International Journal of the Cardiovascular Academy 3 (2017) 34–37

Contents lists available at ScienceDirect

International Journal of the Cardiovascular Academy

journal homepage: www.elsevier.com/locate/ijcac

Case report

Rheumatic valvulitis – Forgotten, but not gone☆

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ARTICLE INFO

Article history:
Received 1 March 2017
Accepted 8 May 2017
Available online 8 May 2017

ABSTRACT

Acute rheumatic fever is an exceedingly rare condition in the developed world. It is thought to have nearly disappeared in the United States. Through the case of a 41-year-old Caucasian female who presented with progressive dyspnea and symptoms of heart failure, due to subacute rheumatic valvulitis, the importance of multimodality cardiovascular imaging assessment of patients presenting with severe, multi-valvular dysfunction is highlighted. This case also serves as a powerful reminder for clinicians that rheumatic valvulitis should remain in the differential diagnoses for patients with otherwise unexplained severe, multi-valvular dysfunction.

Introduction

Acute or subacute rheumatic fever in adults in the developed world is exceedingly rare, such that most clinicians assessing patients presenting with multi-valvular dysfunction would not even consider rheumatic valvulitis as a differential diagnosis. We report the case of a 41-year-old Caucasian female who developed severe multi-valvular regurgitation as a result of subacute rheumatic valvulitis in the United States. This case serves as a powerful reminder for clinicians that rheumatic valvulitis is an important and relevant condition, which is not yet "*gone, but not forgotten*", but rather "*forgotten, but not gone*".

Case record

A 41-year-old Caucasian female first developed dyspnea on exertion in August 2015. Her relevant medical history includes obesity and chronic rhinitis complicated by post-nasal drip. Her dyspnea was initially attributed to possible asthma and lower respiratory tract infections. A trial of inhaled bronchodilators and antibiotics did not help. By March 2016, she was in New York Heart Association functional class III, becoming short of breath with routine activities of daily living. She also reported four-pillow orthopnea, paroxysmal nocturnal dyspnea and peripheral edema. Echocardiography performed at a local hospital demonstrated severe aortic, mitral and tricuspid regurgitation. N-terminal pro-brain-derived natriuretic peptide was significantly elevated at 14,900 (normal: <125 pg/mL). Erythrocyte sedimentation rate (ESR) was moderately elevated at 50 mm/h (normal: 0–15 mm/h). Serum C-reactive protein (CRP) was mildly elevated at 10.5 (normal: 0–1.0 mg/dL). She was managed with standard heart failure therapies. Her symptom status improved following oral diuretic treatment. At this stage, the patient was referred to our center for further assessment.

On further history, the patient recalled an episode of severe pharyngitis six years ago. She had to take time off work for two days at that time. She did not seek medical attention at that time. The patient did not have a prior history of valvular heart disease. There was also no family history of valvular heart disease or sudden cardiac death. The patient did not use illicit substances. The patient has not had any pharmacological anti-obesity treatment. In particular, she has not taken fenfluramine or dexfenfluramine. An extensive auto-immune screen including lupus anticoagulant, anti-cardiolipin, beta-2 glycoprotein, anti-double stranded deoxyribonucleic acid, anti-nuclear, anti-Smith, anti-Jo-1, anti-Ro, anti-La, anti-ribonucleoprotein, cytoplasmic and peri-nuclear anti-neutrophil cytoplasmic antibodies, and rheumatoid factor, were unremarkable. Serum complement levels were within normal limits. Testing for syphilis and human immunodeficiency virus were negative.

The patient underwent further imaging investigations at our center. Repeat transthoracic echocardiography demonstrated a dilated left ventricle with preserved left ventricular ejection fraction. The mitral valve was abnormally thickened with restricted diastolic opening. There was severe (4+) pan-systolic mitral regurgitation (Fig. 1; Supplementary Videos 1 and 2). The aortic valve was also severely thickened with restricted leaflet opening. There was severe (4+) pan-diastolic aortic regurgitation, associated with significant flow reversal within the upper descending thoracic aorta (Fig. 2; Supplementary Video 3). Additionally, the tricuspid valve was also thickened. There was severe tricuspid regurgitation (Fig. 3). Aortic valve morphology was difficult to appreciate on echocardiography, due to abnormal thickening of the

☆ Peer review under responsibility of The Society of Cardiovascular Academy.
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http://dx.doi.org/10.1016/j.ijcac.2017.05.001

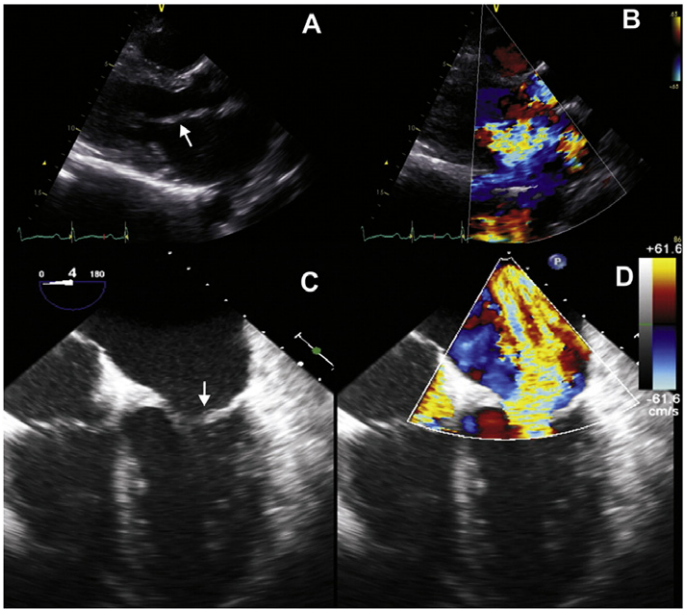

Fig. 1. Abnormally thickened mitral valve leaflets with restricted opening on echocardiography (A: parasternal long-axis view on transthoracic echocardiography; C: mid-esophageal four-chamber view on transesophageal echocardiography; arrows point to thickened mitral valve leaflets). Severe, torrential mitral regurgitation on color Doppler analysis (B: parasternal long-axis view on transthoracic echocardiography; D: mid-esophageal four-chamber view on transesophageal echocardiography).

valve leaflets. Multi-detector cardiac computed tomography (MDCT) demonstrated a thickened trileaflet aortic valve (Fig. 4). Cardiac magnetic resonance imaging (CMR) was performed to exclude pan-aortitis. There were no supportive features of Takayasu arteritis. Significant multi-valvular regurgitation was confirmed by CMR (Fig. 5; Supplementary Videos 4 and 5).

The patient underwent mechanical mitral valve replacement (#25 On-X), mechanical aortic valve replacement (#21 On-X), and tricuspid valve repair (#28 Carpentier Classic annuloplasty ring). At the time of operation, the aortic and mitral valves were found to be severely thickened and retracted. Histological examination of the aortic and mitral valves demonstrated severe fibrosis with neovascularization consistent with post-inflammatory scarring. The gross appearance and microscopic features of the valve pathology were most consistent with rheumatic valvulitis (Fig. 6). Post-operatively, the patient has remained clinically well, in New York Heart Association functional class I. She has been commenced prophylactic antibiotic therapy, as secondary prevention for rheumatic fever. Due to the unusual nature of the patient's presentation, and the rare occurrence of rheumatic fever in adults in the United States, rheumatic fever was not even considered as a differential diagnosis at the time of

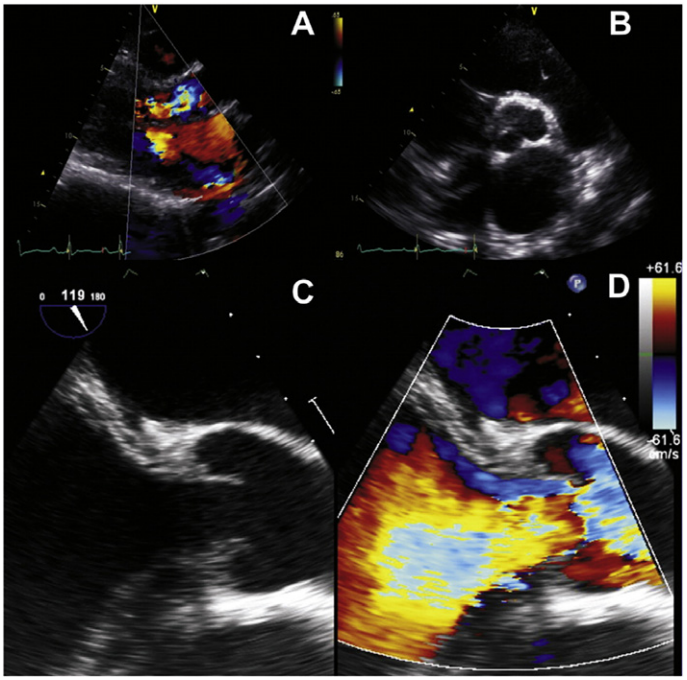

Fig. 2. Severe, torrential aortic regurgitation demonstrated on color Doppler analysis (A: parasternal long-axis view on transthoracic echocardiography; D: mid-esophageal long-axis view on transesophageal echocardiography). Aortic valve leaflets were abnormally thickened (C: mid-esophageal long-axis view on transesophageal echocardiography), however, the morphology of the aortic valve was rather difficult to appreciate on echocardiography (B: parasternal short-axis view on transthoracic echocardiography).

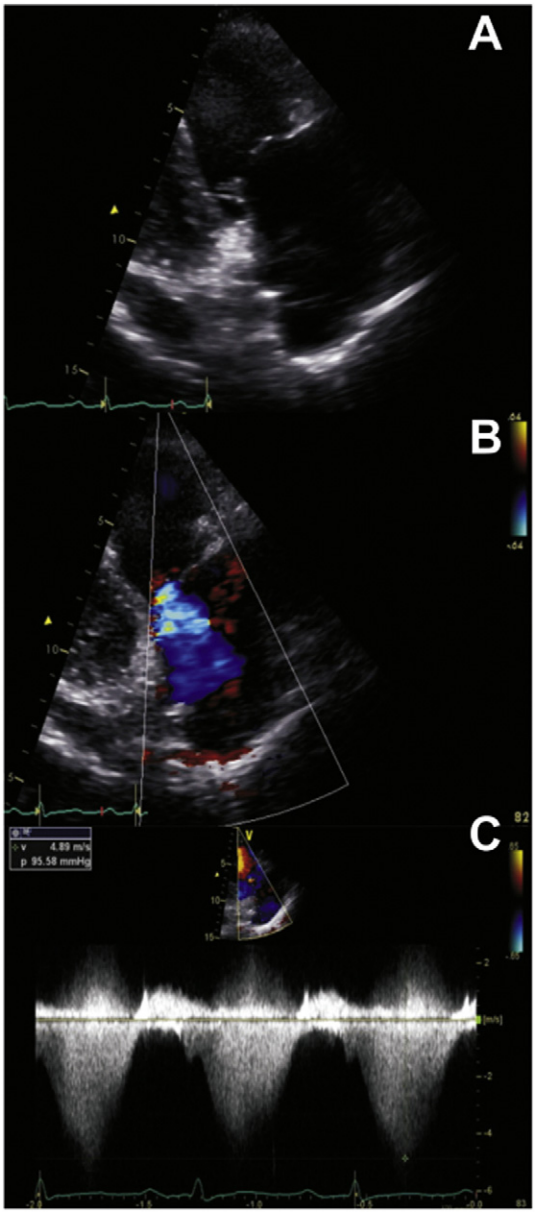

Fig. 3. Mildly thickened tricuspid valve leaflets (A: right ventricular inflow view on transthoracic echocardiography), with significant tricuspid regurgitation (B: color Doppler analysis in right ventricular inflow view on transthoracic echocardiography). Estimated right ventricular systolic pressure was severely elevated (C: continuous wave Doppler recording through tricuspid regurgitant signal in right ventricular inflow view on transthoracic echocardiography).

initial clinical assessment. Six weeks post-operatively, the patient underwent serum anti-Streptolysin O titer and anti DNAse B titer testing. At that stage, her serum anti-Streptolysin O titer was 88 (normal range: 0–530 IU/mL). Her anti DNAse B titer was 165 (normal range: 0–300 U/mL).

Discussion

We report a case of subacute rheumatic valvulitis causing severe aortic, mitral and tricuspid regurgitation in a 41-year-old Caucasian female in the United States. Nowadays, acute rheumatic fever is an exceedingly rare condition in the developed world, and is thought to have nearly disappeared in the United States.[1] To the best of our knowledge, this is the first reported case of rheumatic valvulitis in an adult in the developed world in recent English literature. The global incidence of acute rheumatic fever in children between 5 and 14 years of age is estimated at 300,000 to 350,000 per year.[2] The diagnosis of rheumatic fever can be made using the revised Jones criteria.[3] In low-risk populations, the diagnosis can be made with two major manifestations (carditis, arthritis, chorea, erythema marginatum, subcutaneous nodules), or one major and two minor criteria (polyarthralgia, fever, elevated ESR and/or CRP, prolonged PR interval).[3] The most recent rheumatic fever outbreak in the pediatric population in the United States was due to isolates of the rheumatogenic group A streptococcus M-type in Utah in 1998.[4] The fundamental pathophysiology of rheumatic fever results from molecular mimicry between group A streptococcal antigens and host antigens, in a genetically susceptible host with an abnormal host immune response.[2] However, the specific mechanisms that render each individual host susceptible to developing rheumatic fever are less clear. Even though the patient's serum anti-Streptolysin O and anti DNAse B titers were within the normal range, the tests were performed post-operatively, and it is very likely that the elevated titers may have normalized. The extensive negative auto-immune screen, the history of preceding severe pharyngitis six years ago, the unusual echocardiographic findings of abnormally thickened valves with severe regurgitation, the rheumatic appearance of the aortic and mitral valves at the time of operation, and the severe fibrosis with post-inflammatory scarring on histological examination of the valves, lend support to rheumatic valvulitis being the etiology of the patient's multi-valvular dysfunction.

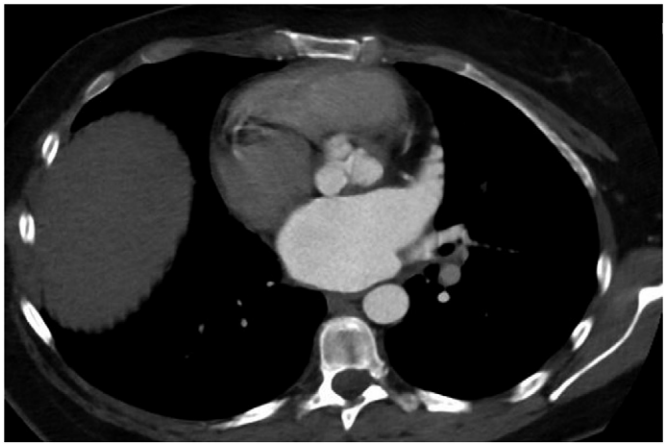

Fig. 4. The morphology of the aortic valve was well demonstrated to be trileaflet on multi-detector computed tomography (contrast-enhanced axial image).

This case is a powerful reminder for clinicians, highlighting the fact that rheumatic valvulitis, although exceedingly rare in the developed world, should still be considered as an etiology for otherwise unexplained severe multi-valvular dysfunction. The comprehensive management of rheumatic valvulitis should incorporate multi-modality cardiovascular imaging assessment, appropriate medical and surgical management of valvular dysfunction, and long-term secondary antibiotic prophylaxis.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijcac.2017.05.001.

Funding source

None.

Conflict of interest statement

The authors have no conflicts of interest to declare.

Acknowledgements

None.

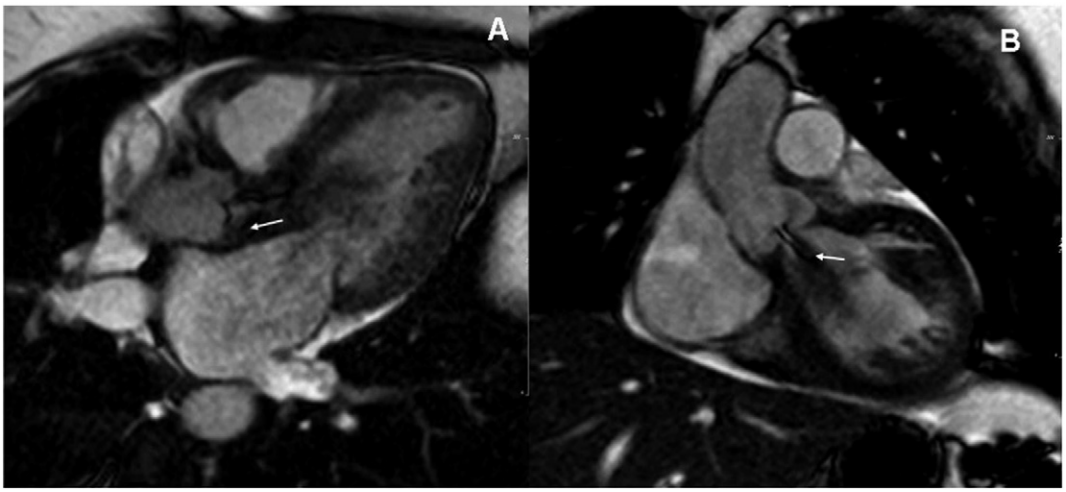

Fig. 5. Cardiac magnetic resonance imaging confirmed the presence of severe aortic regurgitation, represented by signal dephasing (arrows; A: axial image through the left ventricular outflow tract on the steady-state free precession sequence; B: oblique image through the left ventricular outflow tract on the steady-state free precession sequence). There was no evidence of Takayasu's arteritis on cardiac magnetic resonance imaging.

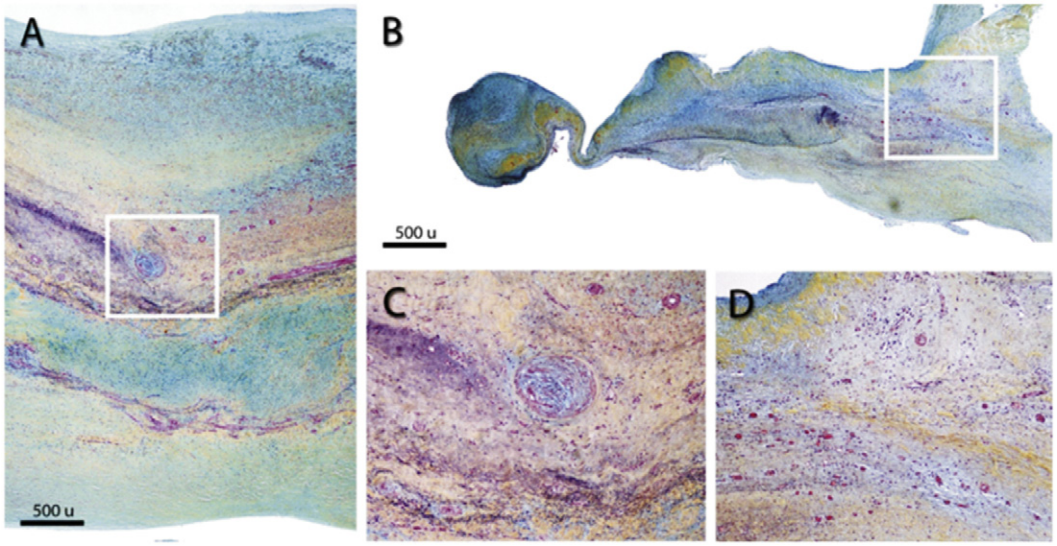

Fig. 6. Histologic sections of the mitral (A) and aortic valves (B) stained with Movat pentachrome shown in the same scale demonstrated fibromyxoid thickening of the leaflets which was more severe in the mitral valve. The boxed areas in A and B are shown in higher magnifications in C and D, respectively. In addition to the fibrosis (yellow material), there was proliferation of numerous small vessels as a result of valvulitis.

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