JoTH Journal of Tropical Health

Case Report

Cutaneous Thrombosis in Paroxysmal Nocturnal Haemoglobinuria: A Rare Manifestation of a Common Complication

Indika Somaratne[1*], Iranthi Kumarasinghe[1], Priyamali Jayasekara[2]

[1]Department of Paraclinical Sciences, General Sir John Kotelawala Defence University, Sri Lanka.

[2]Department of Clinical Sciences, General Sir John Kotelawala Defence University, Sri Lanka.

Abstract

Paroxysmal nocturnal haemoglobinuria (PNH) is a rare clonal disorder of haematopoietic stem cells characterized by complement-mediated intravascular haemolysis and a high risk of thrombosis and bone marrow failure. While venous thrombosis in atypical sites such as intra-abdominal and cerebral veins is well documented, cutaneous thrombosis remains an exceptionally rare manifestation. We report a case of a 72-year-old female with PNH who presented with acute haemolysis and subsequently developed painful, erythematous skin lesions with central necrosis. Skin biopsy confirmed cutaneous thrombosis. Due to the unavailability of complement inhibitors, she was treated with therapeutic low molecular weight heparin followed by long-term anticoagulation with apixaban. The lesions resolved without progression, and she remained thrombosis-free over a three-year follow-up despite ongoing haemolysis requiring transfusions.

This case highlights the importance of considering cutaneous thrombosis in PNH patients presenting with rapidly evolving skin lesions. Early diagnosis and prompt anticoagulation are critical. Although complement inhibitors have revolutionized PNH management, their limited accessibility in low-resource settings necessitates reliance on anticoagulation. Literature reveals varied approaches to managing cutaneous thrombosis, emphasizing individualized care. This report underscores the need for clinical vigilance and tailored treatment strategies in resource-constrained environments.

Keywords: Anticoagulation, Complement inhibitor, Cutaneous thrombosis, Paroxysmal nocturnal haemoglobinuria

Funding: None
Competing interests: None
Received: 24 October 2025 **Accepted:** 09 November 2025 **Published:** 24 November 2025

Corresponding author: Email: somaratnepdis@kdu.ac.lk https://orcid.org/0009-0003-0910-1414

Cite this article as: Somaratne I et al. Cutaneous Thrombosis in Paroxysmal Nocturnal Haemoglobinuria: A Rare Manifestation of a Common Complication. Journal of Tropical Health 2025;1 (3): 42-45. DOI: http://doi.org/10.4038/joth.v1i3.35

Introduction

Paroxysmal nocturnal haemoglobinuria (PNH) is a rare acquired clonal disorder of haemopoietic stem cells with an incidence of about 1–2 per million and prevalence ranging between 10 to 30 per million [1]. An acquired mutation in the phosphatidylinositol glycan class A gene (PIGA) leads to loss of glycosylphosphatidylinositol (GPI) anchored proteins on the cell membrane. Notably, the lack of CD55 and CD59, two key GPI-linked complement regulatory proteins, renders red cells vulnerable to complement-mediated destruction, leading to intravascular haemolysis. Thrombosis and bone marrow failure are the other main complications of the disease. Thrombosis is a major cause of death in PNH, and 29-44% of patients present at least with one thrombotic event during the disease course [2]. The advent of complement inhibitors has significantly lowered thrombotic risk by approximately 80% in regions where

these therapies are accessible. Unfortunately, the high cost of these medications restricts their availability in many low- and middle-income countries. Venous thrombosis is more frequently observed than arterial thrombosis in patients with PNH. While venous thrombosis can affect any site, its occurrence in unusual sites is characteristic. Among these unusual sites, thrombosis of intra-abdominal veins and cerebral venous sinus thrombosis are relatively common. In contrast, cutaneous thrombosis is rare, with only a few cases documented globally and none reported from Sri Lanka to date.

Case report

A 72-year-old female with a history of diabetes mellites, hypertension, chronic renal impairment and PNH diagnosed three years earlier with a large PNH clones in granulocytes (89.5%), monocytes (89.1%) and red cell (99.7%), presented with fever and cough for two days along with features of acute intravascular haemolysis. She was not on anticomplement therapy. Initial investigations revealed severe anaemia (Haemoglobin - 5.4 g/dL), a total white cell count of 5.52 × 10^3/µL with 3.7 × 10^3/µL neutrophils, and a platelet count of 121 × 10^3/µL. Elevated lactate dehydrogenase (1298 u/L) and serum bilirubin levels, along with positive urine haemosiderin, confirmed ongoing intravascular haemolysis. Her C-reactive protein (CRP) was mildly elevated at 10.3 mg/dL, liver enzymes showed aspartate transaminase (AST) 67 U/L and alanine transaminase (ALT) 28 U/L, and renal function was stable with a serum creatinine of 1.03 mg/dL and an estimated glomerular filtration rate (eGFR) of 33 mL/min. She was initially managed with red cell transfusions and empirical antibiotics. Two days into admission, she developed two tender, erythematous, indurated plaques on her forehead and a similar lesion with central necrosis on her lower lip (figure 1). She also reported abdominal pain, prompting evaluation for thrombosis, though abdominal imaging was unremarkable. Given her PNH background, cutaneous thrombosis was suspected, and therapeutic low molecular weight heparin (LMWH) was initiated. A skin biopsy later confirmed cutaneous thrombosis (figure 2). There were no additional clinical features indicative of a connective tissue disorder, and her antinuclear antibody (ANA) test was negative, making vasculitis an unlikely diagnosis. A diagnosis of PNH-associated cutaneous thrombosis was made. Her skin lesions improved with anticoagulation, and after one week of enoxaparin, she was discharged on apixaban 2.5 mg twice daily. She has remained free of thrombotic events for three years while continuing anticoagulation and receiving supportive care with recurrent blood transfusions for ongoing intravascular haemolysis. Furthermore, no anticoagulation-related bleeding events were reported during the three-year follow-up period.

Figure 1: Necrotic skin lesion in the lower lip.

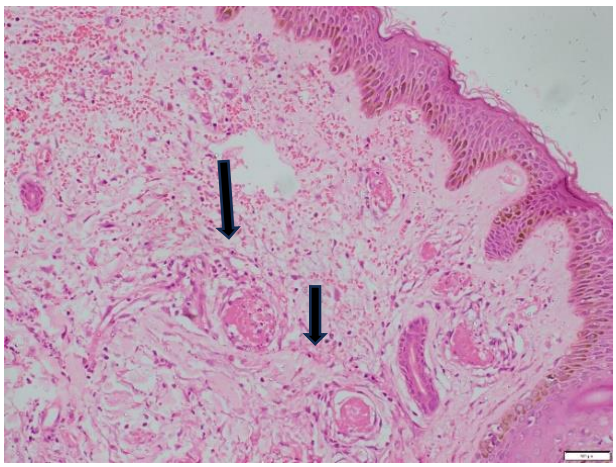

Figure 2: Skin biopsy displaying thrombosis of dermal blood vessels (arrows). (x400, Haematoxylin and Eosin)

Discussion

Here we present a case of cutaneous thrombosis in a patient with PNH, successfully managed with therapeutic anticoagulation and supportive care. Despite the unavailability of complement inhibitors, timely recognition and intervention led to a favourable clinical outcome.

PNH is a clonal hematopoietic stem cell disorder caused by a somatic mutation in the PIGA gene. This mutation disrupts the synthesis of GPI anchors, which are essential for attaching complement regulatory proteins like CD55 and CD59 to the surface of blood cells. Their absence leads to uncontrolled complement activation and intravascular haemolysis, a hallmark of PNH. Other characteristic features are thrombosis and bone marrow failure leading to cytopenia.

Thrombosis remains the leading cause of morbidity and mortality in PNH. A significant proportion of patients experience at least one thrombotic episode during the disease course, and in some cases, multiple vascular sites may be involved. The prothrombotic state in PNH is multifactorial, driven by intravascular haemolysis, complement activation, and impaired fibrinolysis [3]. Thrombosis at the time of infection is common in PNH and can be attributed to pathogen-induced complement activation. The same process could be the triggering event for thrombosis in our patient. Among the recognised risk factors for thrombosis in PNH, the presence of a large clone of CD59-negative polymorphonuclear cells (exceeding 50%) is a significant predictor. Additional risk factors include LDH levels at least 1.5 times the upper limit of normal, a history of prior thrombotic events, and the presence of clinical symptoms related to PNH [3]. Our patient exhibited several of these high-risk features, including a CD59-negative granulocyte clone of 89.5%, elevated LDH levels, and symptomatic chronic intravascular haemolysis, all of which placed her at substantial risk for thrombotic complications

In PNH, thrombosis can affect any vascular site, with venous thrombosis occurring more frequently than arterial thrombosis. It is well known to cause venous thrombosis at unusual sites, most notably within the intra-abdominal and cerebral veins. Hepatic vein thrombosis (Budd-Chiari syndrome), is among the most common thrombotic manifestations, occurring in approximately 7.5% to 25% of PNH patients [4]. Cutaneous thrombosis is a rare complication, with only a few cases documented globally and none previously reported from Sri Lanka. Patients typically present with painful, discoloured skin lesions that may ulcerate. These lesions can be localized or diffuse, sometimes mimicking purpura fulminans [4]. In some case reports, cutaneous thrombosis has been associated with more extensive thrombotic involvement, including mesenteric vein thrombosis and Budd-Chiari syndrome [5,6]. Given these risks, prompt recognition and timely initiation of treatment are essential to prevent progression and improve outcomes.

The introduction of complement inhibitors such as eculizumab and ravulizumab has significantly transformed the management of PNH, reducing the risk of thrombosis by approximately 80% and markedly improving both quality of life and overall survival [2]. However, the high cost of these therapies has restricted access in many low- and middle-income countries, including Sri Lanka. The recommended approach for managing acute thrombosis in PNH involves initiating therapeutic anticoagulation alongside complement inhibition with either eculizumab or ravulizumab. For initial anticoagulation, LMWH or unfractionated heparin (UFH) is preferred [3]. Long-term anticoagulation is typically maintained with vitamin K antagonists such as warfarin, although direct oral anticoagulants (DOACs) are increasingly considered, despite limited data on their use in this context. Importantly, indefinite anticoagulation following a thrombotic event may not be necessary once complement inhibitor therapy is established, depending on individual risk factors and clinical response [3,7]. The literature on cutaneous thrombosis in PNH revealed varied therapeutic approaches, reflecting the rarity and clinical variability of this complication. Some reported cases have shown favourable responses to steroid therapy alone, while others have benefited from a combination of anticoagulation and steroids, or from complement inhibitors used alongside anticoagulation. In all instances, supportive care, including antibiotics or other antimicrobial agents, was administered when clinically indicated [6,8–11]. These findings underscore the need for individualised treatment plans based on scientific evidence, available resources, patient characteristics, and clinical judgment. In our patient, due to the unavailability of complement inhibitors, therapeutic anticoagulation with LMWH (1 mg/kg twice daily) was initiated, resulting in the resolution of skin lesions without further progression. She was subsequently discharged on apixaban 2.5 mg twice daily; the dose was selected in view of her low body mass index and renal impairment. Over a three-year follow-up period, she remained free of thrombotic events, despite ongoing haemolysis that necessitated recurrent red cell transfusions and a few hospital admissions with infections needing antibiotic treatment.

Primary thromboprophylaxis in patients with PNH has demonstrated beneficial outcomes in certain studies. However, with the widespread adoption of complement inhibitors such as eculizumab and ravulizumab, many countries have shifted away from routine use of primary prophylaxis [2,3,12]. In settings where access to these therapies is limited, evaluating patients for high-risk features and considering primary thromboprophylaxis may play a crucial role in preventing thrombotic complications.

Conclusion

PNH is a rare haematological disorder in which thrombosis remains a leading cause of morbidity and mortality. Cutaneous thrombosis is an uncommon manifestation of PNH. Nonetheless, it should be

considered in PNH patients presenting with rapidly developing, painful skin lesions, and a skin biopsy can be instrumental in differentiating it from other causes of skin necrosis. Early recognition, initiation of therapeutic anticoagulation, and complement inhibition with agents such as eculizumab is the mainstay of effective management. However, in resource-limited settings like Sri Lanka, where access to complement inhibitors is restricted, therapeutic anticoagulation at presentation remains the primary treatment strategy, followed by long-term anticoagulation tailored to individual disease characteristics and patient factors. Additionally, in such contexts, primary thromboprophylaxis may be beneficial for patients identified as high risk.

Consent

Informed written consent was obtained from the patient for publishing this case report.

References

1. Cançado RD, Araújo A da S, Sandes AF, Arrais C, Lobo CL de C, Figueiredo MS, et al. Consensus statement for diagnosis and treatment of paroxysmal nocturnal haemoglobinuria. Hematol Transfus Cell Ther. 2021;43(3):341–8. doi: 10.1016/j.htct.2020.06.006.

2. Apodaca Chavez E, Rangel-Patiño J, Tuna-Aguilar EJ, Garcés-Martínez A, Demichelis R. Total oral anticoagulation for classic PNH as primary prophylaxis strategy in a complement inhibitor restricted scenario: A retrospective analysis. Blood. 2021;138(Supplement 1):1118–1118. doi: 10.1182/blood-2021-153515.

3. Kokoris S, Polyviou A, Evangelidis P, Grouzi E, Valsami S, Tragiannidis K, et al. Thrombosis in paroxysmal nocturnal hemoglobinuria (PNH): From pathogenesis to treatment. Int J Mol Sci. 2024;25(22):12104. doi: 10.3390/ijms252212104.

4. Hill A, Kelly RJ, Hillmen P. Thrombosis in paroxysmal nocturnal hemoglobinuria. Blood.;121(25):4985–96. doi:org/10.1182/blood-2012-09-311381.

5. Watt SG, Winhoven S, Hay CRM, Lucas GS. Purpura fulminans in paroxysmal nocturnal haemoglobinuria. Br J Haematol [Internet]. 2007;137(4):271–271. doi:10.1111/j.1365-2141.2007.06522.

6. Hsieh FN, Chen TY, Lee JYY. Severe cutaneous thrombosis with hemorrhagic necrosis in a patient with paroxysmal nocturnal hemoglobinuria: A case report and review of literature. Dermatologica Sinica. 2017;35(3):138–41. doi: 10.1016/j.dsi.2017.01.006.

7. Brodsky RA. How I treat paroxysmal nocturnal hemoglobinuria. Blood. 2021 ;137(10):1304. doi:10.1182/blood.2019003812.

8. May C, O'Rourke K, Jackson K, Francis L, Kennedy GA. Purpura fulminans in a patient with paroxysmal nocturnal haemoglobinuria. Intern Med J. 2013 ;43(1):102.

9. Yang C, Long ZB, Zhang Y, Zhu TN, Han B. Purpura fulminans related to paroxysmal nocturnal haemoglobinuria: a case report and literatures review. Zhonghua Xue Ye Xue Za Zhi. 2018 ;39(11):921–6. doi: 10.3760/cma.j.issn.0253-2727.2018.11.010.

10. Zhao H, Shattil S. Cutaneous thrombosis in PNH. Blood. 2013;122(19):3249–3249. doi:10.1182/blood-2013-05-43668.

11. Cebeci Kahraman F, Özen T, Elibol T. Lip necrosis in a patient with paroxysmal nocturnal hemoglobinuria: Can it be triggered by COVID-19? J Cosmet Dermatol. 2020;19(12):3168–70. doi: 10.1111/jocd.13746.

12. Griffin M, Munir T. Management of thrombosis in paroxysmal nocturnal hemoglobinuria: a clinician's guide. Ther Adv Hematol. 2017;8(3):119–26. doi: 10.1177/2040620716681748.