmun. 2025;11:100309.
11. Walecki J, Mruk B, Nawrocka-Laskus E, Piliszek A, Przelaskowski A, Sklinda K. Neuroimaging of cerebral venous thrombosis – old dilemma and new diagnostic methods. Pol J Radiol. 2015;80:368–373.
12. Gatos C, Fotakopoulos G, Tasiou A, Christodoulidis G, Georgakopoulou VE, Spiliotopoulos T, et al. Efficacy of decompressive craniectomy: a retrospective case series study with 321 patients and an update on controversies. Medicine (Baltimore). 2024;4(6):64.
13.Shukla DP. Complications following decompressive craniectomy. Acta Neurochir Suppl. 2024;133:157–168.
14. Seon MJ, Chung IN, Sei WY, Eun JB, Choong HS, Hae RC, et al. Endothelial dysfunction and microvascular complications in type 1 diabetes mellitus. J Korean Med Sci. 2008;23(1):77–84.
15. Puttarak K, Angchaisuksiri P, Boonyawat K. Delayed diagnosis and treatment of deep vein thrombosis—an underrecognized factor for its related outcomes? Thromb J. 2025;23(1):85.
16. Zhou LW, Dizonno V, Mandzia J, Almekhlafi MA, Bala F, Alhabli I, et al. Multiple health care encounters prior to diagnosis of cerebral venous thrombosis. Ann Emerg Med. 2025.