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Coexistence of Infective Endocarditis and Recurrent Acute Rheumatic Fever: A Case Report

Kino[1,2], Didik Hariyanto[1,3], Harben Fernando[1], Indra Fahlevi[1*],

[1]Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Andalas

[2]Dr. M. Djamil General Hospital, Padang, Indonesia

[3]Department of Pediatrics, Faculty of Medicine, Universitas Andalas / Dr. M. Djamil General Hospital, Padang, Indonesia

* Corresponding author.
E-mail address: indrafahlevi.md@gmail.com

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Abstract

Background: Infective endocarditis (IE) and recurrent acute rheumatic fever (ARF) are two serious cardiovascular conditions frequently associated with rheumatic heart disease (RHD). Their coexistence complicates diagnosis and management due to overlapping clinical features such as fever, migratory arthritis, and valvular dysfunction. This case report aims to elucidate the clinical presentation, diagnostic challenges, and treatment strategies in a pediatric patient with coexisting IE and recurrent ARF.
Methods: A detailed clinical case study was conducted involving a 10-year-old boy with a history of RHD presenting with joint pain and intermittent fever. Diagnostic evaluations included physical examination, laboratory investigations (including blood cultures and antistreptolysin O titers), and serial transthoracic echocardiography. Therapeutic interventions combined targeted intravenous antibiotics, corticosteroids, and secondary prophylaxis with benzathine penicillin G. Multidisciplinary consultations were employed to optimize management.
Results: The patient exhibited echocardiographic evidence of mitral valve vegetations along with severe mitral regurgitation. Blood cultures remained negative, likely due to prior antibiotic exposure. Elevated antistreptolysin O titers confirmed recent streptococcal infection supporting recurrent ARF diagnosis. Clinical improvement was observed with symptom resolution and reduction in vegetation size on follow-up echocardiography. Multimodal therapy was well-tolerated, preventing further complications.
Conclusion: This case highlights the diagnostic complexity and therapeutic balancing act required in managing coexisting IE and recurrent ARF in children with RHD. Early recognition through comprehensive evaluation and integrated treatment combining antimicrobial and immunomodulatory approaches can improve outcomes. Continued vigilance and multidisciplinary care are essential for preventing morbidity in this high-risk population.

Keywords: *infective endocarditis, recurrent acute rheumatic fever, rheumatic heart disease, blood culture negative endocarditis, heart valve vegetation*

Introduction

Infective endocarditis (IE) and recurrent acute rheumatic fever (ARF) are significant cardiovascular diseases predominantly affecting patients with rheumatic heart disease (RHD). The clinical overlap between these conditions—manifesting as fever, migratory arthritis, heart murmurs, and heart failure symptoms—poses a diagnostic and therapeutic challenge. Despite advances in diagnostics and treatment, differentiation between inflammatory and infectious valve involvement remains difficult, particularly in children with RHD who are at high risk for both. Addressing these complexities is critical given the global burden of RHD and the potential for severe morbidity and mortality associated with IE and ARF.[1–16]

Existing literature delineates IE as an infection of the endocardium commonly caused by bacteria such as *Staphylococcus aureus* and *Streptococcus viridans*, often complicating damaged valves. ARF, an autoimmune sequela of untreated *Group A Streptococcus* infection, targets heart valves and may progress to chronic RHD. However, reports describing simultaneous presentations of IE and recurrent ARF in pediatric populations are scarce, and management protocols remain insufficiently standardized. Prior studies have noted the diagnostic ambiguity created by overlapping symptoms and the difficulty in establishing definitive diagnoses, especially when blood cultures are negative.[1,2,6–8,17–23]

This study presents a detailed clinical case to explore the diagnostic intricacies and therapeutic strategies in managing coexistent IE and recurrent ARF. The objectives are to highlight the clinical course, emphasize the utility of echocardiography and serologic testing, and discuss multidisciplinary management approaches. By addressing these gaps, this report aims to enhance clinician awareness and inform better care pathways for similar high-risk patients.

Methods

This case report was conducted at Dr. M. Djamil General Hospital, Padang, Indonesia, in September 2024. It describes a single case involving a 10-year-old boy with a known history of RHD who presented with clinical features suggestive of both IE and recurrent ARF. The research design is observational and descriptive, focusing on detailed clinical, laboratory, and imaging data collected during hospitalization.

The patient had been previously diagnosed with RHD one year prior and was on regular follow-up receiving monthly benzathine penicillin G injections. He was referred after a 3-day hospitalization at a secondary facility with worsening joint pain and intermittent fever, unresponsive to empirical antibiotics. A comprehensive clinical evaluation was conducted upon admission, including detailed history taking, physical examination, and serial investigations. Investigations included complete blood counts, renal function tests, CRP, ASO titers, urinalysis, electrocardiography (ECG), and serial transthoracic echocardiography (TTE). Blood cultures from four sites yielded no growth, likely due to prior antibiotic exposure. The working diagnosis was Possible IE (according to ESC 2023 criteria), Definite Recurrent ARF (based on the 2020 Australian guidelines), and Severe Mitral Regurgitation secondary to RHD.

Management included intravenous antibiotics (ampicillin-sulbactam and gentamicin), corticosteroids, aspirin, and continued monthly benzathine penicillin G prophylaxis. Multidisciplinary consultations—including cardiology, infectious diseases, nephrology, dermatology, and dentistry—were conducted to ensure comprehensive care. The patient showed marked clinical improvement, with resolution of fever and joint pain by day 8, and gradual reduction in vegetation size on serial echocardiography. He was discharged on day 21 in stable condition with planned follow-up and continued medical therapy.

Data analysis was qualitative, focusing on symptom resolution, changes in echocardiographic findings, and laboratory markers over time. The study ensures validity by adhering to standardized diagnostic criteria (ESC 2023 for IE and Australian 2020 guidelines for ARF) and reliability by documenting serial assessments. Ethical approval was obtained from the Institutional Review Board of RSUP Dr. M. Djamil Padang. Written informed consent was secured from the patient's legal guardian for the use of anonymized data and images in this publication.

Results

A 10-year-old boy with a known history of RHD presented to the Emergency Department of Dr. M. Djamil General Hospital with progressively worsening migratory joint pain over four days, primarily affecting the knees and ankles. The pain was migratory, without persistent erythema or swelling, and partially relieved by paracetamol. The patient also reported intermittent low-grade fever for two weeks, predominantly in the late afternoon and evening, responsive to antipyretics. There was no current dyspnea, although exertional dyspnea was reported. No orthopnea, nocturnal dyspnea, wheezing, peripheral edema, or cyanosis was observed. The patient was under regular cardiology follow-up and received spironolactone 12.5 mg daily, ramipril 2.5 mg daily, and monthly

intramuscular benzathine penicillin G since June 2023. There was no history of chest pain, palpitations, syncope, or neurological symptoms.

Prior to referral, he had been hospitalized for three days at Dr. Adnaan WD Payakumbuh Regional Hospital with diagnoses of IE and recurrent ARF, treated with intravenous ampicillin 2 g every 4 hours and gentamicin 75 mg daily. Referral was necessitated by worsening symptoms and the inability to perform blood cultures.

On examination, the patient was moderately ill but cooperative, with stable vital signs: blood pressure 98/63 mmHg, pulse 87 bpm, respiratory rate 20/min, and oxygen saturation 99% on nasal cannula at 1 L/min. Physical examination revealed a visible apical impulse, with the left cardiac border palpable one finger lateral to the midclavicular line, normal S1 and S2 heart sounds, and a high-pitched grade 3/6 pansystolic murmur at the apex radiating to the axilla. Lung auscultation was normal. No peripheral edema or peripheral stigmata of IE were noted.

Electrocardiogram demonstrated sinus rhythm (68 bpm), normal axis and P waves, PR interval 12 seconds, QRS duration 0.06 seconds, T wave inversion in leads aVR, aVL, and V1–V3, evidence of left ventricular hypertrophy, no right ventricular hypertrophy, and a corrected QT interval of 426 ms (Figure 1).

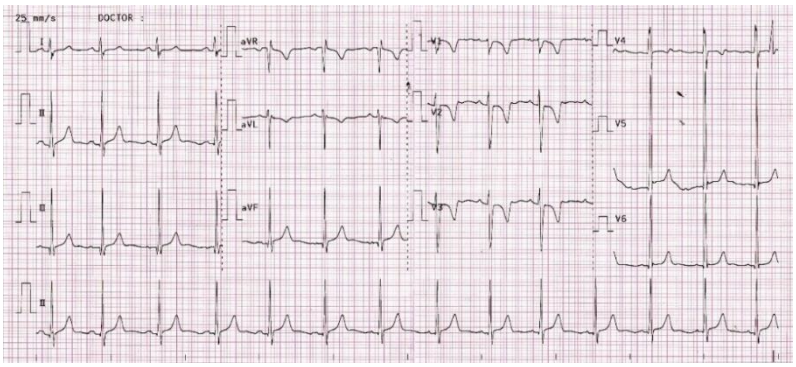

Figure 1. Electrocardiogram in the Emergency Department of M. Djamil General Hospital.

Transthoracic echocardiography performed one day prior to referral revealed situs solitus with all pulmonary veins draining normally into the left atrium, dilated left atrium and left ventricle, severe mitral regurgitation consistent with RHD, mild tricuspid regurgitation, low probability of pulmonary hypertension, preserved left ventricular ejection fraction of 75%, and good right ventricular function (TAPSE 2.7 cm). Vegetations measuring 9x11 mm were noted on the anterior mitral leaflet (Figure 2).

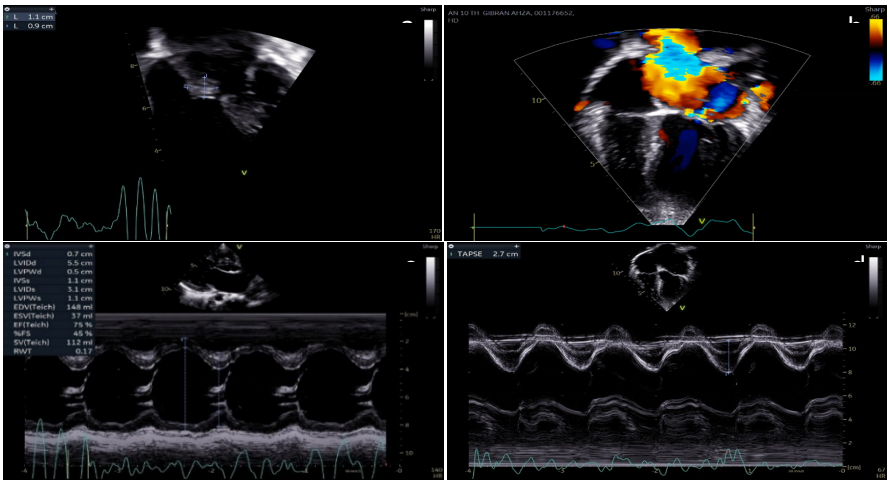

Figure 2. Echocardiography at M. Djamil General Hospital (a) Apical four-chamber view showing vegetation on anterior mitral leaflet (AML) (b) Apical four-chamber view showing severe mitral regurgitation (c) Parasternal long axis M-mode demonstrating ejection fraction 75% (Teichholz method) (d) Apical four-chamber M-mode showing tricuspid annular plane systolic excursion (TAPSE) 2.7 cm

Discussions

This case report addresses a complex diagnostic and therapeutic challenge involving the coexistence of IE and recurrent ARF in a 10-year-old boy with RHD. The primary objective was to examine clinical-diagnostic interactions between these overlapping pathologies and evaluate multidisciplinary management strategies.

The findings emphasize that patients with RHD, particularly in developing countries, remain vulnerable to both ARF and IE. Vegetations detected by echocardiography, intermittent fever, and a history of mitral regurgitation formed the basis for suspecting IE. Meanwhile, migratory joint pain, prior RHD, elevated ASO titers, and the presence of mitral valve regurgitation strongly supported the diagnosis of recurrent ARF. Applying ESC 2023 criteria and the Australian 2020 guidelines helped delineate this dual diagnosis and direct appropriate treatment.[1,2,5,9,10,18,21,22,24,25]

The pathophysiology likely involves an immune-mediated response triggered by streptococcal antigens, resulting in inflammatory damage to the cardiac valves and the development of sterile vegetations. Prior antibiotic use may also lead to culture-negative endocarditis, further complicating the distinction between infection and sterile inflammation.[1,2,5,6,8,24]

The case contributes valuable insights to clinical practice. First, it highlights the diagnostic ambiguity that arises from overlapping symptoms—fever, arthritis, and murmurs—commonly seen in both ARF and IE. Second, it reaffirms the role of echocardiography in revealing characteristic vegetations that are critical for IE diagnosis, particularly in culture-negative cases. Third, it showcases the importance of early empirical antibiotics tailored to likely pathogens and the cautious use of corticosteroids to manage inflammation in ARF without exacerbating infection risks in IE.[1,2,8,9,17,26]

Limitations of this study include the inability to perform advanced diagnostics such as PCR or serologic identification of fastidious organisms. Negative blood cultures, prior antibiotic exposure, and lack of molecular tests constrained the identification of causative pathogens. These limitations reinforce the need for high clinical suspicion and empiric therapy in endemic settings.[2,5–8,18,19,23,24]

This case aligns with existing literature reporting the prevalence of coexisting IE and ARF in RHD patients from developing regions. Studies such as REMEDY confirm similar patterns, with increased IE risk among pediatric patients with chronic valve lesions. Our findings further support previous recommendations advocating strict oral hygiene, routine dental evaluation, and early antibiotic prophylaxis to prevent streptococcal infections.[1,4–6,8,18,19,24,26,27]

In summary, this case underscores the necessity of integrated diagnostic frameworks like the ESC 2023 and Australian 2020 criteria to navigate diagnostic uncertainty. Timely and tailored interventions, including antibiotics, anti-inflammatory agents, and secondary prophylaxis, significantly improved patient outcomes. This highlights the importance of vigilant multidisciplinary collaboration, early detection, and structured follow-up in managing dual diagnoses of IE and recurrent ARF in RHD patients.

Conclusions

This case report highlights the complexity of diagnosing and managing the coexistence of infective endocarditis and recurrent acute rheumatic fever in children with rheumatic heart disease. The combined use of echocardiography and serologic markers is critical for accurate diagnosis, especially in blood culture-negative scenarios. Integrated treatment addressing both infection and autoimmune inflammation can lead to favorable clinical outcomes. Future research should focus on developing standardized protocols for such dual-pathology presentations and enhancing microbiological diagnostics to improve detection rates. Multidisciplinary care remains essential to reduce morbidity and improve prognosis in this vulnerable population.

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Declarations of competing interest

The authors declare that there are no competing interests associated with this publication.

References

1. RHDAustralia. The 2020 Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease. 3rd ed. Currie B, Ralph A, editors. Darwin: Menzies School of Health Research; 2022. p. 1–295.
2. Delgado V, Ajmone Marsan N, De Waha S, Bonaros N, Brida M, Burri H, et al. 2023 ESC Guidelines for the management of endocarditis. Eur Heart J. 2023;44(39):3948–62.
3. Dougherty S, Okello E, Mwangi J, Kumar RK. Rheumatic Heart Disease: JACC Focus Seminar 2/4. J Am Coll Cardiol. 2023;81(1):81–94.
4. Soesanto AM, Almazini P, Ariani R, Rudiktyo E, Ardini TW, Mumpuni H, et al. Characteristics and problems of rheumatic heart disease in Indonesia: The Ina-RHD multicenter study. JACC Asia. 2025;Forthcoming. doi:10.xxxx/xxxx (update with volume/issue/page once available).
5. Costa REMAS, Nicoletti SA, Amaral KSJ, Matola MFSB, Alves SP, Vellano PO, et al. Rheumatic fever and infective endocarditis: A review. J Adv Med Med Res. 2023;35(16):121–7.
6. Alsamarrai A, Saavedra C, Bryce A, Dimalapang E, Leversha A, Briggs S, et al. Infective endocarditis in patients with rheumatic heart disease: a single-centre retrospective comparative study. N Z Med J. 2022;135(1550):62–73.
7. Fowler VG, Durack DT, Selton-Suty C, Athan E, Bayer AS, Chamis AL, et al. The 2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for infective endocarditis: updating the modified Duke criteria. Clin Infect Dis. 2023;1–22.
8. Basaglia A, Kang K, Wilcox R, Lau A, McKenna K, Smith S, et al. The aetiology and incidence of infective endocarditis in people living with rheumatic heart disease in tropical Australia. Eur J Clin Microbiol Infect Dis. 2023;42(9):1115–23.
9. World Health Organization. WHO guideline on the prevention and diagnosis of rheumatic fever and rheumatic heart disease. Geneva: World Health Organization; 2024.
10. Peters F, Karthikeyan G, Abrams J, Muhwava L, Zühlke L. Rheumatic heart disease: Current status of diagnosis and therapy. Cardiovasc Diagn Ther. 2020;10(2):305–15.
11. Charlesworth M, Williams BG, Ray S. Infective endocarditis. BJA Educ. 2023;23(4):144–52.
12. Mills MT, Al-Mohammad A, Warriner DR. Changes and advances in the field of infective endocarditis. Br J Hosp Med. 2022;83(3):1–11.
13. Imazio M. The 2023 new European guidelines on infective endocarditis: Main novelties and implications for clinical practice. J Cardiovasc Med. 2024;25(10):718–26.
14. Ruan R, Liu X, Zhang Y, Tang M, He B, Zhang QW, et al. Global, regional, and national advances toward the management of rheumatic heart disease based on the Global Burden of Disease Study 2019. J Am Heart Assoc. 2023;12(13):e028989.
15. Arafuri N, Murni IK, Julia M, Nugroho S, Soehadi N. Survival of rheumatic heart disease in Indonesian children. Glob Heart. 2022;17(1):1–12.
16. Moe TG. Rheumatic heart disease: A global call to action. JACC Case Rep. 2024;29(20):1–4.
17. Hajsadeghi S, Hassanzadeh M, Hajahmadi M, Kadivar M. Concurrent diagnosis of infective endocarditis and acute rheumatic fever: A case report. J Cardiol Cases. 2018;17(5):147–50.
18. Yılmaz M, Gürses D, Kahraman Ö. The incidence and clinical characteristics of infective endocarditis in children: A five-year, single-centre retrospective evaluation. Cureus. 2022;14(5):e24879.
19. Parham S, Barbara H, Michelle F, Ursula F, Katia B, Benoit G, et al. Infective endocarditis: prevention and antibiotic prophylaxis. Swiss Med Wkly. 2021;151:w30001.

20. Kamde SP, Anjankar A. Pathogenesis, diagnosis, antimicrobial therapy, and management of infective endocarditis, and its complications. Cureus. 2022;14(9):e28976.
21. Simpson MT, Kachel M, Neely RC, Erwin WC, Yasin A, Patel A, et al. Rheumatic heart disease in the developing world. Struct Heart. 2023;7(6):1–9.
22. Guan C, Xu W, Wu S, Zhang J. Rheumatic heart disease burden, trends, and inequalities in Asia, 1990–2019. Glob Health Action. 2023;16(1):2189487.
23. Ralph AP, Currie BJ. Therapeutics for rheumatic fever and rheumatic heart disease. Aust Prescr. 2022;45(4):104–12.
24. Cox DA, Tani LY. Pediatric infective endocarditis: A clinical update. Pediatr Clin North Am. 2020;67(5):875–88.
25. Zhuang S, Guo D, Yu D. A mini review of the pathogenesis of acute rheumatic fever and rheumatic heart disease. Front Cell Infect Microbiol. 2025;15:1552900.
26. Rwebembera J, Marangou J, Mwita JC, Mocumbi AO, Mota C, Okello E, et al. 2023 World Heart Federation guidelines for the echocardiographic diagnosis of rheumatic heart disease. Nat Rev Cardiol. 2024;21(4):250–63.
27. Kumar RK, Antunes MJ, Beaton A, Mirabel M, Nkomo VT, Okello E, et al. Contemporary diagnosis and management of rheumatic heart disease: Implications for closing the gap. A scientific statement from the American Heart Association. Circulation. 2020;142(20):e337–57.