

Embolic stroke in young adults: Investigating the role of rheumatic mitral stenosis in cerebrovascular events

Rizaldy Taslim Pinzon^{1,2}, Kenzie Ongko Wijaya¹

¹Faculty of Medicine Duta Wacana Christian University Yogyakarta, Indonesia

²Departement of Neurology Bethesda Hospital Yogyakarta, Indonesia

ABSTRACT

We report a case of early-onset ischemic stroke in a previously healthy 39-year-old female, attributed to rheumatic mitral stenosis (MS) and atrial fibrillation (AF). The patient presented with acute-onset hemiparesis, dysarthria, and facial asymmetry, with symptoms developing within six hours prior to hospital admission. Comprehensive cardiac assessment revealed severe mitral valve stenosis, a rapid ventricular response secondary to atrial fibrillation, and marked left atrial enlargement. Management involved anticoagulation therapy, statin administration, and rhythm control. The patient demonstrated a favorable recovery, achieving a modified Rankin Scale (mRS) score of 2 at discharge after a 10-day hospitalization. This case underscores the importance of identifying rheumatic mitral stenosis as a significant etiological factor for ischemic stroke in young adults.

Keywords: stroke, mitral stenosis, warfarin, rheumatic heart disease

INTRODUCTION

Ischemic stroke represents a severe complication of rheumatic heart disease (RHD), leading to substantial morbidity and mortality [1]. In developing regions, while RHD is relatively infrequent, it remains a significant risk factor for early-onset ischemic stroke. Epidemiological studies estimate that RHD contributes to 3–7.5% of all ischemic strokes [1,2]. Moreover, systematic reviews indicate that RHD accounts for 7–9% of ischemic stroke cases [2]. These figures highlight the persistent burden of RHD-related strokes in low- and middle-income countries, where delayed diagnosis and suboptimal management often exacerbate outcomes. Early diagnosis and appropriate management are critical in preventing such outcomes, but many regions lack the resources or infrastructure to provide adequate care.

Suboptimal anticoagulation therapy and delayed diagnosis are prevalent challenges among patients with RHD, increasing the risk of stroke [3,4]. A population-based investigation revealed that 6 of 15 cases of RHD-related ischemic stroke were underdiagnosed [3,5]. This underdiagnosis may be linked to the inad-

equate use of anticoagulants, compounded by subtle clinical presentations and complexities in maintaining therapeutic international normalized ratio (INR) levels [4,5]. Furthermore, socioeconomic factors, including limited access to healthcare services and lack of awareness about secondary prophylaxis, further contribute to this gap, highlighting the need for targeted public health interventions. Improving awareness among clinicians and the general population is essential in preventing the long-term consequences of RHD-related strokes.

Atrial fibrillation (AF) frequently complicates mitral stenosis (MS), affecting 40–75% of individuals with MS, and significantly elevates the risk of stroke and systemic embolism [2,3]. This case highlights a rare occurrence of ischemic stroke in a young adult female with mitral stenosis secondary to RHD. Stroke incidence among patients with both MS and AF is approximately 18 times higher than in age-matched controls without AF. However, the occurrence of ischemic stroke due to RHD in younger populations remains uncommon, emphasizing the need for heightened clinical vigilance in identifying RHD as a contributing factor in this subset. Moreover, in-

Corresponding author:

Kenzie Ongko Wijaya

E-mail: kenzieowpersonal@gmail.com

Article History:

Received: 3 December 2024

Accepted: 27 December 2024



FIGURE 1. Cardiomegaly in chest X ray

corporating echocardiographic screening and timely initiation of anticoagulation therapy could significantly mitigate the risk of such life-threatening complications, especially in resource-limited settings. Strengthening healthcare infrastructure to address diagnostic and therapeutic gaps will be crucial in improving outcomes for affected populations. This may include the use of telemedicine and mobile health technologies to enhance screening, follow-up, and management of RHD, especially in remote areas. Education on preventive care and timely intervention can help reduce the burden of ischemic strokes and improve the quality of life for young patients affected by RHD.

CASE PRESENTATION

A 39-year-old previously healthy female presented to the emergency department with acute-onset right-sided hemiparesis, dysarthria, and facial asymmetry. The symptoms began within the prior six hours. The patient had no history of hypertension, diabetes, smoking, alcohol use, oral contraceptive

use, migraine, or known cardiac disorders. Notably, she had not undergone prior comprehensive cardiac evaluation. On examination, a diastolic rumbling murmur was auscultated at the cardiac apex, consistent with mitral stenosis. Electrocardiography (ECG) demonstrated atrial fibrillation with a rapid ventricular response and an irregularly irregular pulse. The patient's blood pressure was 110/70 mmHg, with a heart rate of 110 beats per minute. Neurological assessment revealed a National Institutes of Health Stroke Scale (NIHSS) score of 10, indicative of moderate stroke severity. Laboratory findings were unremarkable.

Chest radiography identified cardiomegaly (Figure 1). Transthoracic echocardiography revealed severe mitral stenosis with a hockey stick appearance of the mitral valve, a Wilkins Score of 8, severe mitral regurgitation, left atrial and ventricular dilation, an ejection fraction of 43%, moderate tricuspid regurgitation, and a moderate probability of pulmonary hypertension. Despite these severe echocardiographic abnormalities, the patient had no prior symptoms of cardiac disease, which is atypical given the severity

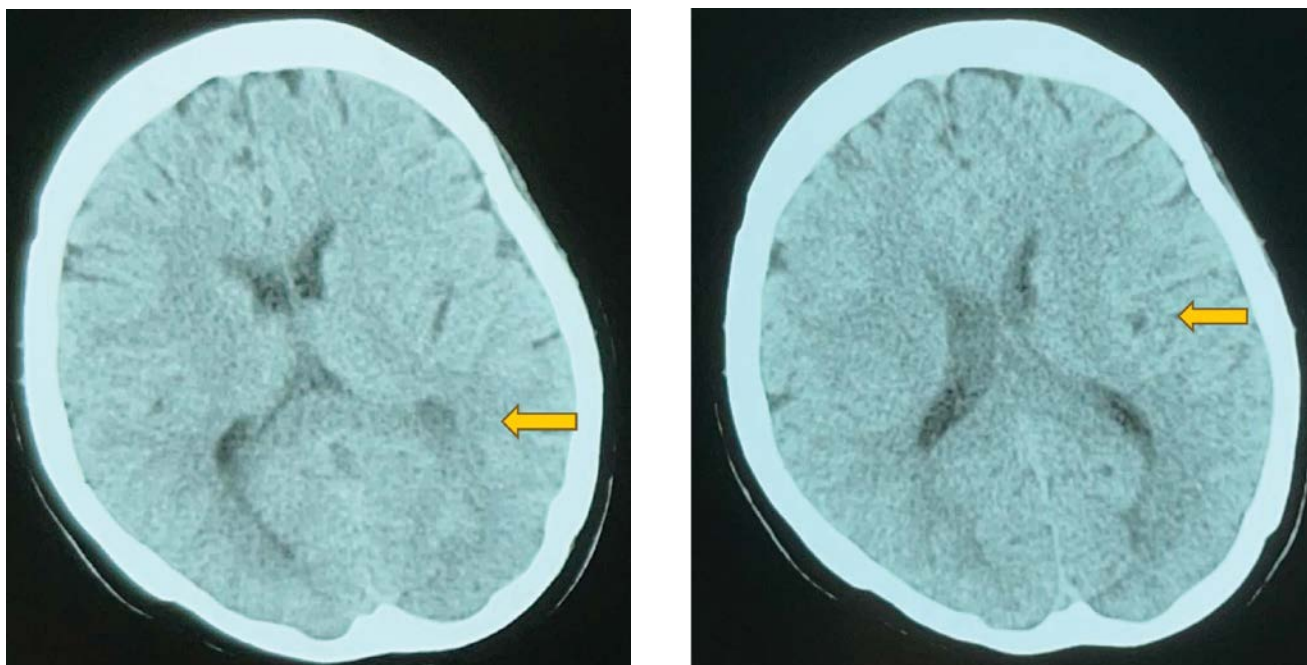


FIGURE 2. Left parietal and occipital infarction from brain CT

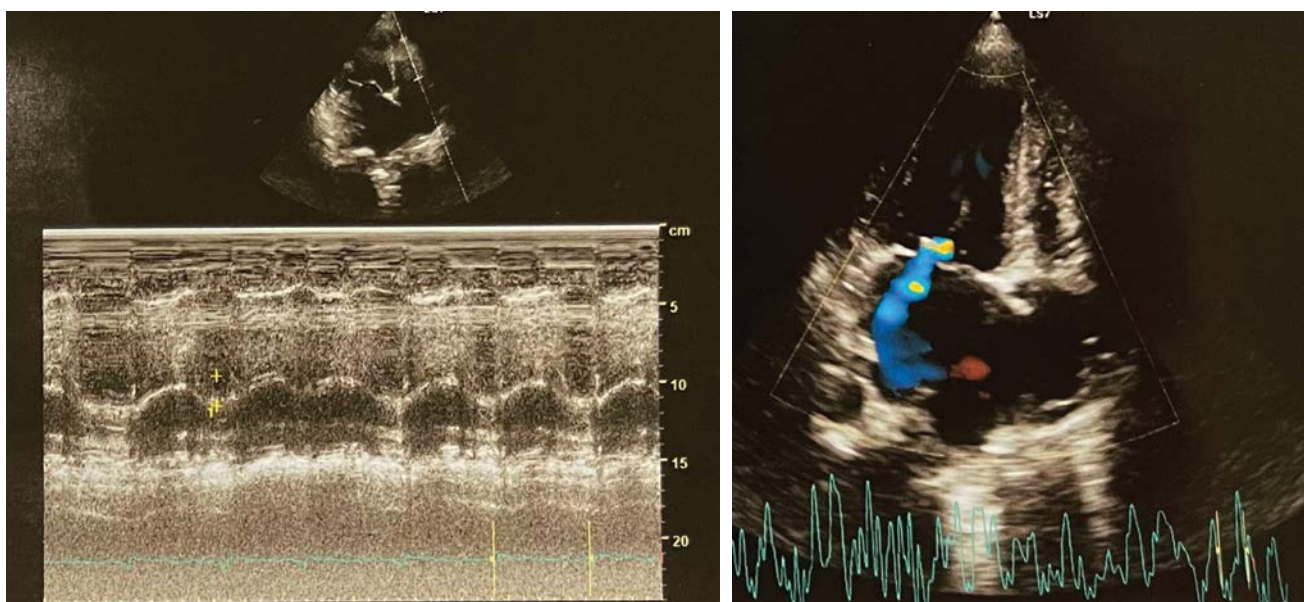


FIGURE 3. Echocardiography: MS Severe, MR Severe, TR Moderate, Moderate Probability of PH

of the findings. Clinical history further revealed previous rheumatic fever, supporting the diagnosis of rheumatic heart disease (RHD).

Management included parenteral anticoagulation with weight- and renal function-adjusted dosing, transitioning to oral warfarin with a bridging dose of low-molecular-weight heparin. Statins were administered for cardiovascular protection, and a rhythm control strategy with antiarrhythmic therapy addressed atrial fibrillation. Physical therapy was initiated to promote functional recovery. Additionally, the patient was closely monitored for potential complications such as recurrent embolism and heart failure due to the extent of her underlying cardiac pathology.

The patient achieved clinical stabilization and was discharged on day 10 with a modified Rankin Scale (mRS) score of 2, indicating minimal disability. Her discharge regimen included warfarin (target INR: 2.7–3.5), digoxin, and furosemide. Outpatient follow-up focused on anticoagulation monitoring and secondary stroke prevention, as well as regular echocardiograms to assess the progression of her mitral stenosis and overall cardiac function.

DISCUSSION

This report presents a rare but clinically significant case of ischemic stroke in a young adult female, where severe mitral stenosis secondary to rheumatic

heart disease (RHD) was identified as the primary etiological factor. This case underscores the importance of comprehensive diagnostic evaluation in young stroke patients, particularly in regions where RHD remains a significant public health concern. It also highlights the intricate relationship between mitral stenosis, atrial fibrillation (AF), and thromboembolism, necessitating an integrated approach to management.

Rheumatic mitral stenosis and stroke risk

RHD, particularly rheumatic mitral stenosis, is a well-documented significant risk factor for ischemic stroke. The narrowing of the mitral valve orifice in rheumatic mitral stenosis leads to increased left atrial pressure, dilation, and stasis of blood flow, which predisposes patients to thrombus formation. The co-occurrence of AF exacerbates this risk by reducing atrial contractility and promoting blood stasis. Studies show that patients with mitral stenosis and AF face a thromboembolic risk 17–18 times higher than their peers without AF [5][7].

This case aligns with existing data, which show a disproportionate burden of RHD-related strokes in low- and middle-income countries (LMICs). Feigin et al. (2014) estimated that RHD accounts for 7–9% of ischemic strokes globally, with the majority occurring in regions where RHD prevalence remains high due to delayed diagnoses and limited healthcare access [6]. Similarly, a study by Myint et al. (2018) reported that over 30% of strokes in young adults in Southeast Asia were attributable to RHD, emphasizing the regional disparities in disease burden [7].

Gaps in anticoagulation management

While anticoagulation therapy is established as effective in reducing stroke risk, significant gaps persist in its application, especially in resource-limited settings. Vitamin K antagonists (VKAs), such as warfarin, remain the cornerstone of anticoagulation therapy in RHD patients with AF. However, achieving and maintaining therapeutic INR levels proves challenging. Studies from LMICs reveal that fewer than 50% of eligible patients receive anticoagulation therapy, and only 30–50% achieve therapeutic INR targets [4][5].

Karthikeyan et al. (2020) demonstrated that suboptimal anticoagulation management in RHD patients led to a 13% annual recurrence rate of thromboembolic events. In contrast, a well-coordinated anticoagulation program in high-resource settings reduced recurrence rates to less than 5% [6]. These findings highlight the need for systemic improvements in anticoagulation services, particularly in endemic regions.

Emerging evidence also highlights the potential role of novel oral anticoagulants (NOACs), such as da-

bigatran and rivaroxaban, as alternatives to VKAs. NOACs offer advantages, including predictable pharmacokinetics, fewer dietary restrictions, and reduced monitoring requirements. However, their use in RHD populations remains limited due to high costs and the lack of large-scale clinical trials in this specific cohort. A systematic review by Mohanty et al. (2021) suggested that while NOACs may provide comparable efficacy to VKAs, their safety profile in RHD patients with mechanical heart valves or severe mitral stenosis requires further investigation [8].

Diagnostic challenges in RHD

This case also highlights the challenges in the early detection and diagnosis of RHD. The patient presented with advanced mitral stenosis, characterized by left atrial dilation and moderate pulmonary hypertension, yet had no prior symptoms. Subclinical RHD often progresses silently, making it difficult to identify affected individuals until significant complications, such as ischemic stroke or congestive heart failure, arise.

Screening programs using echocardiography have been proposed as an effective strategy for early detection of subclinical RHD, particularly in endemic regions. Wang et al. (2013) demonstrated that echocardiographic screening of schoolchildren in high-prevalence areas identified early RHD in 1.5% of participants, many of whom were asymptomatic [7]. Early identification through such programs allows for timely initiation of secondary prophylaxis with penicillin, which has been shown to halt disease progression in early stages [8].

Multidisciplinary approach to management

The therapeutic approach adopted in this case exemplifies the importance of multidisciplinary care in managing RHD-associated ischemic stroke. The use of parenteral anticoagulation, followed by transition to oral warfarin, effectively mitigated the risk of recurrent thromboembolism. Maintaining a target INR of 2.7–3.5 was crucial, as subtherapeutic INR levels are associated with a threefold increase in stroke recurrence risk [6].

In addition to anticoagulation, rhythm control strategies were employed to manage the patient's AF and prevent hemodynamic instability. Mohan et al. (2011) reported that optimal rhythm control strategies, combined with anticoagulation, reduced recurrence rates of RHD-related strokes from 13.6% to under 10% [3]. Non-pharmacological interventions, such as catheter ablation, may also play a role in select patients with refractory AF, though their applicability in RHD populations remains limited due to anatomical challenges and resource constraints [7].

Future directions and public health implications

Addressing the high burden of RHD-associated ischemic stroke requires a multifaceted approach, encompassing public health interventions, healthcare system improvements, and advancements in clinical care. Early detection through echocardiographic screening programs should be prioritized in endemic regions, as these initiatives have demonstrated cost-effectiveness in reducing long-term morbidity and mortality [6]. For instance, the Rheumatic Heart Disease Screening and Prevention Program in Uganda successfully reduced RHD-related complications by over 20% within five years of implementation [8].

Improving access to anticoagulation therapy is another critical priority. This includes expanding the availability of VKAs and monitoring infrastructure, as well as exploring innovative delivery models, such as community-based anticoagulation clinics and telemedicine platforms. The development of predictive analytics tools, such as machine learning algorithms for stroke risk stratification, holds promise for enhancing personalized care. Rauf et al. (2023) demonstrated the potential of such tools to identify high-risk patients with over 90% accuracy [8].

Emerging therapies, such as NOACs and newer-generation rhythm control agents, should also be explored through rigorous clinical trials in RHD populations. While these therapies offer convenience and potential efficacy, their cost-effectiveness and safety profiles in low-resource settings need to be established. Collaborative efforts between governments, non-governmental organizations, and pharmaceutical companies will be essential to ensure equitable access to these innovations.

Finally, increasing awareness of RHD and its complications among both healthcare providers and the general population is crucial. Educational campaigns and capacity-building initiatives can empower communities to seek timely care and enable healthcare providers to implement evidence-based management strategies. These efforts, combined with robust public health policies, have the potential to significantly reduce the burden of RHD-associated ischemic stroke globally.

This case underscores the complex interplay of rheumatic mitral stenosis, AF, and ischemic stroke in young adults, highlighting the need for early diagnosis, optimized anticoagulation, and multidisciplinary care. Despite advances in understanding and managing RHD, significant gaps remain, particularly in LMICs, where the disease burden is highest. Addressing these gaps through public health interventions, innovative therapies, and personalized care strategies will be pivotal in improving outcomes for patients with RHD-associated ischemic stroke.

Rheumatic heart disease (RHD) remains a leading cause of ischemic stroke in younger populations,

particularly in low- and middle-income countries (LMICs). Despite advances in diagnostic and therapeutic strategies, the global burden of RHD-related strokes continues to be significant due to delayed or missed diagnoses, inadequate access to medical care, and suboptimal treatment adherence. Research shows that RHD accounts for approximately 7–9% of all ischemic strokes globally, with the majority occurring in regions where healthcare access is limited and awareness is low [2].

The underutilization of anticoagulation therapy remains a key challenge in managing RHD-associated strokes. Many patients with atrial fibrillation (AF) secondary to mitral stenosis (MS) do not receive adequate anticoagulation, placing them at significant risk for thromboembolic events, including ischemic stroke. Studies have shown that underuse of oral anticoagulants in patients with AF is a major contributor to the increased risk of stroke in this population [1].

In addition to anticoagulation, early detection remains a cornerstone of effective management. Regular screening, particularly through echocardiography, has shown to identify subclinical RHD before complications arise. Timely initiation of secondary prophylaxis with antibiotics, such as penicillin, can halt or slow disease progression [7].

In conclusion, while management strategies have improved in some areas, significant challenges remain, particularly in LMICs. Early detection, appropriate anticoagulation, and a multidisciplinary approach are crucial to reducing stroke risk in young adults with RHD. Public health initiatives aimed at increasing awareness, improving healthcare infrastructure, and promoting early screening will be pivotal in mitigating the impact of this condition. Additionally, further research into the use of novel anticoagulants and digital health tools may provide promising solutions for improving stroke prevention and outcomes in this vulnerable population.

CONCLUSION

In conclusion, this report emphasizes the critical role of rheumatic mitral stenosis and atrial fibrillation as significant risk factors for ischemic stroke in young adults. Rheumatic heart disease (RHD) contributes to 7–9% of ischemic strokes globally, with a disproportionately high burden in low- and middle-income countries. The presented case underscores the necessity of early diagnosis and comprehensive management strategies, including effective anticoagulation therapy, to reduce the elevated thromboembolic risk associated with this condition.

The patient's favorable clinical outcome, reflected in a modified Rankin Scale (mRS) score of 2 at discharge, highlights the effectiveness of a multidisciplinary

nary approach integrating anticoagulation, rhythm control, and physical rehabilitation. Nevertheless, substantial challenges persist in the management of RHD. Studies reveal that fewer than 50% of patients receive appropriate anticoagulation therapy, and recurrence rates for RHD-related strokes exceed 13% in certain populations, underscoring critical gaps in care delivery.

To enhance patient outcomes, healthcare systems in endemic regions must prioritize systematic RHD screening, ensure the optimization of anticoagulation management, and consider innovative interventions such as the use of non-vitamin K oral

anticoagulants (NOACs) or predictive analytics, for personalized risk stratification. This case further underscores the importance of heightened clinical vigilance in investigating the etiology of ischemic stroke in young adults, particularly in resource-limited settings where RHD prevalence remains significant.

Ethics statement:

Verbal informed consent was obtained from the patient and family. No identifiable patient information is disclosed in this manuscript.

Conflict of interest: none declared

Financial support: none declared

REFERENCES

1. Vasconcelos M, Vasconcelos L, Ribeiro V, Campos C, Di-Flora F, Abreu L, et al. Incidence and predictors of stroke in patients with rheumatic heart disease. *Heart*. 2021 May;107(9):748-754. doi: 10.1136/heartjnl-2020-318054.
2. Liu M. Epidemiology of stroke in patients with rheumatic heart disease: A systematic review. *Cerebrovasc Dis*. 2011; 32(Suppl 2):26–27.
3. Mohan KM, Wolfe CD, Rudd AG, Heuschmann PU, KolominskyRabas PL, Grieve AP. Risk and cumulative risk of stroke recurrence: A systematic review and meta analysis. *Stroke*. 2011; 42:1489–1494. doi: 10.1161/STROKEAHA.110.602615.
4. Ogilvie IM, Newton N, Welner SA, Cowell W, Lip GY. Underuse of oral anticoagulants in atrial fibrillation: A systematic review. *Am J Med*. 2010; 123:638–645.e4. doi: 10.1016/j.amjmed.2009.11.025.
5. Wang D, Liu M, Lin S, Hao Z, Tao W, Chen X, et al. Stroke and rheumatic heart disease: a systematic review of observational studies. *Clin Neurol Neurosurg*. 2013 Sep;115(9):1575-82. doi: 10.1016/j.clineuro.2013.06.017.
6. Myint NPST, Aung NM, Win MS, Htut TY, Ralph AP, Cooper DA, et al. The clinical characteristics of adults with rheumatic heart disease in Yangon, Myanmar: An observational study. *PLoS One*. 2018 Feb 21;13(2):e0192880. doi: 10.1371/journal.pone.0192880.
7. Rauf A, Ullah A, Rathi U, Ashfaq Z, Ullah H, Ashraf A, et al. Predicting stroke and mortality in mitral stenosis with atrial flutter: A machine learning approach. *Ann Noninvasive Electrocardiol*. 2023 Sep;28(5):e13078. doi: 10.1111/anec.13078.
8. Karthikeyan G, Connolly SJ, Yusuf S. Overestimation of Stroke Risk in Rheumatic Mitral Stenosis and the Implications for Oral Anticoagulation. *Circulation*. 2020 Nov 3;142(18):1697-1699. doi: 10.1161/CIRCULATIONAHA.120.050347.