WebLog Journal of Clinical Case Reports

Case Report
Published: 05 Aug, 2026

Vildagliptin-Induced Thrombocytopenia: A Case Report with Pharmacovigilance Perspective

*Rahul Garg**

Professor, Department of Medicine, FH Medical College and Hospital, Agra, Uttar Pradesh, India

Abstract

Vildagliptin, a Dipeptidyl Peptidase-4 (DPP-4) inhibitor widely used in type 2 diabetes mellitus, is generally considered well-tolerated. We report a case of a 62-year-old woman who developed progressive, isolated thrombocytopenia approximately ten months after initiating vildagliptin 50 mg twice daily as an add-on to her existing antidiabetic regimen. Extensive haematological evaluation excluded alternative aetiologies including immune thrombocytopenic purpura, viral infections, haematological malignancies, and drug interactions with concurrent medications. Discontinuation of vildagliptin led to sustained platelet recovery within twelve weeks without any haematological intervention. The Naranjo Adverse Drug Reaction Probability Scale yielded a score of 6, indicating a probable causal relationship, corroborated by WHO-UMC causality assessment. A search of the VigiBase pharmacovigilance database identified 20 reports of vildagliptin-associated thrombocytopenia globally. This case reinforces the need for periodic platelet monitoring in patients receiving vildagliptin.

Keywords: Vildagliptin; DPP-4 Inhibitors; Thrombocytopenia; Adverse Drug Reaction; Pharmacovigilance

Introduction

Dipeptidyl Peptidase-4 (DPP-4) inhibitors represent a well-established class of oral antidiabetic agents that exert their glucose-lowering effect by inhibiting the enzyme responsible for rapid degradation of Glucagon-Like Peptide-1 (GLP-1) and Glucose-dependent Insulinotropic Peptide (GIP) [1]. By prolonging the half-life of endogenous incretins, these agents augment glucose-dependent insulin secretion, suppress glucagon release, and promote modest weight neutrality [1, 2]. Vildagliptin, licensed in the European Union in 2007, is commonly prescribed either as monotherapy or in fixed-dose combination with metformin.

The tolerability profile of vildagliptin is generally favourable; commonly reported adverse effects include nasopharyngitis, headache, dizziness, and rarely elevated hepatic transaminases and polyarthritis [1, 3, 4]. Haematological adverse effects, particularly thrombocytopenia, are absent from the drug's summary of product characteristics. However, the DPP enzyme family includes not only the extracellular DPP-4 but also the cytosolic enzymes DPP-8 and DPP-9, selective inhibition of which has been associated with thrombocytopenia, reticulocytopenia, splenomegaly, and mortality in animal models [5]. Pharmacovigilance data from VigiBase, the WHO global database of individual case safety reports, contain 20 reports of thrombocytopenia associated with vildagliptin [6]. Published case reports documenting this adverse reaction remain scarce; Siddiqi and Saad reported the first in 2016, describing a 58-year-old woman whose platelet count declined progressively over 21 months of vildagliptin use and normalised following discontinuation [7]. We add to this sparse literature with the present report, structured in accordance with CARE guidelines.

Case Presentation

A 62-year-old woman with a 15-year history of T2DM and a 10-year history of hypertension presented to the outpatient diabetes clinic for routine review. Her antidiabetic regimen comprised metformin 1000 mg twice daily, glimepiride 2 mg once daily, and vildagliptin 50 mg twice daily, the last introduced approximately ten months earlier for suboptimal glycaemic control. Antihypertensive medications included telmisartan 40 mg once daily and amlodipine 5 mg once daily, both unchanged for over three years. She also received atorvastatin 20 mg once daily. No herbal preparations, over-the-counter agents, or nutritional supplements were used. There was no history of recent viral illness, blood transfusion, alcohol consumption, or toxic exposures. The

OPEN ACCESS

Correspondence:
Dr. Rahul Garg, MBBS, MD, Professor, Department of Medicine, FH Medical College and Hospital, Agra, Uttar Pradesh, India,
E-mail: gargrahul27@gmail.com

Received Date: *15 Jun 2026*
Accepted Date: *03 Aug 2026*
Published Date: *05 Aug2026*

Citation:
Rahul Garg. Vildagliptin-Induced Thrombocytopenia: A Case Report with Pharmacovigilance Perspective. WebLog J Clin Case Rep. wjccr.2026.h0504. https://doi.org/10.5281/zenodo.21852173

Table 1: Serial platelet counts in relation to vildagliptin exposure.

Timepoint	Platelet count (×10⁹/L)	Clinical context
Baseline (vildagliptin initiation)	198	Pre-exposure baseline
10 months after initiation	74	Presentation; vildagliptin identified as suspect agent
1 week post-presentation	71	Repeat confirmation (second analyser)
2 weeks post-presentation	69	Repeat confirmation (third analyser)
Vildagliptin discontinued		
2 weeks post-discontinuation	88	Recovery begins
4 weeks post-discontinuation	127	Continued recovery
6 weeks post-discontinuation	168	Near-normalisation
12 weeks post-discontinuation	193	Complete recovery confirmed

patient denied spontaneous bleeding, petechiae, ecchymoses, or excessive bruising.

Routine haemogram revealed a platelet count of 74×10^9/L, a significant decline from a baseline of 198×10^9/L documented at vildagliptin initiation. Haemoglobin (11.8 g/dL) and total leucocyte count (6,400/μL) with differential were within normal limits. Peripheral blood smear confirmed thrombocytopenia and excluded pseudo-thrombocytopenia, showing no platelet clumping, abnormal leucocyte morphology, or microangiopathic changes. Repeat counts on two occasions at one-week intervals on different analysers yielded 71×10^9/L and 69×10^9/L, corroborating the finding.

Investigations to identify an alternative aetiology included: antinuclear antibody (negative), antiplatelet antibody testing (negative), dengue NS1 antigen and IgM serology (negative), hepatitis B surface antigen and anti-hepatitis C virus antibody (both negative), HIV serology (non-reactive), serum vitamin B12 and folate (normal), thyroid-stimulating hormone (2.1 mIU/L), and liver function tests (normal). Coagulation parameters were normal. Ultrasound abdomen showed no hepatosplenomegaly or lymphadenopathy. A haematology opinion was sought; given isolated thrombocytopenia without constitutional symptoms or organomegaly, bone marrow examination was deferred pending a drug withdrawal trial.

Medication review identified vildagliptin as the only agent introduced in the ten months preceding thrombocytopenia. All concurrent medications had been continued unchanged for three to seven years without prior haematological abnormality. Vildagliptin was discontinued and the patient observed on remaining medications with intensified glycaemic monitoring. Serial platelet counts are summarised in Table 1. Complete recovery to 193×10^9/L was confirmed at twelve weeks without platelet transfusion or immunosuppressive therapy.

Causality assessment using the Naranjo Scale yielded a score of 6, placing the reaction in the probable category [8]. WHO-UMC causality assessment likewise categorised the association as probable, given the plausible temporal relationship, consistent dechallenge response, and absence of a more credible alternative explanation [9]. The reaction was classified as Type B (idiosyncratic), as it was not predictable from the known pharmacology of DPP-4 inhibitors and occurred at a standard therapeutic dose [10].

Discussion

This case presents a temporally coherent association between vildagliptin use and isolated, gradually progressive thrombocytopenia. Several features strengthen causal inference: thrombocytopenia developed exclusively during vildagliptin exposure with all concurrent medications unchanged; platelet counts declined progressively over ten months in a pattern consistent with drug-induced marrow suppression or peripheral destruction rather than acute immune-mediated thrombocytopenia; complete and sustained recovery occurred within twelve weeks of discontinuation without haematological intervention; and comprehensive evaluation excluded viral, autoimmune, nutritional, and haematological aetiologies.

The existing case literature is notably sparse. Siddiqi and Saad described a strikingly similar clinical course, with gradual platelet decline over 21 months normalising after vildagliptin discontinuation. Importantly, subsequent use of sitagliptin did not reproduce the haematological abnormality over 14 months of follow-up, suggesting agent-specific rather than class-specific toxicity [7]. This selectivity aligns with established biochemical heterogeneity within the DPP inhibitor family. Davis et al. demonstrated that sitagliptin exhibits high selectivity for DPP-4 over DPP-8 and DPP-9 and functions as a purely competitive, rapidly reversible inhibitor - pharmacodynamically distinct from the slow-binding, near-irreversible inhibition produced by vildagliptin [2]. Animal studies by Lankas et al. demonstrated that selective inhibition of DPP-8 and DPP-9 produced a consistent toxicity syndrome comprising thrombocytopenia, reticulocytopenia, splenomegaly, and mortality, whereas selective DPP-4 inhibition did not [5]. Brandt et al., further characterised vildagliptin's selectivity profile, finding inhibitory activity against DPP-8 at micromolar concentrations despite nanomolar potency at DPP-4, with Ki values for DPP-9 and DPP-8 of 95 nM and 810 nM respectively, compared to 3 nM for DPP-4 [3]. This pharmacological margin, while protective in most individuals, may be insufficient in rare patients with pharmacokinetic variability or polymorphic drug metabolism, providing a mechanistically plausible basis for idiosyncratic toxicity at standard therapeutic doses.

The clinical presentation of vildagliptin - induced thrombocytopenia - insidious onset, absence of bleeding symptoms despite significantly reduced platelet counts, and lack of associated cytopenias - poses a diagnostic challenge. Without routine haematological monitoring, the diagnosis may be delayed, prompting unnecessary invasive investigation such as bone marrow biopsy, as was considered in the present patient. A structured drug withdrawal trial before proceeding to invasive haematological evaluation may spare patients considerable morbidity. The pharmacovigilance signal supports clinical vigilance: given well-recognised under-reporting in spontaneous pharmacovigilance systems, the actual incidence of this adverse effect is likely higher than current VigiBase data reflect.

The primary limitations are inherent to the case report design: absence of formal rechallenge (withheld for ethical reasons), single-patient observation, and the theoretical possibility of spontaneous resolution coinciding with drug discontinuation. However, the progressive and sustained platelet decline during exposure, complete and durable recovery following withdrawal, absence of any identifiable alternative aetiology, and the precedent in prior published data collectively render spontaneous resolution an unlikely explanation.

Conclusion

This case documents probable vildagliptin-induced thrombocytopenia characterised by insidious onset, progressive

platelet decline during drug exposure, and complete recovery following discontinuation without haematological intervention. Supported by a Naranjo score of 6, WHO-UMC probable causality classification, and 20 corresponding VigiBase reports, this report highlights an underappreciated adverse effect of vildagliptin. Clinicians should consider periodic platelet monitoring in patients receiving this agent and maintain a low threshold for drug withdrawal in cases of unexplained thrombocytopenia.

Patient Perspective

The patient expressed concern on being informed of the possibility of a blood disorder and reported significant anxiety during the period of investigation. She was relieved by resolution of the abnormality following drug change and consented to publication of this report to help other patients.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report.

Declaration of Competing Interests

None declared.

Funding

None.

References

1. Kasina SVSK, Baradhi KM. Dipeptidyl Peptidase IV (DPP IV) Inhibitors. StatPearls. 2026.
2. Davis JA, Singh S, Sethi S, Roy S, Mittra S, Rayasam G, et al. Nature of action of Sitagliptin, the dipeptidyl peptidase-IV inhibitor in diabetic animals. Indian J Pharmacol. 2010; 42(4): 229-33.
3. Brandt I, Joossens J, Chen X, Maes MB, Scharpé S, De Meester I, et al. Inhibition of dipeptidyl-peptidase IV catalyzed peptide truncation by Vildagliptin. Biochem Pharmacol. 2005; 70(1): 134-143.
4. Garg R, Thakre A. Vildagliptin-induced polyarthritis: First documented case with positive rechallenge and complete reversal. J Diabetol 2026; 17: 203-206.
5. Lankas GR, Leiting B, Roy RS, Eiermann GJ, Beconi MG, Biftu T, et al. Dipeptidyl peptidase IV inhibition for the treatment of type 2 diabetes: potential importance of selectivity over dipeptidyl peptidases 8 and 9. Diabetes. 2005; 54(10): 2988-2994.
6. Uppsala Monitoring Centre. VigiAccess. Uppsala. 2015.
7. Siddiqi AI, Saad K. Thrombocytopenia: Could it be Vildagliptin. Ann Case Rep. 2016.
8. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981; 30(2): 239-245.
9. The Uppsala Monitoring Centre. The WHO-UMC causality assessment system. Uppsala. 2026.
10. Iasella CJ, Johnson HJ, Dunn MA. Adverse Drug Reactions: Type A (Intrinsic) or Type B (Idiosyncratic). Clin Liver Dis. 2017; 21(1): 73-87.