

## CASE REPORT

# Lone Aortic Insufficiency and Conduction Disease: A Marker of Reactive Arthritis

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A 48-year-old male with history of chronic arthritis and uveitis presented with 1 year of progressively reduced exercise capacity and nonexertional chest pain. Physical examination was consistent with severe aortic insufficiency. An electrocardiogram demonstrated sinus rhythm with first degree atrioventricular block. Transthoracic and transesophageal echocardiography demonstrated severe lone central aortic insufficiency of a trileaflet valve due to leaflet thickening, retraction of leaflet margins and mild aortic root dilation in the setting of left ventricular dilatation. In addition, computed tomographic angiography revealed a small focal aneurysm of the distal transverse arch. He was found to be positive for the immunogenetic marker HLA-B27. The patient subsequently underwent uncomplicated mechanical aortic valve replacement. The diagnosis of HLA-B27 associated cardiac disease should be entertained in any individual with lone aortic insufficiency, especially if accompanied by conduction disease. (Echocardiography 2014;00:1–4)

**Key words:** reactive arthritis, Reiter's syndrome, HLA-B27, aortic insufficiency

## Case Report:

A 48-year-old man with reported history of rheumatic heart disease, recurrent joint pain and uveitis presented with progressive exertional dyspnea over the past year and a 1-month history of nonexertional chest pain. His exercise tolerance had recently decreased to less than 1 city block. The physical examination was notable for a wide pulse pressure (130/50 mmHg), a systolic ejection murmur (without ejection click) radiating to the clavicles, and a soft early diastolic decrescendo murmur radiating down the left sternal border. Furthermore, the Corrigan pulse and the Quincke sign were present.

Transthoracic echocardiography revealed severe central aortic insufficiency with left ventricular dilatation (end-diastolic diameter 6.0 cm), no right or left ventricular wall motion abnormalities and a left ventricular ejection fraction of 55%. The aortic valve was trileaflet and the aortic root was mildly dilated (4.1 cm at the level of

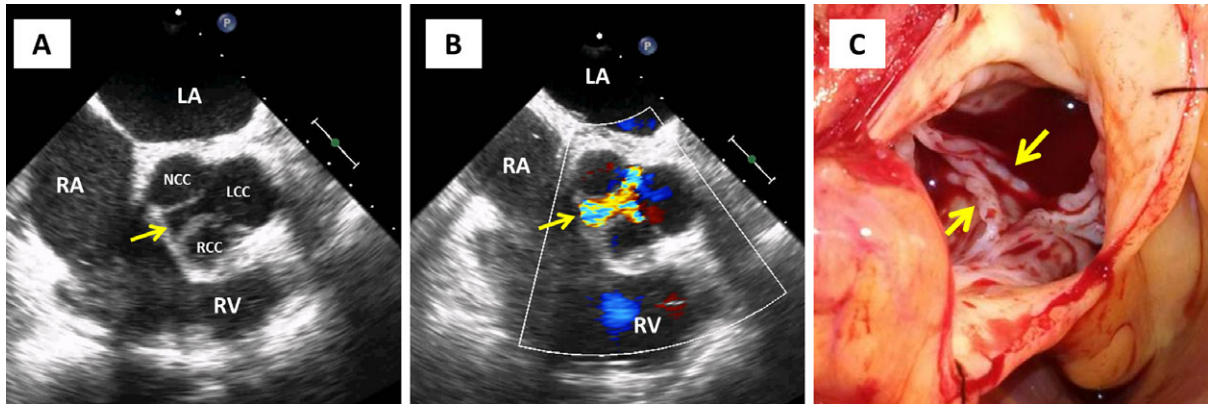
sinuses of Valsalva). The leaflet margins were thickened and retracted; however, aortic valve calcification, commissural fusion and stenosis were absent. There were no other significant echocardiographic findings (Fig. 1, movie clips S1 and S2).

An electrocardiogram demonstrated normal sinus rhythm with first degree atrioventricular block and left ventricular hypertrophy. Computed tomographic angiography (GE Healthcare, Fairfield, CT, USA) demonstrated focal dilatation at the junction of the distal transverse arch and the proximal descending thoracic aorta with a largest diameter 3.9 cm, as well as focal calcification and thickening of the aortic wall, consistent with aortitis (Fig. 2).

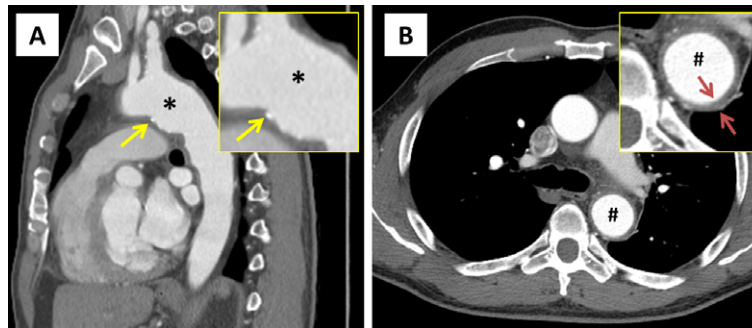
There was no clinical or serologic evidence of prior syphilis. Thereafter, a clinical diagnosis of reactive arthritis (Reiter's syndrome) was established and he was found to be positive for the immunogenetic marker HLA-B27.

Because of severe symptomatic aortic insufficiency, the patient was referred for surgery (Fig. 3); he underwent uncomplicated mechanical aortic valve replacement (St. Jude Medical, St Paul, MN, USA). He has subsequently returned to an active lifestyle.

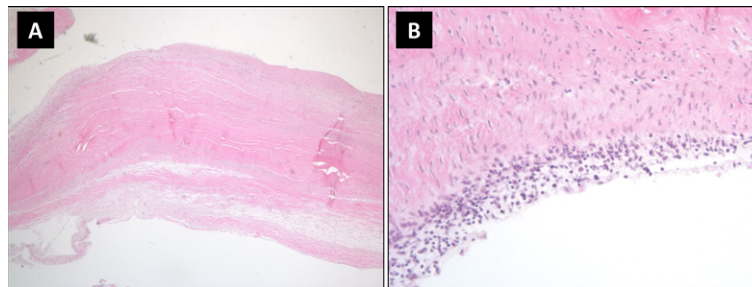
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**Figure 1.** Echocardiographic and surgical findings. **A.**, **B.** demonstrate the short-axis view of the abnormal aortic valve on a transesophageal echocardiogram. The aortic leaflets are thickened and retracted giving rise to a central regurgitant orifice (arrow). (Movie clips S1 and S2 correspond to these panels.) **C.** Surgical view of the aortic valve from the ascending aorta perspective of the aortic valve that corresponds to echocardiographic images in (**A** and **B**). Note the leaflet thickening and rolled leaflet margins (arrows). LA = left atrium; LCC = left coronary cusp of the aortic valve; NCC = noncoronary cusp; RA = right atrium; RCC = right coronary cusp; RV = right ventricle.



**Figure 2.** Computed tomography. **A.** Sagittal view of a contrast-enhanced computed tomographic image which shows a focal aneurysm of the distal aortic arch (asterisk), and calcification of the aortic wall (arrows). **B.** Demonstrates an axial view of descending thoracic aorta (#) with circumferential thickening of the aortic wall (arrows).



**Figure 3.** Histopathology of aortic valve. **A.**, **B.** Photomicrographs of hematoxylin-eosin stained sections of surgically explanted native aortic valve. **A.** Demonstrates nonspecific aortic leaflet thickening with myxoid degeneration (10× magnifications). **B.** 40× magnification reveals a nonspecific inflammatory infiltrate.

**Discussion:**

The case illustrates characteristic cardiovascular manifestations of reactive arthritis: a combination of lone central aortic regurgitation and cardiac conduction delay. Reactive arthritis, previously

referred to Reiter’s syndrome, is a microbial infection-triggered autoimmune disorder typically presenting with a triad of urethritis, arthritis, and uveitis. Many spondyloarthropathies including reactive arthritis, ankylosing spondylitis, and

psoriatic arthritis are commonly associated with the immunogenetic marker HLA-B27.

In 1936, the Boston-trained pathologist Tracy Mallory (brother of Kenneth Mallory of the Mallory–Weiss syndrome) was the first to report an association between aortic insufficiency and the spondyloarthropathies.<sup>1</sup> Subsequently, a combination of lone aortic insufficiency (not associated with aortic stenosis) and atrioventricular conduction defects has been characterized as HLA-B27-associated cardiac disease.

An autopsy series<sup>2</sup> and later echocardiographic studies<sup>3,4</sup> have shown that aortic valvular abnormalities can be detected in a substantial proportion of spondyloarthropathy patients without evidence of overt cardiac disease. Case series suggest that aortic insufficiency is present in 2% to 10% of patients with ankylosing spondylitis.<sup>5,6</sup> The prevalence of aortic insufficiency among patients with other rheumatoid factor negative spondyloarthropathies such as Reiter's syndrome is less clear. A relationship between the duration of the arthropathy and the likelihood of aortic insufficiency has been suggested.<sup>7</sup> However, lone aortic insufficiency has been described in HLA-B27 positive individuals in the absence of typical clinical rheumatic or ocular manifestations.<sup>8</sup>

Dilation of the aortic root, fibrotic thickening, downward retraction of the bases of the cusps, and inward rolling of the cusp margins are the primary causes of HLA-B27 associated aortic insufficiency as seen in our patient.<sup>9,10</sup> Notably, there is a lack of associated aortic stenosis. While involvement of the aortic root has been most commonly reported, involvement of more distal segments of the aorta, as in our patient, has also been described.<sup>11</sup> Computed tomography or magnetic resonance imaging can be helpful for evaluating the entire aorta and its branch vessels.

Since the 1940s, atrioventricular conduction blocks have been associated with the rheumatoid factor negative spondyloarthropathies and are recognized as the most common cardiac manifestation of these diseases. In a 1949 electrocardiographic study of 190 patients with ankylosing spondylitis, the prevalence of first- and third-degree atrioventricular block was 15% and 1.6%, respectively.<sup>12</sup>

Subsequently, atrioventricular, and intraventricular blocks were identified in 33% of ankylosing spondylitis patients followed up for 25 years.<sup>13</sup> This study was unique in that it emphasized the intermittent nature of conduction disease in these patients, supporting the involvement of a reversible inflammatory process (as opposed to fibrosis) in its causation. Furthermore, up to 20% of male patients with permanent pacemakers may have bradycardia related to an HLA-B27 associated pathology.<sup>14</sup>

In summary, the diagnosis of HLA-B27 associated cardiac disease must be entertained in any individual with lone aortic insufficiency, especially if accompanied by conduction disease. HLA-B27 cardiac disease may be dramatically underdiagnosed as cardiac manifestations may be present when characteristic rheumatologic or ocular findings are absent.

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## Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Movie clip S1.** Transesophageal echocardiogram of aortic valve in short axis. This movie clip corresponds to Figure 1A and B. It demonstrates the short axis of the aortic valve (asterisk) severe lone aortic regurgitation due to leaflet thickening, retraction of leaflet margins and mild aortic root dilation.

**Movie clip S2.** Transesophageal echocardiogram of aortic valve in long axis. This movie clip demonstrates the long-axis view of the aortic

valve with pathologic findings as described for movie clip S1. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.