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Case Report

Acute on chronic severe aortic insufficiency due to rheumatoid arthritis-associated valvulitis

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Abstract: Rheumatoid Arthritis associated valvular heart disease (RA-VHD) may occur in patients in varying degrees of severity. Aortic valve involvement leading to severe symptomatic aortic insufficiency is a rare complication of rheumatoid arthritis. This entity has not been well characterized and its clinical predictors are undefined. The pathology of RA-VHD can extend from benign nodular development to acute valvulitis with late-stage leaflet fibrosis and severe valvular regurgitation. In this report, we describe a rare case of acute heart failure (AHF) resulting from severe aortic valve destruction and insufficiency due to persistent chronic inflammation in a patient with long-standing RA. Persistent systemic inflammation of RA involved the aortic valve causing nodular thickening and leaflet destruction. Our patient had compensated chronic heart failure due to progressive aortic insufficiency resulting from gradual leaflet destruction. However, she suddenly developed AHF requiring valve replacement. Her clinical presentation, gross and histological images suggest an acute/subacute disruption of the friable aortic leaflets that resulted in AHF.

Keywords: Rheumatoid arthritis, aortic insufficiency, heart failure, valvular destruction

Introduction

Rheumatoid Arthritis (RA) has been previously established as a potential cause of valvular destruction and insufficiency but rarely result to symptomatic heart failure. The diagnosis and clinical predictors of symptomatic rheumatoid arthritis associated valvular heart disease (RA-VHD) is not well established. The valvular destruction seen in RA-VHD may also occur due to age related valvular degeneration, prior infective endocarditis, or immunologic phenomena as seen in rheumatic fever [1]. Thus, the diagnosis of RA-VHD can be very challenging. In addition, some of the histologic findings in RA, anitschkow cells, are not specific and may be seen in other disease entities [2]. Although a subclinical and indolent course of RA-associated valvulitis have been reported in most literature [3, 4], there are only few reports of acute heart failure due to severe aortic insufficiency resulting from RA-associated valvulitis. Rapidly progressive aortic valvular disease leading to heart failure has been reported in few studies [5]. Rarely, rheumatoid granuloma can develop on the aortic valve [6] and this may cause fatal acute aortic insufficiency. Therefore, rheumatoid arthritis needs to be considered as an important risk factor for acute valvular disease. We report a case of acute on chronic heart failure due to RA-VHD and present a peculiar gross imaging and histologic features of aortic valve involvement in a patient with long standing rheumatoid arthritis. Finally, we provide insight on surveillance, management strategy, and clinical follow-up.

Case report

A 55-year-old African American woman with a history of hypertension and longstanding rheumatoid arthritis was admitted with complaints

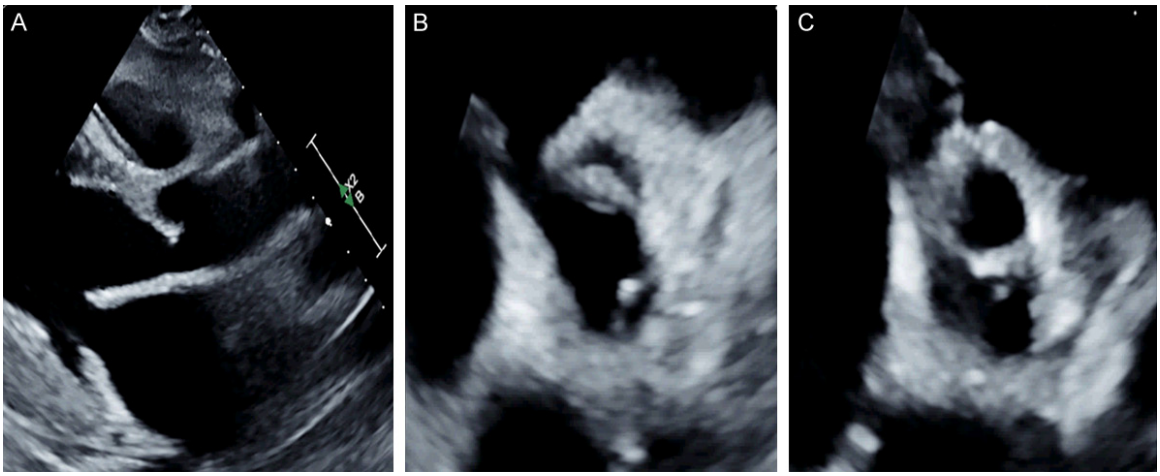

Figure 1. A. Parasternal long axis view (PLAX) of AV on TTE. B. Parasternal short axis (PSAX) on TTE of AV in systole. C. PSAX TTE of AV in diastole.

of exertional dyspnea, orthopnea, and decreased exercise tolerance. The patient had polyarticular seropositive erosive RA, which was treated with long-term steroids daily for recurrent worsening flairs of inflammation. On admission, her blood pressure was 140/58 mmHg, heart rate 76 beats/minute, and temperature 36.4 degrees Celsius. The cardiac exam was significant for a 2/4 early diastolic heart murmur, audible at the 4th intercostal space, with a 4/6 holosystolic murmur heard throughout the precordial space. Physical exam was pertinent for bilateral pitting lower extremity edema, bibasilar crackles and significantly elevated jugular venous pressure. Chest radiograph showed cardiomegaly, cephalization of pulmonary vessels and perihilar patchy opacities consistent with pulmonary edema. Brain natriuretic peptide was 770 pg/mL, troponin-I was 0.03 ng/ml, erythrocyte sedimentation rate was 84 mm/hr, and her C-reactive protein was >24 mg/dl. Rheumatoid factor ranged between 675 IU/ml (current value) to 2520 IU/ml over the past several years (reference normal value is <43 IU/ml). All other blood work, including blood cultures, was negative.

Transthoracic (TTE) and Transesophageal echocardiogram (TEE) was significant for an EF of 60%, severe AR with jet width/LVOT diameter ratio of 0.67, a pressure half-time of 184 ms, a vena contracta >10 mm, effective regurgitant orifice area (ERO) >0.5 cm^2 , left ventricular end diastolic diameter of 6.2 cm, and left ventricular end systolic diameter of 4.1 cm (**Figures 1**-**5**).

According to the American College of Cardiology/American Heart Association practice guidelines, this patient has a Class I indication for aortic valve replacement surgery (SAVR) [7]. The patient has Stage D AR associated with structural indicators of severe AR (Vena Contracta >0.6 cm, ERO >0.3 cm^2, left ventricular dilatation), along with symptomatic heart failure.

The choice of prosthetic heart valve is based on a shared decision-making process that accounts for the patient's preferences, anticoagulant therapy indications/risk, and the potential need/risk for a reintervention (Class I) [7]. Our patient was 55 years of age without contraindications for anticoagulation, with ongoing issues from progressive RA. The patient and team decided it was reasonable to proceed with a mechanical valve prosthesis. She underwent a SAVR with a 21 mm St. Jude Regent mechanical aortic valve. The patient had an uneventful post-operative recovery with significant improvement of symptoms.

Gross examination of excised aortic valve (AV) leaflets revealed significant destruction, nodular thickening with areas of erythematous foci suggesting ongoing inflammation (**Figure 6**). There was no evidence of aortic valve vegetations and the tissue culture was negative for any bacterial organisms. The histology was significant for focal fibrin deposition with chronic changes and superimposed acute neutrophilic infiltration suggestive of acute on chronic inflammation (**Figure 7A**, **7B**). There was evi-

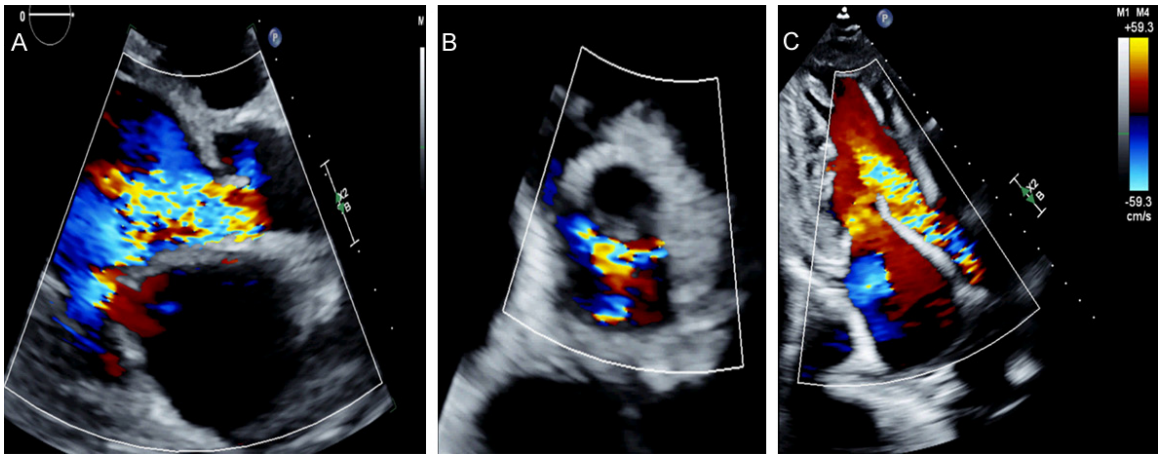

Figure 2. A. PLAX of AV with color flow doppler (CFD) displaying severe aortic regurgitation on TTE. B. PSAX TTE of AV with CFD. C. Apical three-chamber on TTE of AV with CFD.

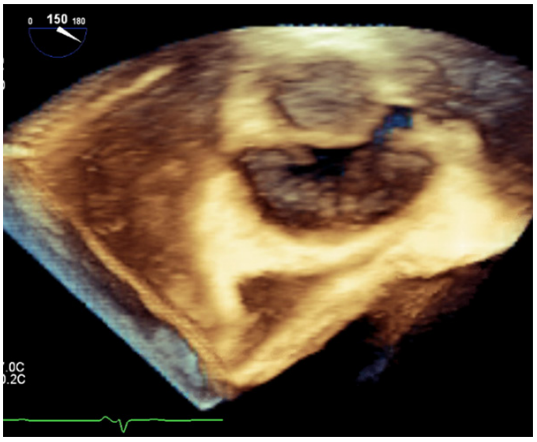

Figure 3. 3D TEE imaging of the AV in diastole (150 degrees angle mid to upper esophageal level) displaying thick right coronary cusp and least-well defined non-coronary cusp.

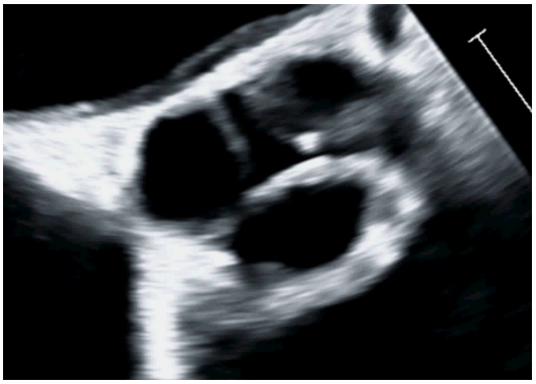

Figure 4. Short-axis (SAX) on TEE of AV in diastole at 15 degrees angle in the upper esophagus. Nodular thickening noted along the left coronary cusp and thickening of the right coronary cusp.

dence of some fibrosis, and angiogenesis with fibroblast proliferation. Anitschkow cells were also present, which are usually seen in the rheumatic heart disease valvular histology (**Figure 7C**).

Immediate post-operative echocardiography revealed a mechanical prosthetic AV without regurgitation. The mean pressure gradient was 23 mmHg with a velocity ratio was 0.54. The LVEF was normal and unchanged. The patient did well with post-op recovery and has followed-up at the cardiology clinic for 9 months without complications.

Discussion

This patient presented with acute on chronic heart failure due to severe AR resulting from RA-VHD. Although the possibility of age-related VHD and a prior infective endocarditis were entertained as possible etiologies of the valvular destruction, the gross examination, microbiologic testing, and histologic features of excised native AV leaflets favored RA-VHD. Homogenous valve nodules [3] and fibrinoid necrosis [6], as seen in our patient, have been described as distinctive features of RA-VHD. Libman-Sacks endocarditis was considered less likely in the absence of obvious vegetations and/or supporting clinical scenario. In this case, persistently elevated inflammatory markers, histologic features and absence of other possible etiology helped confirm the relationship between RA activity and acute aortic insufficiency. In addition, the calculated clinical disease activity scores using the DAS28 for ESR and CRP were 6.2 and 5.8 respectively. These scores indicate high disease activity.

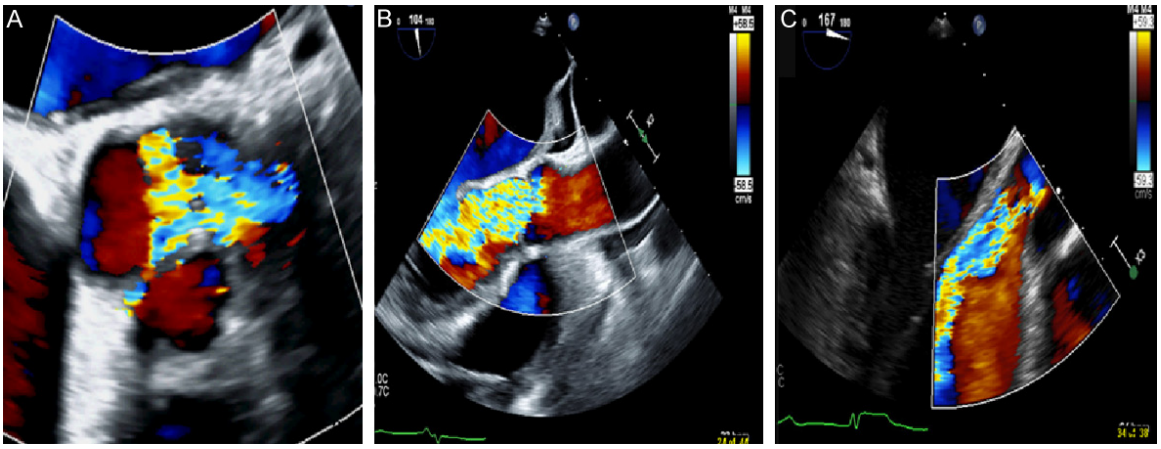

Figure 5. A. SAX on TEE of AV in diastole at 0 degrees in the upper esophagus with color flow doppler. B. TEE of AV in diastole with CFD at 104 degree angle displaying AR of the non-coronary cusp. C. TEE of AV in diastole with CFD at 167 degree angle displaying AR of the non-coronary cusp.

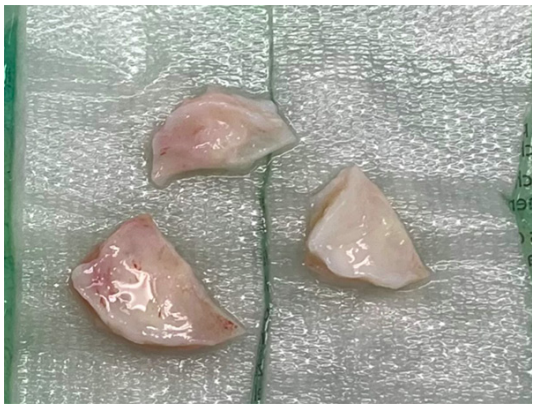

Figure 6. AV leaflets displaying significant destruction and nodular thickening.

RA-VHD manifesting with mild valvular insufficiency is common [3], although symptomatic severe or acute VHD is an infrequent occurrence in this population. Most patients with RA-VHD have chronic progressive valvular insufficiency due to slowly progressive valvulitis that occurs within several months to years [5]. Our patient is a rare case in which the inflammation of the cardiac valves progressed to the acute phase within approximately 2.5 weeks. She was successfully managed with a SAVR using a mechanical prosthetic valve. We speculate that chronic inflammation in RA patients contributes to the progressive valvular damage and regurgitation. Although data are limited, some studies have not demonstrated correlation between VHD and clinical, laboratory, or therapeutic variables of RA [1, 3, 4, 8, 9] (**Table 1**). Anitschkow cells, large macrophages characterized by a 'caterpillar-like' or 'owl-eye' chromatin pattern of the nucleus was also seen in the histology of this patient. Anitschkow cells, first described by von Opel in 1901, where later further characterized in cardiac tissue by Nikolay Anitschkow (or Anichov) in 1913 [2].

Although Anitschkow cells and Aschoff bodies are more commonly associated with rheumatic heart disease, this cell pattern is not specific for rheumatic heart disease. Whereas the pathology of rheumatic VHD is associated with an autoimmune process triggered by infection with group A streptococci, RA-VHD occurs due to the innate autoimmune pathology of rheumatoid arthritis. The process by which the valvular destruction occurs in RA-VHD and rheumatic VHD are initiated by completely different processes, without infection being the nidus for RA-VHD pathology. In a study by Whebens and colleagues, vesicular nuclei displaying an Anitschkow chromatin pattern were the predominant cell type in fetal and neonatal myocardium. A similar pattern was also observed in laryngeal cartilage of fibrous tissue of the fetal tissue, leading the investigators to conclude the Anitshckow pattern probably indicates cellular immaturity rather than a specific cell type [10].

Conclusion

Although RA-VHD is more common than previously thought, severe symptomatic or acute

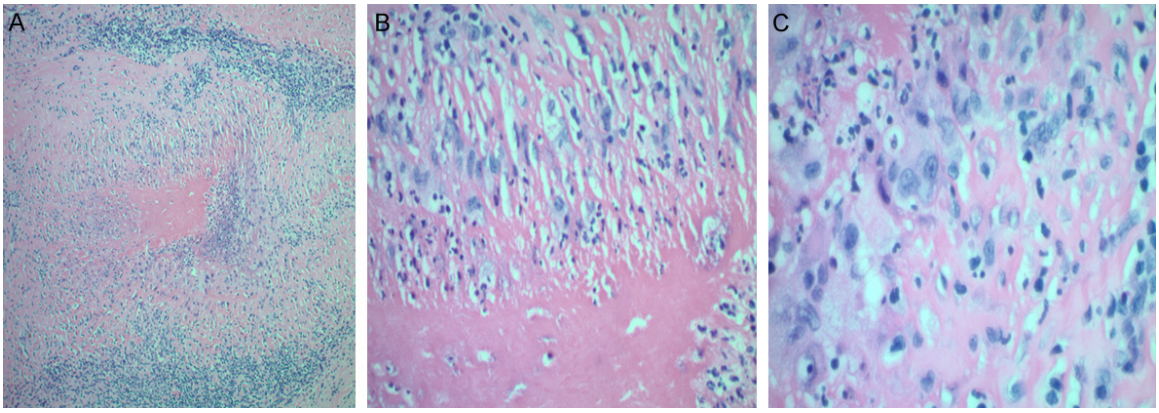

Figure 7. A. Histology of the AV left coronary cusp displaying granulomas with necrotic foci and central fibrinoid necrosis (40×). B. Histology AV tissue with central area of fibrinoid necrosis with surrounding plasma cells, lymphoid, and Anitschkow cells (100×). C. Histology of AV Anitschkow cells (black arrows) (400×).

Table 1. Summary and discussion of main findings of similar previous studies

Ref*	Findings	Comments
1	Granulomatous and nonspecific aortic valvulitis due to rheumatoid arthritis is often clinically and macroscopically indistinguishable from rheumatic valve lesions. The aortic valvulitis may culminate in significant hemodynamic abnormality	Our case similarly highlights granulomatous aortic valvulitis resulting to acute on chronic heart failure
3	RA-VHD is common. Cardiac valve nodules and thickening are its distinctive features, and it is not associated with clinical variables of RA	Our patient had persistent long-standing elevation of clinical variables of RA. Gross imaging of aortic valvular leaflets revealed nodular thickening
4	Involvement of the mitral valve is extremely common in RA-VHD. Nodular thickening of mitral and aortic valve leaflets was noted	We did not note any gross or hemodynamically significant mitral valve lesion in our patient
6	RA-VHD with high seropositive rheumatoid factor resulting to severe aortic valve regurgitation and significant stenosis requiring valve replacement	Similarly, our case highlights severe aortic valve regurgitation in a patient with RA and persistently high seropositive rheumatoid factor
8	Echocardiographic evidence of valvular heart abnormalities in patients with RA-VHD is more common with nodular RA when compared to non-nodular RA	Although our case highlights nodular thickening of the aortic valve leaflets, our study did not compare findings between nodular and non-nodular RA
9	Cardiac involvement in patients with RA did not result to any clinically significant diagnosis, heart failure or constrictive pericarditis, over a follow-up period of 4 years. However, non-specific valvular abnormalities were noted	Contrary to the finding in our case, our patient developed RA-VHD with clinically significant heart failure requiring aortic valve replacement

REF* Number corresponds to the referenced article at the end of the manuscript; RA Rheumatoid arthritis; RA-VHD Rheumatoid arthritis-associated valvular heart disease.

VHD requiring surgical intervention is rare. RA-VHD is typically a progressive destructive process, which can eventually lead to valvular regurgitation of varying severity. Clinicians should be aware of this rare etiology of VHD and AR in patients with chronic RA.

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Verbal consent for publication was obtained from patient on the grounds that report does not contain any personal data nor protected health information. The authors confirm that this report does not contain any personal data nor protected health information.

Disclosure of conflict of interest

None.

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