Case Report

Dabigatran-associated drug exanthema and its increasing prevalence

Shashank Jaiswal[1], Aditi Jaiswal[2], Subhash Kaul[3]

From [1]Consultant, Department of Neurology, Care Hospital, [2]Consultant, Department of Dermatology, Jaiswal Hospital, [3]Consultant, Department of Neurology, KIMS, Hyderabad, Telangana, India

ABSTRACT

Anticoagulants are commonly associated with hemorrhagic complications. However, rare hypersensitivity drug reactions associated with direct oral anticoagulants (DOACs) in the form of cutaneous reactions such as vasculitis, exanthema, and urticaria are also being reported. With the increase in the use of DOACs over warfarin as the choice of anticoagulant in the treatment of atrial fibrillation, as well as venous thromboembolism, recently, there has been a rise in the number of reported cutaneous adverse effects. This case report describes the clinical course of a 29-year-old postpartum patient being treated for cerebral venous sinus thrombosis, who experienced Dabigatran-induced exanthema. We further provide a review of all the cases reported so far.

Key words: Dabigatran, Drug reaction, Pregnancy-associated stroke

Cerebral venous sinus thrombosis (CVT) is an uncommon cause of stroke, accounting for approximately 0.5–1% of all strokes, with pregnancy and the puerperium representing well-recognized risk factors [1]. Pregnancy-associated physiological hypercoagulability, vascular endothelial injury, and hemodynamic alterations substantially increase the risk of venous thromboembolism (VTE), including CVT. Anticoagulation remains the cornerstone of treatment, preventing thrombus propagation and facilitating venous recanalization. Direct oral anticoagulants (DOACs) have increasingly emerged as alternatives to Vitamin K antagonists due to their predictable pharmacokinetic profiles, fewer drug interactions, fixed dosing regimens, and lack of requirement for routine laboratory monitoring. Dabigatran etexilate, a direct thrombin inhibitor (DTI), has demonstrated efficacy and safety in the prevention and treatment of thromboembolic disorders, including atrial fibrillation (AF) and VTE. Although evidence supporting its use in CVT remains limited, recent studies suggest comparable efficacy and safety to conventional anticoagulants, resulting in increasing off-label utilization. The adverse effect profile of dabigatran is generally favorable, with bleeding complications and dyspepsia being the most frequently reported events. However, rare hypersensitivity reactions, including urticaria, leukocytoclastic vasculitis, drug exanthema, and drug reaction with eosinophilia and systemic symptoms (DRESS), have been increasingly recognized through post-marketing surveillance and isolated case reports. As the use of DOACs continues to expand globally, clinicians are likely to encounter a growing number of such uncommon adverse cutaneous reactions.

We report a case of dabigatran-associated drug exanthema in a young postpartum woman treated for CVT. The diagnosis was supported by the temporal relationship between drug exposure and symptom onset, eosinophilia, histopathological findings, and complete resolution following drug withdrawal. We also review the available literature on dabigatran-induced cutaneous hypersensitivity reactions and discuss their clinical implications in the era of increasing DOAC utilization. Given the rapidly expanding use of DOACs in diverse thromboembolic disorders, recognition and reporting of rare cutaneous hypersensitivity reactions are important to improve clinician awareness, facilitate early diagnosis, and guide decisions regarding alternative anticoagulant therapy.

CASE REPORT

A 29-year-old primiparous woman presented 5 days after a lower-segment cesarean section with severe headache followed by generalized tonic–clonic seizures. She had been previously healthy, with an uneventful antenatal course and no prior history of thromboembolic disease, autoimmune disorders, atopy, or drug allergies.

On examination, she was hemodynamically stable with a blood pressure of 130/80 mmHg, pulse rate of

Access this article online

Received - 24 December 2025
Initial Review - 07 January 2026
Accepted - 30 June 2026

Quick Response code

DOI: 10.32677/ijcr.v12i7.8019

Correspondence to: Aditi Jaiswal, 128/A, Jaiswal Hospital, Kalyan Nagar Phase 3, Hyderabad, Telangana, India, E-mail: drjaiswalshashank@gmail.com

84 beats/min, and temperature of 98.2°F. Neurological examination revealed no focal deficits, and there were no clinical signs of meningeal irritation.

Magnetic resonance (MR) imaging brain with MR venography demonstrated extensive CVT involving the superior sagittal sinus, right transverse sinus, right sigmoid sinus, and proximal right internal jugular vein, associated with a right parietal hemorrhagic venous infarction. Baseline hematological and biochemical investigations, including renal and liver function tests, were within normal limits.

The patient was initially treated with low-molecular-weight heparin and subsequently transitioned to oral dabigatran 150 mg twice daily. Within 24 h of initiating dabigatran, she developed pruritus accompanied by erythema and mild swelling over the face. Despite continuation of therapy, the symptoms progressively worsened over the next 3 days, extending to involve the scalp and neck. Dabigatran was discontinued at that stage; however, the eruption continued to progress over the following several days, eventually involving the trunk and extremities. Five days later, she presented with diffuse rash, facial edema, and fever.

Dermatological examination revealed widespread ill-defined blanchable erythematous plaques with associated pruritus and fine scaling involving the face, neck, chest, abdomen, back, and upper and lower limbs (Figs. 1 and 2). Mild periorbital edema was present. Mucosal involvement was limited to the oral cavity, while the palms were involved and the soles and genital mucosa were spared (Fig. 3). Detailed history failed to identify any alternative triggers, including newly introduced medications, over-the-counter drugs, dietary changes, detergents, cosmetics, or other environmental exposures.

Laboratory investigations demonstrated marked eosinophilia (35%) with preserved renal and hepatic function. Given the presence of fever, eosinophilia, and extensive cutaneous involvement, a skin biopsy was performed to evaluate for DRESS syndrome. Histopathological examination showed epidermal hyperkeratosis, acanthosis, and spongiosis with superficial perivascular mixed inflammatory infiltrates containing eosinophils, findings consistent with a drug-induced hypersensitivity reaction (Fig. 4).

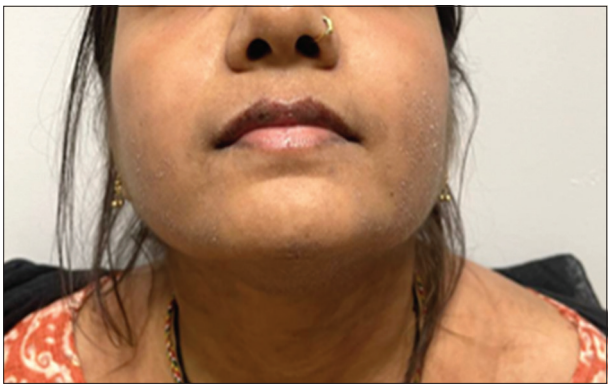

Figure 1: Erythema and excoriation of the face

The patient was treated with dexamethasone for symptomatic relief, and therapeutic anticoagulation

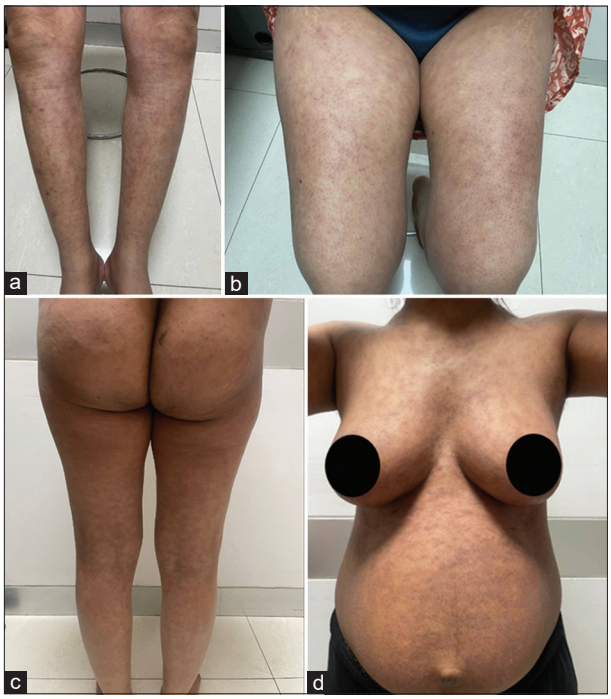

Figure 2: Multiple erythematous blanchable patches present (a) anteriorly on Bilateral Lower limb, (b) bilateral thigh, as well as (c) posteriorly and on (d) chest

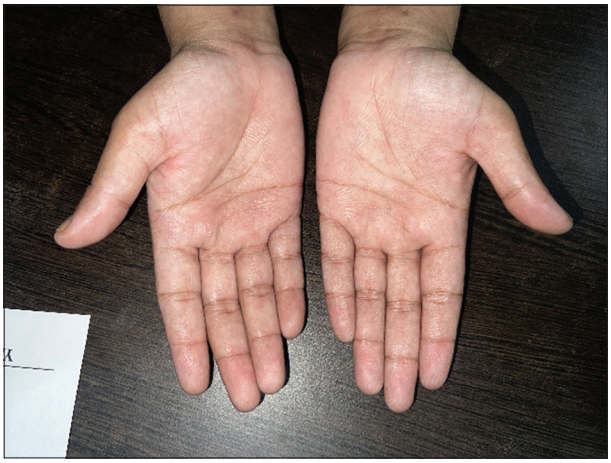

Figure 3: Multiple blanchable erythematous macules on bilateral palms

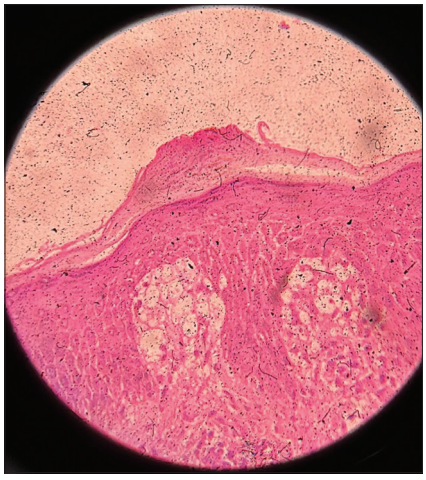

Figure 4: Histopathological specimen of the lesion from the left leg

Table 1: Review of literature of cases

References	Symptom of rash	Location of rash	Management of rash	Time of occurrence of rash	Time for resolution of rash	Rechallenge test	Naranjo score interpretation	Skin biopsy
To *et al*. [2]	Diffuse, non-pruritic	Trunk and lower extremities	Discontinuation of the drug	5 days	~ 7 days	No	N/A	Not done
Whitehead *et al*. [11]	Raised, pruritic, erythematous	Inner thigh and forearm	Discontinuation of dabigatran, initiation of prednisone	~ 2 wks.	~ 2 days	No	Probable	Not done
Eid and Shah [12]	Pruritic	Diffuse throughout body	Discontinuation of dabigatran, diphenhydramine 50 mg i.m. dose followed by diphenhydramine 50 mg p.o. every 6 hrs	1 day	<9 days	No	Probable (score of 7)	Not done
Cucurull *et al*. [13]	Pruritic	Shoulder and lower extremities	Discontinuation of the antibiotic and dabigatran etexilate	Not reported	Not reported	Yes	Probable	Not done
Lee *et al.* [14]	Non-blanching erythematous palpable petechiae and purpura	Thighs, arms, and the lower abdomen	Discontinuation of drug	10 days	Several days	No	N/A	Not done
Rao *et al.* [15]	Painful erythematous plaques and nodules	Bilateral upper extremities	Systemic steroids	10 years	Waxing and waning	No	N/A	Dermal edema and neutrophilic infiltrate with occasional eosinophils
Schleichert *et al*. [16]	Discreet pustules with minimal erythema of the underlying skin	Palms and soles	Discontinuation of drugs	1 day	After discontinuation	No	Probable (score of 7)	Mild hyperkeratosis, spongiosis with lymphocyte exocytosis, intraepidermal vesiculation, and a sparse upper dermal and perivascular lymph histiocytic infiltration
Patil and Ikekwere [17]	Pruritic morbilliform exanthemas	Elbows, axillae, and lower extremities	Discontinuation of drugs	10 days	1 week	No	N/A	Not done
An *et al.* [18]	Palpable purpura, petechiae	Lower extremities, torso, and distal upper extremities	N/A	3 days	N/A	No	N/A	Not done

was maintained with enoxaparin for 3 days before transition to apixaban. Progressive clinical improvement occurred following withdrawal of dabigatran, with complete resolution of the rash within 1 week, leaving only mild post-inflammatory hyperpigmentation. The Naranjo Adverse Drug Reaction Probability Scale score was 7, indicating a probable adverse drug reaction. At follow-up, the patient remained asymptomatic and tolerated apixaban without recurrence of cutaneous manifestations.

DISCUSSION

Dabigatran etexilate and its acyl glucuronides are reversible, competitive, DTIs. Because thrombin (serine protease) enables the conversion of fibrinogen into fibrin during the coagulation cascade, its inhibition prevents the development of a thrombus. Both free and clot-bound thrombin, and thrombin-induced platelet aggregation are inhibited by the active moieties [2,3].

It is an oral drug with primarily renal clearance. It has been shown to be as effective as Warfarin, with a decreased risk of untoward bleeding. Dabigatran etexilate was approved by the United States Food and Drug Administration (FDA) in October 2010. It is a direct thrombin antagonist that has been proven to be efficacious and to have a good safety profile when used for stroke prevention in patients with AF [4], as well as when used for treatment and prevention of recurrent DVT and PE [5]. Dabigatran and other non-Vitamin K oral anticoagulants are occasionally used off-label in patients with CVT. A trial found that CVT patients who were started on either dabigatran or warfarin had a low risk of recurrent VTEs, and the risk of bleeding was similar with both medications, suggesting that both dabigatran and warfarin may be safe and effective for preventing recurrent VTEs in patients with CVT [6]. The evidence for DOAC use in CVT is limited, although it suggests sufficient safety and efficacy despite variability in timing and dose of treatment [7]. When compared to warfarin, the 150-mg dose of dabigatran significantly reduced the primary composite endpoint of stroke and systemic embolism (1.11%/year vs. 1.69%/year) as seen in the RE-LY study [8].

In the RE-LY study, the most common adverse drug reactions reported for patients receiving dabigatran etexilate 150 or 110 mg were bleeding and dyspepsia. Drug hypersensitivity reactions were reported in <0.1% patients receiving dabigatran [8]. One out of 60 patients receiving dabigatran experienced urticaria in the RE-SPECT CVT trial [6]. To date, there have been a few reported cases of dabigatran etexilate–associated rash. One case was reported to the FDA during post-marketing surveillance [9]. Another case was reported in an observational study [10], and a few were published case reports [2,11-18] (Table 1). One case report had evidence of cross-reactivity between Rivaroxaban and Dabigatran. Our patient, however, did not develop a rash on switching to the Factor Xa inhibitor Apixaban.

In conclusion, the number of reported cutaneous adverse reactions associated with dabigatran remains small; however, an increasing trend has been observed over the past decade, likely reflecting both expanded clinical use and improved pharmacovigilance. Most reported reactions have occurred within days to weeks of drug initiation and have resolved after drug withdrawal. Recognition of these reactions is important because early discontinuation can prevent progression to severe hypersensitivity syndromes such as DRESS. Furthermore, available evidence suggests that switching to an alternative DOAC may be feasible in selected patients, although isolated reports of cross-reactivity warrant careful monitoring. This is possibly the first such case report in the South Asian population.

CONCLUSION

Although the most common adverse effects of dabigatran are bleeding and dyspepsia, clinicians should also be aware of the potential for cutaneous hypersensitivity reactions to this drug.

REFERENCES

1. Breteau G, Mournier Vehier F, Godefroy O, Gauvrit JY, Mackowiak-Cordoliani MA, Girot M, *et al*. Cerebral venous thrombosis 3-year clinical outcome in 55 consecutive patients. J Neurol 2003;250:29-35.
2. To K, Reynolds C, Spinler SA. Rash associated with dabigatran etexilate. Pharmacotherapy 2013;33:e23-7.
3. Pradaxa [Package Insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2011. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/022512s004lbl.pdf [Last accessed on 2026 Mar 14].
4. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, *et al*. RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361:1139-51.
5. Schulman S, Kearon C, Kakkar AK, Mismetti P, Schellong S, Eriksson H, *et al*. Dabigatran versus warfarin in the treatment of acute venous thromboembolism. N Engl J Med 2009;361:2342-52.
6. Ferro JM, Coutinho JM, Dentali F, Kobayashi A, Alasheev A, Canhão P, *et al*. Safety and efficacy of dabigatran etexilate vs dose-adjusted warfarin in patients with cerebral venous thrombosis. JAMA Neurol 2019;76:1457-65.
7. Bose G, Graveline J, Yogendrakumar V, Shorr R, Fergusson DA, Gal GL, *et al*. Direct oral anticoagulants in treatment of cerebral venous thrombosis: A systematic review. BMJ Open 2021;11:e040212.
8. Connolly SJ, Ezekowitz MD, Yusuf S, John E, Oldgren J, Parekh A, *et al*. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361:1139-51.
9. Food and Drug Administration Advisory Committee Briefing Document: Dabigatran for AF; 2010. Available from: http://www.fda.gov/downloads/advisorycommittees/committees/meetingmaterials/drugs/cardiovascularandrenaldrugsadvisory committee/ucm247244.pdf [Last accessed on 2011 Apr 25].
10. Winkle RA, Mead RH, Engel G, Kong MH, Patrawala RA. The use of dabigatran immediately after atrial fibrillation ablation. J Cardiovasc Electrophysiol 2011;23:264-8.
11. Whitehead H, Boyd JM, Blais DM, Hummel J. Drug-induced exanthem following dabigatran. Ann Pharmacother 2011;45:e53.
12. Eid TJ, Shah SA. Dabigatran-induced rash. Am J Health Syst Pharm 2011;68:1489-90.
13. Cucurull I, Canosa J, Vega-Molpeceres S, Garcia E. [Dabigatran induced exanthema]. Rev Clin Esp 2010;210:590-1.

14. Lee HL, Kim L, Kim CW, Kim JS, Nam HS, Ryu JS. Case of both rivaroxaban- and dabigatran-induced leukocytoclastic vasculitis, during management of pulmonary thromboembolism. Respir Med Case Rep 2019;26:219-22.
15. Rao M, Méndez A, Rahnama-Moghadam S. Drug-induced sweet syndrome likely secondary to dabigatran. J Allergy Clin Immunol Pract 2022;10:3315-6.e1.
16. Schleichert R, Goldner R, Dickfeld T. Palmoplantar pustular eruption due to dabigatran. Cutis 2016;97:E10-1.
17. Patil T, Ikekwere C. A case report of rivaroxaban-induced urticaria and angioedema with possible cross-reaction to dabigatran. J Med Cases 2019;10:359-63.
18. An J, Garje R, Wanat KA, Leone JP. Dabigatran-related leukocytoclastic vasculitis. BMJ Case Rep 2017;2017:bcr2016217423.

Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Jaiswal S, Jaiswal A, Kaul S. Dabigatran-associated drug exanthema and its increasing prevalence. Indian J Case Reports. 2026;12(7):482-486.