

Chronic rheumatic heart disease with recrudescence of acute rheumatic fever on histology: a case report

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Background

Rheumatic heart disease (RHD) is endemic in sub-Saharan Africa where it is the leading cause of cardiovascular mortality in the young. Rheumatic heart disease results from recurrent episodes of acute rheumatic fever (ARF), which are often difficult to diagnose clinically. Acute rheumatic fever may be diagnosed based on the revised Jones Criteria 2015 for the diagnosis of ARF. Histologically, acute rheumatic valvulitis manifests with active inflammation characterized by lymphocytic infiltration, Aschoff bodies, and Anitschkow cells. Chronic rheumatic valvulitis is associated with neovascularization, and/or dystrophic calcification. The combination of histological features of both ARF and chronic RHD is a rare finding.

Case summary

Here we report on a case of a 59-year-old woman with mixed aortic and mitral valve disease of probable rheumatic aetiology (elevated C-reactive protein and prolonged PR interval) and with histological evidence of lymphocytic infiltration, Aschoff bodies, and fibrinoid necrosis admixed with features of chronic RHD.

Discussion

Cases of chronic RHD admixed with ARF are very rare; however, they should be considered in regions with a high prevalence of RHDs.

Keywords

Case report • Rheumatic heart disease • Valvular heart diseases • Histopathology

ESC Curriculum

4.1 Aortic regurgitation • 4.3 Mitral regurgitation • 4.9 Multivalvular disease • 7.5 Cardiac surgery • 9.1 Aortic disease

Learning points

- In high-risk areas, consideration of acute rheumatic fever (ARF) in the differential diagnosis should not be ruled out despite not meeting the criteria for definite ARF diagnosis as per revised Jones Criteria 2015.
- Infective endocarditis or ARF should be considered in the differential diagnosis of patients presenting with rapidly declining ventricular function in rheumatic heart disease endemic areas in all regions of the world.

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Introduction

Rheumatic heart disease (RHD) is endemic in low- and middle-income countries (LMICs).¹ Rheumatic heart disease follows repeated acute rheumatic fever (ARF) episodes resulting in valvular stenosis, regurgitation, heart failure, left ventricular (LV) dysfunction, arrhythmias, and pulmonary hypertension.² Incidents of ARF are mostly prevalent among children aged 5–14 years and uncommon in persons 45 years and older.^{2,3} Rheumatic heart disease is an important cause of infective endocarditis in LMICs, including sub-Saharan Africa (SSA). Rheumatic heart disease is diagnosed clinically and confirmed echocardiographically or using other imaging modalities; ARF is diagnosed based on the revised Jones Criteria.⁴

Pathologically, chronic RHD shows features of chronicity such as stromal neovascularization, fibrosis, calcification, and/or chronic inflammation. It is rare for histological features of ARF to coincide with those of RHD.⁵ Here we report on a patient diagnosed with RHD who underwent elective aortic and mitral valve (MV) replacement and was confirmed histologically to have RHD as well as coincident ARF, with evidence of acute valvulitis.

Timeline

June–August 2019	<ul style="list-style-type: none"> A 59-year-old woman presented with poorly controlled diabetes and hypertension presents with heart failure The patient was afebrile
15 October 2019	<ul style="list-style-type: none"> Patient presented with New York Heart Association (NYHA) functional Class IV (decompensated) heart failure She was normotensive and afebrile She had an elevated C-reactive protein (CRP) On electrocardiogram (ECG) she had ST-segment elevation and a prolonged PR interval On echocardiography, she demonstrated severe aortic regurgitation (AR) and mitral regurgitation (MR) suspected to be of rheumatic aetiology. She also had calcified aortic valve (AV) leaflet and a large vegetation on the anterior MV leaflet and AV, and an ejection fraction of 60% On cardiac catheterization, she had normal coronaries, severe AR, severe MR, with normal LV function She was referred for valve replacement surgery
22 October 2019	<ul style="list-style-type: none"> Double valve replacement surgery was done Intraoperative observations showed a small AV root abscess with chronic infective endocarditis, large vegetations on the non-coronary AV cusp. The MV showed

18 November 2019	<ul style="list-style-type: none"> anterior leaflet vegetation, and both AV and MV were replaced with bioprosthetic valves Surgery went well and had uneventful ICU and ward stay Patient was started on antibiotics treatment for infective endocarditis Patient was booked for follow-up appointment in 6 months' time and has remained well
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Case report

A 59-year-old woman of sober habits with a 10-year history of poorly controlled Type 2 diabetes, hypertension, and no history of ARF, prior myocarditis, or other known structural heart disease presented with acutely decompensated heart failure. She reported in the past 2 months symptoms of breathlessness, shortness of breath, declining effort tolerance, orthopnoea, bipedal oedema, and paroxysmal nocturnal dyspnoea. Her performance status declined from a NYHA functional Classes II–IV within 3 months.

Physical examination revealed no fever, no arthritis, no chorea, no erythema magnatum nor subcutaneous nodules. Further examination showed a normal blood pressure of 140/60 mmHg with a wide pulse pressure, a heart rate of 98 bpm, a collapsing pulse, displaced apical impulse, and elevated jugular venous pressure. Cardiac auscultation showed a normal soft S1, a normal S2, and an S3 gallop. A 3/6 pansystolic murmur in the mitral area, loudest on expiration, was heard, in keeping with MR. She also had a 2/4 early diastolic murmur with arterial findings of severe AR and a widened pulse pressure. The 12-lead ECG showed abnormal QRS wave pattern, repolarization changes, and 1st degree atrioventricular (A-V) block (PR 330 ms) (*Figure 1*). On chest radiography, there was cardiomegaly, bilateral pleural effusions, upper lobe pulmonary venous diversion in keeping with heart failure, and prominent pulmonary arteries (*Figure 2A and B*). Transthoracic echocardiography (TTE) with two-dimensional (2D) Doppler imaging showed mildly dilated LV size and normal LV function (LV dimension in diastole (d) 54 mm, and LVEF 60%). The echocardiographic assessment of the right ventricle (RV) and the pulmonary valve showed pulmonary hypertension with normal sized RV with normal RV function and normal pulmonary valve with mild tricuspid regurgitation (TR – TR V_{max} 3.66 m/s, TR P_{max} 54 mmHg, right atrial (RA) pressure 20 mmHg, RV systolic pressure 74 mmHg, RA area 19.7 cm²). Further, left atrial assessment showed a mildly dilated left atrium (43 mm). Preoperative TTE showed a tri-leaflet AV with calcified lesions on the non-coronary cusps (NCC), and severe AR. Transthoracic echocardiography of MV showed thickened leaflet tips with severe MR (*Figure 3A–H* and *Supplementary material*). Coronary angiography showed unobstructed epicardial coronary vessels and confirmed severe AR and MR. Laboratory examination showed elevated CRP 9 mg/dL, and normal white blood cells $7.62 \times 10^9/L$. Anti-DNAse B and anti-streptolysin O-titres were not performed. Blood cultures were performed but the bacterial growth had not occurred by the time the patient underwent valve replacement surgery.

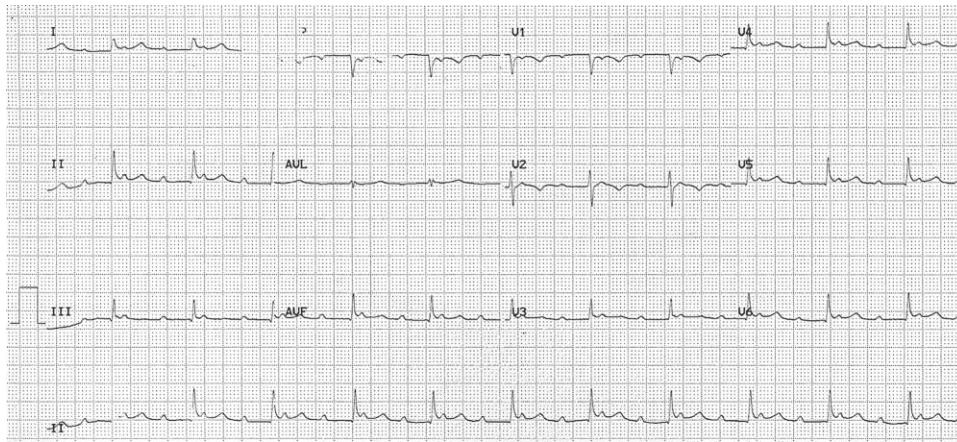


Figure 1 The 12-lead electrocardiogram with abnormal QRS wave pattern (QRS 82 ms), repolarization changes, and 1st degree a–v block (PR 330 ms).

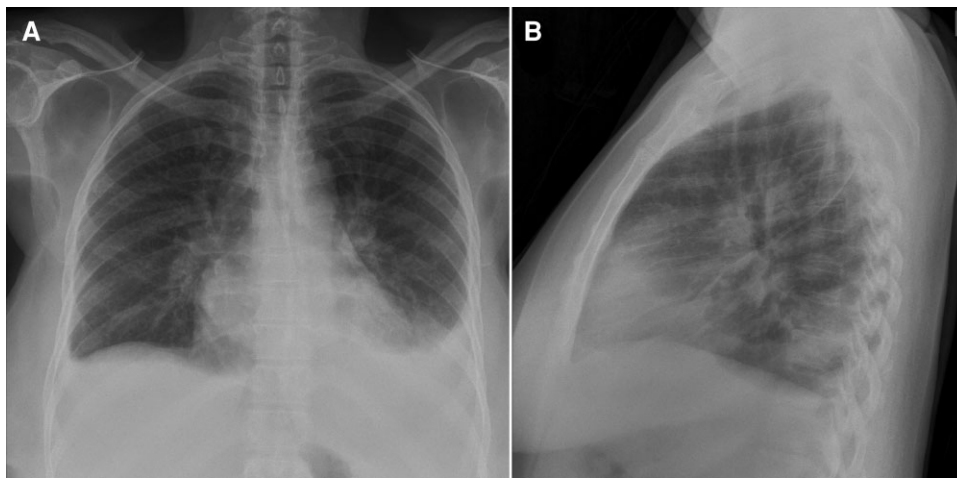


Figure 2 (A and B) chest X-ray transverse view showing cardiomegaly and upper lobe pulmonary venous diversion (A) and bilateral pleural effusions (B).

Microbiology tests for gram-negative bacteria were negative and polymerase chain reaction testing for common bacteria was also negative.

The patient was diagnosed with valvular heart disease of probable rheumatic aetiology and with severe AR and MR complicated by heart failure. She was started on heart failure pharmacotherapy and referred for double valve replacement surgery. On-table, transoesophageal echocardiography was performed and showed a large vegetation on the anterior MV leaflet, and another on the NCC of the AV. In addition, Grade III diastolic dysfunction was noted, a large pleural effusion on the right was also seen. She underwent open-heart surgery and had AV and MV replacement, both with bioprosthetic tissue valves, based on patient's preference. During the operation, it was evident that below the AV there was small root abscess and vegetation on the AV and MV, confirming chronic infective endocarditis. The patient was

treated for culture-negative infective endocarditis. The patient was started on an antibiotic therapy (penicillin G 5 million Unit IV 6 hourly for 4 weeks, gentamycin 80 mg IV three times a day for 2 weeks, doxycycline 100 milligrams orally twice a day for 4 weeks), discharged home well, and has been doing well on follow-up visits. Her post-surgical course was uneventful.

The histopathological assessment showed features of concomitant ARF in a background of chronic RHD. The MV showed evidence of a chronic RHD, with moderate-to-severe fibrosis of the valves, scattered stromal histiocytes, and foci of neovascularization with characteristic thick-walled vessels (*Figure 4A and B*). The AV showed chronic RHD with stromal neovascularization, fibrosis, and chronic inflammation. Additionally, discrete foci of acute rheumatic valvulitis were evident, with Aschoff bodies containing Anitschkow cells and central fibrinoid necrosis (*Figure 5A–D*).

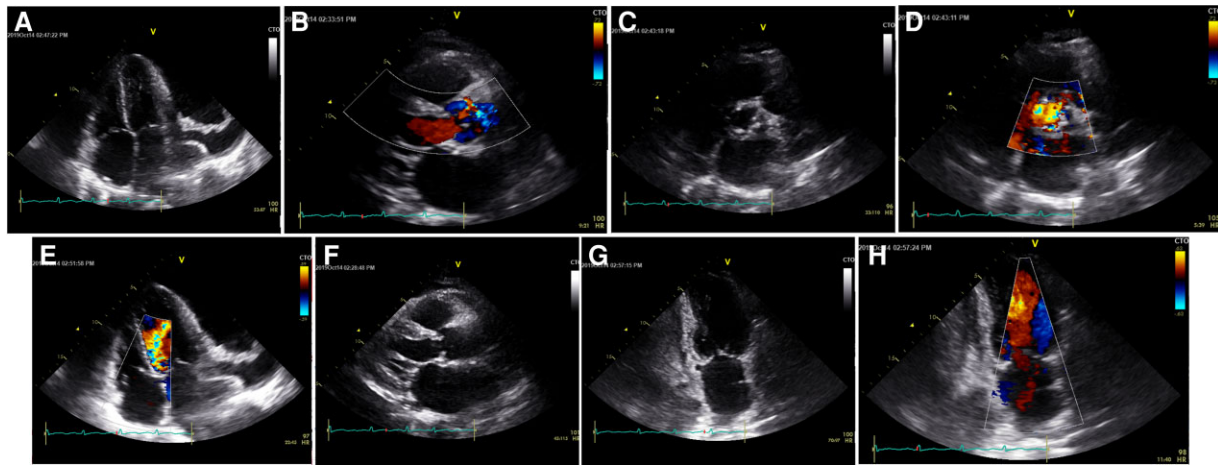


Figure 3 (A–H) Preoperative 2D Doppler TTE showing mildly dilated left ventricular, and normal right ventricular and right atrial. (A) Normal pulmonary valve with mild TR. (B) Calcified tri-leaflet aortic valve (C) with severe AR (D and E), thickened mitral valve (F and G) with severe MR (H).

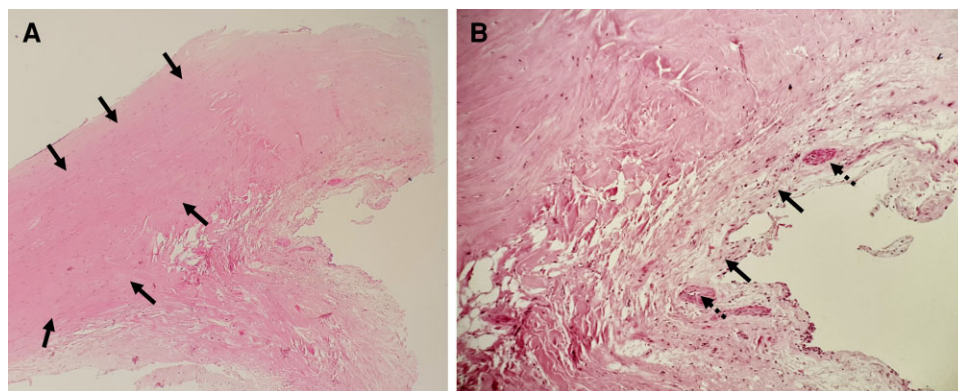


Figure 4 (A and B). Haematoxylin and eosin staining of mitral valves. (A) Severe fibrosis (solid arrows) (magnification 40 \times), (B) scattered stromal histiocytes (solid arrows) and foci of neovascularization with thick-walled vessels (dotted arrows) (magnification 200 \times).

Discussion

Rheumatic heart disease is endemic in LMICs, including SSA.^{1,6} Prevalence of RHD in SSA was 864/100 000 in 2017.⁷ The reported incidence of ARF is declining, and likely reflects underdiagnosis and improving public health.⁸

In RHD, MV lesions (stenosis and/or regurgitation) are found in 50–60%, while mixed MV and AV disease (as in our patient) occurs in ~20% of RHD patients.⁹ As per the revised Jones Criteria 2015 for diagnosis of ARF, a combination of two major criteria or one major plus two minor criteria is required to diagnose a definitive ARF.⁴ In this case, however, the patient presented with two minor criteria and had no history of ARF, therefore, at best was diagnosed with probable ARF.

We report on a case of chronic RHD with acute recrudescence of ARF confirmed histologically, with infective endocarditis, severe AR, and severe MR, and complicated by heart failure. The fact that ARF is rare in individuals older than 45 years makes it unique that here we report a 59-year-old individual with histologically confirmed ARF.

In this case, preoperative TTE could not rule out or confirm ARF and preoperative TEE was not suggested since there was no doubt on the diagnosis of RHD. On-table TEE provided a better assessment of the MV by showing the presence of vegetations on the MV and confirmed intraoperatively. Preoperative TEE would have provided more findings than did TTE towards the workup of the patient by indicating the presence of infective endocarditis. Transthoracic echocardiography has a better sensitivity and provides a clearer assessment of valve morphology which would otherwise have been impeded in TTE due to acoustic shadowing.^{10–12} This underscores the importance of the role of preoperative TEE in the diagnosis of valvular heart disease especially in RHD endemic regions.

Histologically RHD is characterized by neovascularization and lymphocytic cell infiltration. On the other hand, ARF is characterized histologically by fibrinoid necrosis, Aschoff bodies, and Anitschkow cells. In this case, histological findings confirmed chronic RHD in both aortic and MVs. In addition, the AV showed Aschoff bodies, fibrinoid necrosis, neovascularization, moderate to severe stromal

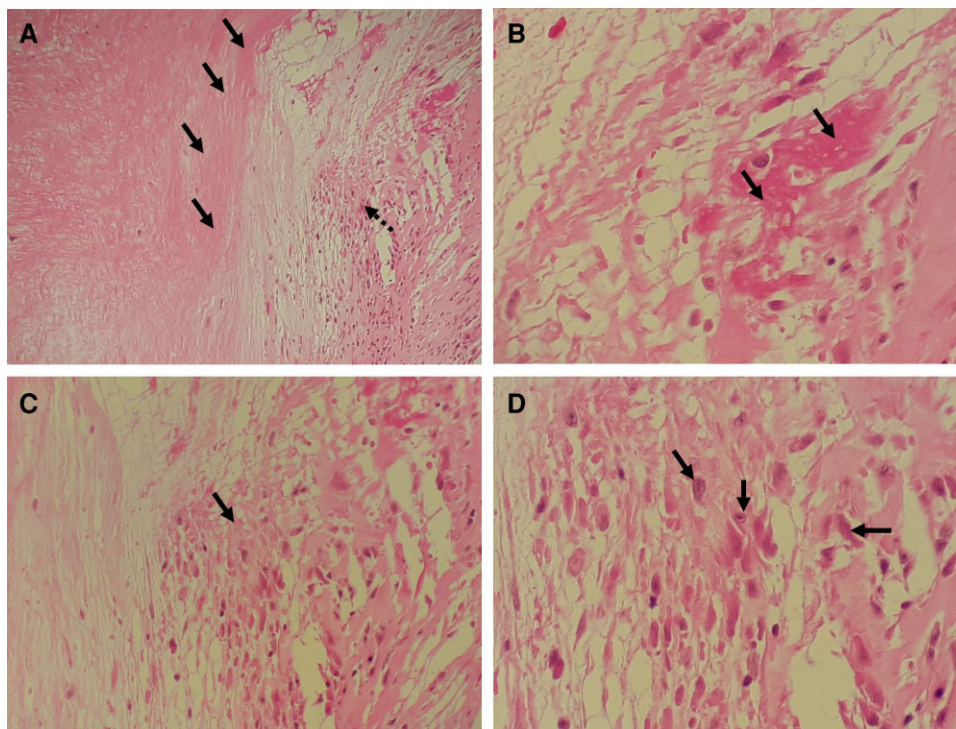


Figure 5 (A–D) Haematoxylin and eosin staining of aortic valve. (A) Hyalinization (solid arrows) and Aschoff bodies (dotted arrow) (magnification 100×), (B) fibrinoid necrosis (magnification 400×), (C) Aschoff body (magnification 200×). (D) Aschoff body with characteristic Anitschkow cells (magnification 400×).

fibrosis, and macrophages compatible with acute rheumatic valvulitis on a background of chronic rheumatic valvulopathy. While Aschoff bodies in acute valvulitis and carditis have been reported elsewhere,^{13,14} admixed of acute on chronic rheumatic valvulitis is exceptionally rare. Therefore, our report intends to create awareness of existing ARF cases that may go unnoticed especially in endemic areas.

Conclusion

Cases of chronic RHD admixed with ARF are very rare, however, they should be considered in regions with a high prevalence of RHD.

Lead author biography



Daniel W. Mutithu is currently a PhD fellow at the Department of Medicine, University of Cape Town, South Africa. Daniel does research on understanding the pathogenesis of valvular heart diseases using histopathology and metabolomics (LC-mass spectrometry and MALDI imaging). He is interested in multi-omics biomarker research. Daniel has a MSc Medical Biotechnology from Wageningen University & Research, Netherlands, and a BSc (Hons) Biotechnology

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Supplementary material

Supplementary material is available at European Heart Journal – Case Reports online.

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Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance. The study was approved by UCT's Faculty of Health Human Research Ethics Committee (HREC REF:574/2018).

Conflict of interest: None declared.

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