Case Report

Nepalese Heart Journal 2025; Vol 22(2), 75-78

The Invisible Clot Maker: Eosinophilia Causing Recurrent Prosthetic Valve Thrombosis- A Case Report

Rheecha Joshi, Sujan Bohara, Sachin Devkota, Jay Mangal Chaudhary, Esna Thapa, Manish Kumar Shah, Navin Chandra Gautam

Department of Cardiovascular Surgery, Shahid Gangalal National Heart Center, Bansbari, Kathmandu

Corresponding Author:
Rheecha Joshi
Department of Cardiovascular Surgery
Shahid Gangalal National Heart Center, Bansbari, Kathmandu
Email: rheechajoshi@gmail.com
ORCID iD: https://orcid.org/0009-0004-9145-045X

Cite this article as: Joshi R, Bohara S, Devkota S, Chaudhary JM, Thapa E, Shah MK, Gautam NC. The Invisible Clot Maker: Eosinophilia Causing Recurrent Prosthetic Valve Thrombosis – A Case Report. Nepalese Heart Journal. 2025;22(2):75–78.

Submission Date: 18 Aug, 2025
Acceptance date: 21 Oct, 2025

Submitted using Care checklist

Abstract

Prosthetic valve thrombosis is a devastating complication, most often related to inadequate anticoagulation. Rare etiologies such as eosinophilia, antiphospholipid syndrome, and myeloproliferative disorders should be considered in recurrent or refractory cases. We report a 17-year-old male with a mechanical mitral valve who developed three episodes of prosthetic valve thrombosis over 9 years, the last two despite therapeutic anticoagulation. Evaluation revealed persistent eosinophilia, and tropical hypereosinophilia was diagnosed. Targeted anti-helminthic therapy resolved eosinophilia and prevented recurrence over 18 months.

Beyond their role in allergic and inflammatory conditions, eosinophils release cytotoxic granule proteins, which can directly damage endothelial surfaces and disrupt the integrity of prosthetic material, facilitating platelet adhesion and aggregation. Eosinophil-derived tissue factor and inflammatory mediators further enhance local thrombogenicity. Clinically, eosinophil-driven prosthetic valve thrombosis manifests as recurrent events despite adequate anticoagulation, underscoring an immunothrombotic mechanism distinct from conventional pathways. Optimal management requires not only anticoagulation but also treatment of the underlying eosinophilic disorder to prevent recurrence.

Keywords: Prosthetic valve thrombosis; Eosinophilia; Recurrent thrombosis; Eosinophil-mediated thrombosis

DOI: https://doi.org/10.3126/nhj.v22i2.85798

Introduction

Prosthetic valve thrombosis (PVT) and anticoagulation-related bleeding are the principal complications following mechanical heart valve replacement.[1] Recurrent PVT can happen infrequently and is typically caused by insufficient anticoagulation for several causes, such as genetic polymorphism, hypercoagulability, and inadequate anticoagulation medication monitoring.[2] Despite being infrequently documented, eosinophilia is not widely recognized as a cause of recurrent PVT.

We describe a young man who experienced recurrent mitral valve PVT as a result of hypereosinophilia. In the context of mechanical heart valves, the interplay between a non-endothelialized prosthetic surface and persistent eosinophil-mediated vascular injury creates an ideal substrate for recurrent thrombus formation, even in the presence of therapeutic anticoagulation. Recognition of this distinct pathogenic mechanism is critical, as management strategies extend beyond standard anticoagulation to include immunosuppressive or targeted biologic therapies aimed at controlling eosinophil activity.

Case presentation

A 17-year-old male underwent mitral valve replacement (MVR) with a 27 mm St. Jude mechanical prosthetic valve via median sternotomy for symptomatic severe mitral regurgitation with moderate mitral stenosis. The perioperative course was uneventful, and the patient was discharged on therapeutic warfarin with instructions for regular international normalized ratio (INR) monitoring.

Two months later, the patient presented to the emergency department with acute worsening dyspnea. On auscultation, prosthetic valve clicks were absent. Transthoracic echocardiography demonstrated markedly elevated trans-mitral gradients (mean: 36 mmHg, peak: 53 mmHg) with preserved left ventricular ejection fraction. Fluoroscopy showed restricted anterior leaflet motion. With a subtherapeutic INR of 1.9, a diagnosis of acute prosthetic mitral valve thrombosis was established.

@Nepalese Heart Journal. Nepalese Heart Journal retains copyright and work is simultaneously licensed under Creative Commons Attribution License CC - BY 4.0 that allows others to share the work with an acknowledgement of the work's authorship and initial publication in this journal.

He underwent successful thrombolysis with streptokinase (STK) — a 250,000 IU intravenous (IV) bolus over 1 hour, followed by continuous infusion at 100,000 IU/hour for 12 hours. Repeat echocardiography demonstrated normalization of gradients with marked symptomatic improvement. Low molecular weight heparin (LMWH) 60 mg subcutaneously every 12 hours was initiated, and he was subsequently discharged with a mean gradient of 12 mmHg and normal leaflet motion. Warfarin dose was adjusted accordingly to keep the target INR 3.0–3.5.

Seven years later, he re-presented with progressive orthopnea and cough. This time, INR was within therapeutic range with documented regular monitoring. Echocardiography revealed restricted prosthetic mitral valve motion (mean gradient: 28 mmHg, peak: 46 mmHg).

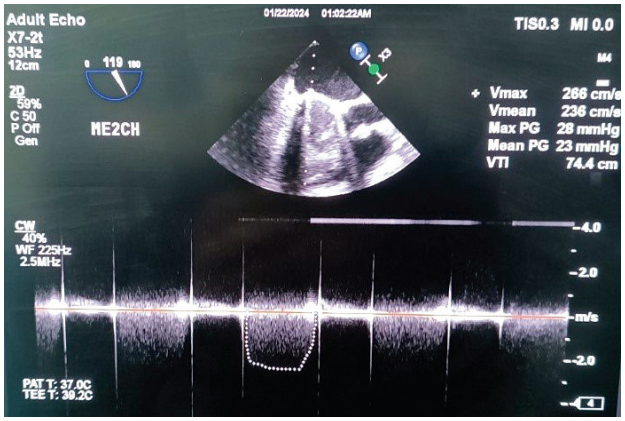

Figure 1: *Intraoperative transesophgeal echocardiographic view showing increased gradient across prosthetic mitral valve.*

Given the therapeutic INR, pannus formation was suspected on echocardiography. Management of pannus-related prosthetic valve dysfunction primarily involves surgical reintervention.[1] As the patient was symptomatic, a redo mitral valve replacement (MVR) was planned. Given the patient's young age, redo MVR with a 27 mm St. Jude mechanical prosthetic valve was performed. The postoperative course was uneventful, and echocardiography demonstrated a well-functioning valve, with a peak gradient of 15 mmHg and a mean gradient of 6 mmHg.

Nine months after the redo MVR, he presented with restricted prosthetic leaflet motion and a mean gradient of 32 mmHg with the supratherapeutic INR of 4.0 — his third episode of prosthetic valve obstruction. He underwent repeat thrombolysis with STK, which reduced the mean gradient to 8 mmHg.

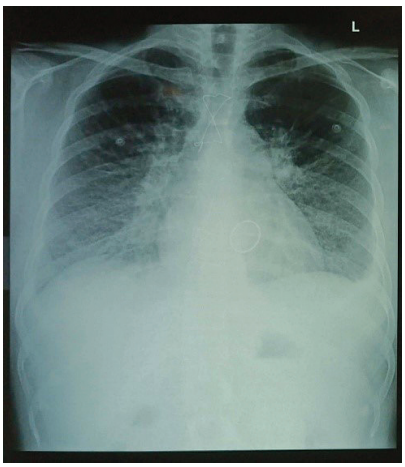

Figure 2: *Chest Xray (PA View) with PVT during 3rd admission showing pulmonary venous hypertension*

This recurrence raised the question: why was PVT recurring despite adequate anticoagulation?

A meticulous review of prior records revealed persistent eosinophilia, which had been overlooked. His first complete blood count (CBC) before initial surgery showed a total leukocyte count (TLC) of 11,200/µL with 20% eosinophils (absolute eosinophil count [AEC]: 2,240/µL). No further evaluation was performed at that time. At the second surgery, TLC was 9,910/µL with 16% eosinophils (AEC: 1,585/µL). During the third admission, CBC again revealed eosinophilia (20%; AEC: 1,420/µL).

Table 1. Summary of recurrent prosthetic valve thrombosis episodes

Episode	INR at presentation	Mean mitral gradient (mmHg)	Absolute eosinophil count (/µL)	Intervention	Outcome
1st	1.9 subtherapeutic	36	2,240	Thrombolysis with streptokinase (STK)	Resolution, discharged on a higher INR target
2nd	3.03 therapeutic	28	1,585	Redo mitral valve replacement with a mechanical prosthesis	Uneventful recovery, well-functioning valve
3rd	4.0 suprathera-peutic	32	1,420	Thrombolysis with STK and treatment of eosinophilia	Resolution, asymptomatic on follow-up

Peripheral smear showed macrocytic red cells, normal total WBC count, and no atypical cells or hemoparasites. Stool examination was negative for ova, cysts, and parasites. There was no history of atopy, asthma, recent travel, or drug exposure.

Hematology consultation was considered crucial for this patient. In the context of prosthetic valve thrombosis, early hematology input can influence management and reduce the risk of recurrence. Following hematology consultation, a diagnosis of tropical hypereosinophilia was established, and the patient was treated with diethylcarbamazine for 21 days. Bone marrow aspiration/biopsy and genetic testing for clonal eosinophil proliferation were not performed, as eosinophilia resolved with anti-helminthic therapy.

At 18 months follow-up, he remained asymptomatic with a normally functioning prosthetic valve and normalised AEC of 320/µL.

Discussion

Prosthetic valve thrombosis (PVT) is one of the most feared complications of mechanical heart valves, with an incidence ranging from 0.1% to 6% per patient-year for left-sided valves.[3] The risk of PVT depends on valve type, position (tricuspid > mitral > aortic),

adequacy of anticoagulation, and the presence of prothrombotic states such as factor V Leiden mutation, prothrombin gene mutation, protein C/S deficiency, eosinophilia, pregnancy, atrial fibrillation, and left ventricular dysfunction.[4] Inadequate anticoagulation remains the most common cause.

Recurrent PVT is potentially lethal. When it occurs despite therapeutic anticoagulation, occult prothrombotic states should be sought. In our patient, persistent hypereosinophilia was the likely cause. Eosinophilia is often overlooked as a contributor to PVT unless specifically considered. In this case, earlier episodes were managed without targeted treatment for eosinophilia, leading to repeated thrombosis despite adequate anticoagulation. Activated eosinophils release mediators and cytokines with potent thrombogenic potential.[5] Normally, eosinophils constitute <7% of circulating leukocytes[6], have a short half-life in blood (8–18 h), but may persist in tissues for weeks.[7,8] Eosinophilia is defined as an absolute eosinophil count (AEC) >500/mm3, and its causes are classified by the British Committee for Standards in Haematology into:

- Primary (clonal hematologic disorders)
- Secondary (allergic, infectious, autoimmune, gastrointestinal, respiratory, drug-induced, or malignant causes)
- Idiopathic when no etiology is identified.[9]

Hypereosinophilia (AEC > 1500/mm³) with target organ injury is termed as hypereosinophilic syndrome (HES).[3] Thrombotic events are a major cause of morbidity and mortality in HES[4], especially with cardiac involvement, which occurs in up to 25% of cases.[10]

Eosinophils promote thrombosis through three main mechanisms:[11-13]

1. degranulation proteins like major basic protein (MBP), eosinophil cationic protein (ECP), eosinophil peroxidase (EPO), and eosinophil-derived neurotoxin (EDN) injure endothelium and enhance coagulation,
2. tissue factor expression with release of platelet-activating mediators, and
3. CD40/CD40L interactions driving endothelial dysfunction, platelet activation, and thrombin generation.

MBP inhibits thrombomodulin-dependent protein C activation, amplifying thrombin generation and favoring prosthetic valve thrombosis.[11] In our patient, marked eosinophilia likely contributed to recurrent thrombosis despite adequate anticoagulation. Similar eosinophil-mediated events have also been described in bioprosthetic valves, highlighting eosinophilia as a prothrombotic trigger across different valve types.[5]

Limitation

This report describes a single patient with short follow-up. While this report highlights a compelling association between eosinophilia and recurrent prosthetic valve thrombosis, the generalizability remains limited. Hence, this observation may prompt further investigation into eosinophil-mediated thrombotic mechanisms.

Conclusion

Mechanical prosthetic heart valves carry an inherent risk of both valvular thrombosis and anticoagulation-related hemorrhage. Eosinophil-mediated prosthetic valve thrombosis represents an exceptionally rare but clinically important entity, with only a few cases documented in the literature. Clinicians should maintain a high index of suspicion for this entity in patients presenting with recurrent or unexplained thrombotic events, even when therapeutic anticoagulation levels are achieved. Prompt recognition of eosinophilia as a potential contributor, coupled with timely initiation of targeted anti-inflammatory therapy, may mitigate recurrence and improve patient outcomes. This case underscores the need for heightened clinical awareness and further investigation into eosinophil-driven prosthetic valve thrombosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Praz F, Borger MA, Lanz J, et al. 2025 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2025 Aug 29;ehaf194. doi:10.1093/eurheartj/ehaf194.
2. Gencbay M, Turan F, Degertekin M, et al. High prevalence of hypercoagulable states in patients with recurrent thrombosis of mechanical heart valves. J Heart Valve Dis. 1998;7(6):601-9.
3. Spry CJ, Davies J, Tai PC, Olsen EG, Oakley CM, Goodwin JF. Clinical features of fifteen patients with the hypereosinophilic syndrome. Q J Med. 1983;52(205):1-22.
4. Hii MW, Firkin FC, MacIsaac AI, Yii M. Obstructive prosthetic mitral valve thrombosis in idiopathic hypereosinophilic syndrome: a case report and review of the literature. J Heart Valve Dis. 2006;15(5):721-5.
5. Kothari SS, Deepti S, Rai N. Reversible bioprosthetic valve thrombosis from eosinophilia. BMJ Case Rep. 2018;2018:bcr2017222937. doi:10.1136/bcr-2017-222937.
6. Simon D, Simon HU. Eosinophilic disorders. J Allergy Clin Immunol. 2007;119(6):1291-300; quiz 1301-2. doi:10.1016/j.jaci.2007.02.010.
7. Beeken WL, Northwood I, Beliveau C, Baigent G, Gump D. Eosinophils of human colonic mucosa: C3b and Fc gamma receptor expression and phagocytic capabilities. Clin Immunol Immunopathol. 1987;43(3):289-300. doi:10.1016/0090-1229(87)90138-3.
8. Kovalszki A, Weller PF. Eosinophilia. Prim Care. 2016;43(4):607-17. doi:10.1016/j.pop.2016.07.010.
9. Butt NM, Lambert J, Ali S, Beer PA, Cross NC, Duncombe A, et al. Guideline for the investigation and management of eosinophilia. Br J Haematol. 2017;176(4):553-72. doi:10.1111/bjh.14488.
10. Kleinfeldt T, Nienaber CA, Kische S, et al. Cardiac manifestation of the hypereosinophilic syndrome: new insights. Clin Res Cardiol. 2010;99(7):419-27. doi:10.1007/s00392-010-0144-8.
11. Mukai HY, Ninomiya H, Ohtani K, et al. Major basic protein binding to thrombomodulin potentially contributes to the thrombosis in patients with eosinophilia. Br J Haematol. 1995;90(4):892-9. doi:10.1111/j.1365-2141.1995.tb05211.x.

12. Samoszuk M, Corwin M, Hazen SL. Effects of human mast cell tryptase and eosinophil granule proteins on the kinetics of blood clotting. Am J Hematol. 2003;73(1):18-25. doi:10.1002/ajh.10323.

13. Moosbauer C, Morgenstern E, Cuvelier SL, et al. Eosinophils are a major intravascular location for tissue factor storage and exposure. Blood. 2007;109(3):995-1002. doi:10.1182/blood-2006-02-004945.