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Rheumatic Valve Disease And Atrial Fibrillation: A Case Report And Review

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Abstract
Background*: Rheumatic Valve Disease is corresponding for the highest cardiovascular disease-related loss of disability. It is more prevalent in low-middle ang high-income countries, strongly associated with socioeconomic disadvantage. Mitral Regurgitation is the most common cardiac involvement and can progress to stenosis. Rivaroxaban 15mg once daily was administered in addition to optimizing heart failure medical therapy in order to prevent cardiovascular events in this patient until surgery. She was submitted to replacement mechanical mitral valve, remaining hemodynamically stable.*
Case summary*: a 50-year-old woman was accepted at a university policlinic with hyperthyroidism, arterial hypertension (HTN) and signs/symptoms of heart failure (nocturnal paroxysmic dyspnoea, orthopnoea, lower limb oedema, S3, and mitral regurgitation). X-ray Chest showed cardiomegaly, inversion of the pulmonary vascular pattern; echocardiogram showed severe mitral regurgitation, moderate tricuspid regurgitation, PAP 59mmHg. Patient was treated with beta-blocker, RAASi, Spironolactone, loop diuretic and Rivaroxaban, up-titrating until tolerated maximal doses. She will be submitted to cardiac catheterization to near future cardiac intervention. The patient is still stable.*
Conclusion*: Treatment with Rivaroxaban in addition to heart failure therapy was administered and maintain patient stabilized, despite of some short-scale studies had proven Rivaroxaban not superior to Warfarin in rheumatic valve disease. The authors know that large-scale randomized clinical trials are necessary to elucidate the difference in mortality and cardiovascular events between the two pharmaceutical classes in atrial fibrillation due to rheumatic valve disease in long-term follow-up.*
Our group know that exist short-term internationals studies addressing this topic. This case report is part of a follow-up of a patient with Heart Failure due to Rheumatic Valve Disease and Atrial Fibrillation at a university policlinic in Rio de Janeiro.

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I. Case Presentation

A 50-year-old lady, afro-descent, born in Rio de Janeiro, came to the Medical Clinic office to evaluation. In 2019, she was diagnosed with hyperthyroidism (used Tapazol once a day, but she suspended for her on) with struma and exophthalmos. Hypertensive foy five years using irregularly Enalapril 10mg twice a day. In 2023 presented worsening of the endocrinological condition, sudoresis, tachycardia, extremity tremors, generalized asthenia, lower limb oedema with difficulty walking, associated with hyperactivity and hypertension peaks, as well as odynophagia and dysphasia for solid foods. She came to a tertiary hospital (HUPE), and Levothyroxine 112 mcg once daily and Enalapril 20mg twice daily, Carvedilol 6,25mg twice daily were prescribed. X-ray chest (**Figure 1**), transthoracic echocardiogram (**Figure 2**) and ECG (**Figure 3**) were requested. The echocardiogram measurements were as follows: LA 8,0/Ao 2,2/ LVD 6,8/ LVS 3,9/ IVS=PW 0,8/ LVEF 72,5%/ LV mass 232g. Concentric left ventricular hypertrophy, normal contractility, normal systolic function, normal size aorta, normal tricuspid, aortic and pulmonary valves. Mitral valve with prolapse. Enlarged right atrium and ventricle. TAPSE 1,9 cm (**Figure 2**).

One month ago, she presented worsening of symptoms, with nocturnal paroxysmic dyspnoea, orthopnoea, and greater lower limb oedema. She sought out the University's polyclinic for evaluation.

Past history of Rheumatic Fever at age 15, being treated with Benzetacil from age 15 to 20. Eclampsia in second pregnancy with pre-delivery. Family history of father who died due to heart failure, had Graves' disease

and type II diabetes mellitus (type-II DM). Mother died from COVID-19, had systemic hypertension, chronic kidney disease and hypotireoidism. A sister died at the age of 32 due to a stroke and myocardial infarction. She has four brothers, hypertensives.

On examination: lucid, oriented in time and space, tachypnoea (28 irpm), irregular pulse, heart rate 83 bpm. BP: 130/90 mmHg. Thyroid mobile, centred, without palpable nodules. Jugular turgidity 60° (patient intolerant to 0°decubitus). Cardiovascular system: palpable ictus cordis in the 5th intercostal space in the left axillary line, ± 5cm, irregular rhythm (Atrial Fibrillation), 3T (third sound-S3), systolic murmur 3+/6+ in mitral focus, with irradiation to the back. Respiratory system with audible vesicular murmur, with crackling rales at the bases. Abdomen with liver palpable 3cm from the right costal margin, negative ascites manoeuvres. Lower limbs with free calves, bilateral oedema 2+/4+ soft, cold, with locks.

Carvedilol 6,25mg twice daily, Spironolactone 25mg once daily, Furosemide 40mg BID, Enalapril 20mg BID, Levothyroxine 150mcg daily were prescribed, and new laboratory tests and transthoracic echocardiogram were requested. A Consent Form was signed.

Figure 1. X-Ray chest: four-chambers cardiomegaly, inversion of the pulmonary vascular pattern, Kerley B lines, enlargement of lung hila.

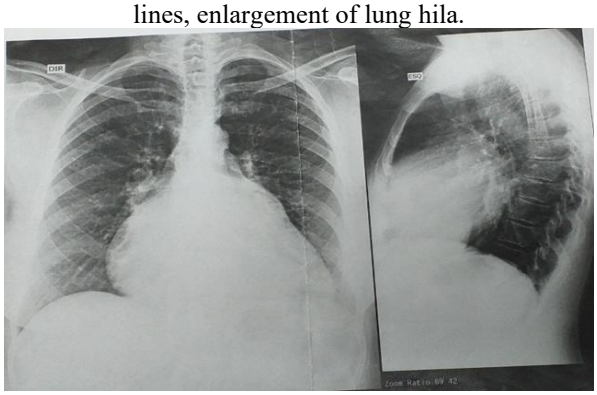


Figure 2. Transthoracic echocardiogram.

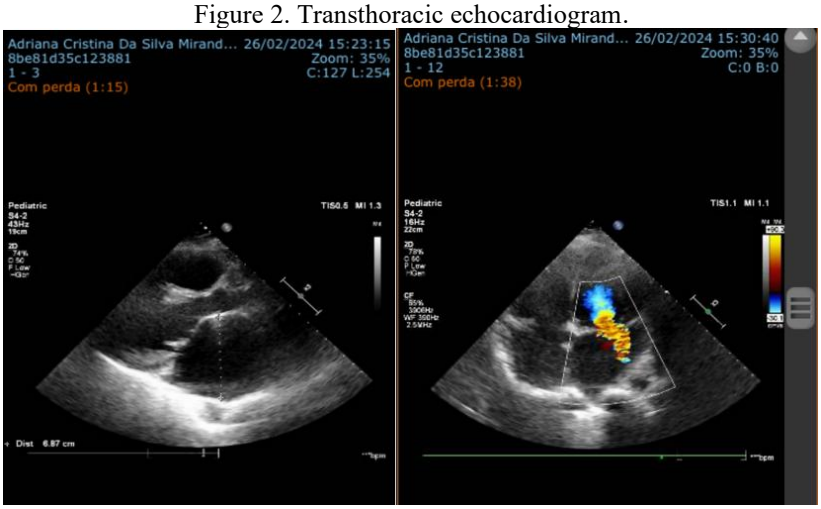
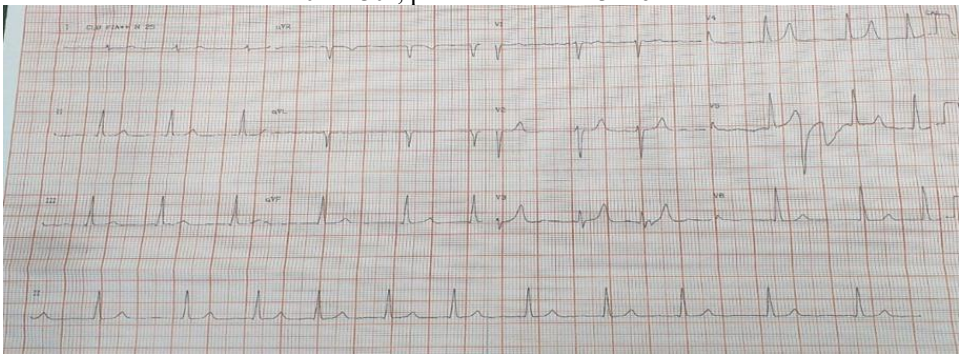
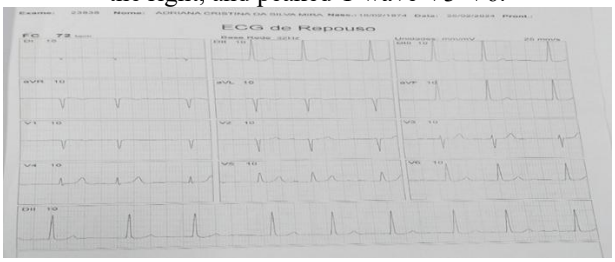


Figure 3. Electrocardiogram (ECG): atrial fibrillation rhythm, average heart rate 80bpm, electrical axis between 0 to -30°, peaked T wave V3-V6.



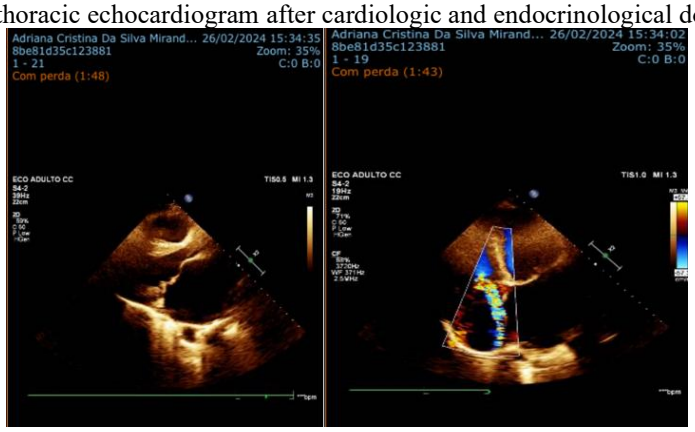
After 30 days, patient returns with exams, and with improved nocturnal paroxysmal dyspnoea, orthopnoea. Respiratory system with vesicular murmurs without adventitious noises. Cardiovascular system: jugular turgidity 0°, irregular cardiac rhythm, S3, systolic murmur 3+/6+ mitral focus, with irradiation to the back. Abdomen presenting non-palpable liver, and without visceromegaly. Lower limbs with no oedema. Medication doses were reduced: Levothyroxine 150mcg/day, Carvedilol 12,5mg BID, Spironolactone 25mg/day, Enalapril 10mg BID, Furosemide 40mg/day, and Rivaroxaban 15mg/day was started (considering non-valvular AF). Evolutionary laboratory tests are listed in Table 1.

Figure 4. ECG with atrial fibrillation (AF) rhythm, average heart rate 80bpm, deviation of the electrical axis to the right, and peaked T wave V3-V6.



Transthoracic echocardiogram (mar/24): Ao 2,2/ LA 6,8// DLV 6,8/ SLV 3,8/ LVEF 73%, left ventricle (LV) mass 281g/ IVS=PW 0,9 (all measures in cm). Increased left cavity dimensions (LA and LV). Thickened mitral valve and leaflet coaptation failure and reduced mobility of the posterior leaflet, suggesting rheumatic involvement, with valve area 3,6cm. Right atrium (RA) enlarged, right ventricle (RV) normal function, Dilated inferior vena cava (IVC). Normal aortic valve. Left ventricle with normal global and segmental contractility. Tricuspid valve mildly thickened. Estimated pulmonary artery pressure 59mmHg. Doppler: severe mitral regurgitation with eccentric jet and presence of remora. Mild mitral stenosis (MS). Moderate tricuspid regurgitation (RT). Double mitral lesion with predominance of insufficiency, of rheumatic etiologic (Figure 5).

Figure 5. Transthoracic echocardiogram after cardiologic and endocrinological dose adjustments.



The thyroid ultrasound revelled thyroid centred, mobile, topic, normal volume, regular contours with heterogeneous texture at the expense of two colloid cysts with regular contours and well-defined limits, measuring 8,6 cm in the left lobe and 5,6 cm in the right lobe.

Table 1. Evolutive laboratorial tests.

LAB parameters	jul/23	fev/24	mar/24
T3	1,1	1,05	
Free T4	0,49	0,91	1,01
TSH	49,96	10,63	7,63
Creatinine	0,78	0,9	1,2
Glucose	86	87	84
HbA1c (%)	6	5,6	5,4
Hto	30	31,2	31
Hb	10,2	11,2	11,5
Potassium	3,9	3,8	3,8
Anti-TPO	Reactive	reactive	reactive

TSH: thyroid stimulating hormone; HbA1c: glycated haemoglobin; Hto haematocrit; Hb haemoglobin. Anti-TPO, anti-thyroperoxity.

After 60 day-treatment, she came to the office with improved symptoms, no nocturnal dyspnoea, supporting decubitus at 0°, no tachypnoea. The group opted to up-titrate carvedilol to 25mg BID, and maintain Enalapril 10 mg BID, Spironolactone 25 mg once daily, Rivaroxaban 10mg once daily (patient with dizziness and altered creatinine in dose 15 mg) with. Furosemide was suspended. The patient referred no side effects neither with Rivaroxaban nor the optimized medical treatment. Transoesophageal echocardiogram were requested. Cardiac catheterization was performed, which revealed unobstructed coronary arteries, left main coronary artery free of lesions, biatrial enlargement with pulmonary artery pressure of 46 mmHg (parameters below).

She underwent mechanical mitral valve replacement surgery and tricuspid valve repair. She was discharged from the hospital with outpatient follow-up for adjustment of medications. In the post-operative period, Warfarin was chosen because is was a mechanical valve in a patient with atrial fibrillation at o dose of 5mg once daily, adjusted to 7,5 mg OD three times a week and 10 mg on the remaining four days (RNI between 2,8-3,3). The patient returns to daily work activities with mild to moderate intensity and remains asymptomatic.

II. Discussion

Rheumatic Fever (RF) is an autoimmune reaction mediated by group A streptococcal-specific antibodies, most seen two to five weeks after acute group A streptococcal infection-pharyngitis. Acute rheumatic fever (ARF) frequently affects children between 5-14 years old, more common in females. This disease is caused by inflammation in the skin, joints, neurologic and cardiovascular systems, causing major clinic manifestations (carditis, arthritis) and minor criteria (arthralgia, fever, biomarkers of inflammation)[1,2,3].

Epidemiologically rheumatic heart disease (RHD) is more prevalent in low-to-middle- income settings, but also affects high-income countries, strongly associated with socioeconomic disadvantage[4]. It is estimated thar 50 million people worldwide and 300.000 death/year, 80% cases is concentrated in South Hemisphere. Around the world, rheumatic heart disease corresponds for the highest cardiovascular disease-related loss of disability[1,5]. Most of acute rheumatic fever symptoms resolve spontaneously, even without intervention in some weeks. In contrast, cardiac involvement is progressive, developing rheumatic valve disease. More than half percent of patients who presents with acute rheumatic fever will develop rheumatic carditis[6,7,8].

Rheumatic heart disease (RHD) mortality is largely based on diagnosis, medical treatments, and cardiac interventions. Its mortality among women is at least explained, in part, by the morbidity during pregnancy or chronic valve disease, mainly fibrosis and thickening[7,8,9]. RHD may contribute to maternal morbidity and mortality in low-middle-high income countries. The most common cardiac involvement is mitral regurgitation, followed by aortic regurgitation, or both[8,10,11]. Progressively, with continued fibrosis, mitral regurgitation (MR) can progress to stenosis (MS), considered trademark of rheumatic heart disease[9,10,12].

In this case presented, the patient used antibiotics (Benzathine penicillin G - Benzetacil) for only five years to treat and prevent repeated infections as secondary prevention. Unfortunately, her adherence remained a great challenge to improve understanding the urgently needed. With the progression of the disease, RHD tends to present high morbidity and mortality due to heart failure (HF), stroke, infective endocarditis (IE), and arrhythmia (atrial fibrillation more common)[13,14].

The use of echocardiogram in rheumatic cardiac (and valve) disease improves diagnosis and assessment of complications during carditis and treatment[10,15]. The diagnosis requires morphologic abnormalities of mitral and/or aortic regurgitation. The criteria are the same used in the World Heart Federation criteria for chronic rheumatic heart disease (**Table** 2). The ability to assess the severity of valve regurgitation and its impact on left ventricular (LV) function is vital in HF due to acute rheumatic fever (ARF) and identifying patients who benefit from surgery in addition to medical therapy[16].

Table 2. World Heart Federation criteria for the diagnosis of rheumatic heart disease.

MORPHOLOGY	DEFINITE RHEUMATIC HEART DISEASE	BORDERLINE RHEUMATIC HEART DISEASE
Mitral: - valve thickening >3mm	Pathological MR and more than 2 morphological criteria	AR/ MR with no morphologic abnormalities
- chordal abnormality		
- restricted posterior leaflet	Pathological AR and more than 2 morphological criteria	Two mitral abnormalities with no pathological MR/MS
- leaflet tip		
	Borderline RHD of mitral and aortic valves	
Aortic: - leaflet thickening		
- coaptation defect	Mitral Stenosis mean gradient more than 4mm	
- restricted leaflet motion		
- prolapse		
Regurgitation: - pansystolic		
- jet length ≥ 2cm		
- jet velocity > 2 views		
- jet velocity in Doppler > 3m/s		

Particularly in this case, was chosen to initiate Rivaroxaban 15mg once daily in addition to optimizing heart failure medical therapy according to the ACC/AHA and ESC Guidelines for the treatment of chronic heart failure (beta-blocker carvedilol, RAASi, MRA, loop diuretic) in order to stabilize signs and symptoms for intervention procedures (percutaneous or surgical)[12].

According to some clinical studies, many choose vitamin K antagonist (Warfarin) for rheumatic valve disease with Atrial Fibrillation (AF). Our group opted for Factor Xa inhibitor Rivaroxaban for the prevention of cardiovascular events in this patient. The REMEDY trial was the first study enrolled South Hemisphere 25 countries[17]. This prospective study concluded that there is suboptimal utilization of oral anticoagulant and antibiotic prophylaxis, and the use of valve interventions. The INVICTUS Trial enrolled 4531 patients with rheumatic valve disease (RVD) across 24 countries in the Rivaroxaban group (2256 patients) versus Vitamin-K antagonist group (2275 patients), the mean follow-up was 3.1 $\pm$ 1.2 years, and mean age 50.5 years, 72,3% were women. This study showed thar vitamin-K antagonist was superior to Rivaroxaban in AF due to rheumatic valve[18]. Large-scale randomized clinical trials are necessary to elucidate the difference in mortality and cardiovascular events between the two pharmaceutical classes in atrial fibrillation due to rheumatic valve disease in long-term follow-up.

Our group know that exist short-term internationals studies addressing this topic. This case report is part of a follow-up of a patient with Heart Failure due to Rheumatic Valve Disease and Atrial Fibrillation at a university policlinic in Rio de Janeiro.

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