

CASE REPORT



Large endocardial rheumatoid nodules: a case report and review of the literature

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ABSTRACT

Rheumatoid nodules occur frequently in patients with rheumatoid arthritis and are the most common cutaneous manifestation of the disease. Although uncommon, rheumatoid nodules may also occur on cardiac valves, where they may be large and clinically significant. They may embolize and cause stroke. They may cause regurgitant murmurs, or they may result in valvular destruction. Echocardiographically, they may mimic an atrial myxoma or appear as a vegetation. We present a patient with seronegative rheumatoid arthritis who developed an acute embolic stroke; he had peripheral stigmata of infective endocarditis on physical examination and echocardiography revealed a mitral valve vegetation. We illustrate that these findings were due to a large, highly destructive mitral valve rheumatoid nodule. We review the literature on macroscopic endocardial nodules and emphasize their diverse clinical behavior.

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Endocarditis; rheumatoid nodule; embolic stroke



1. Case report

A 56-year-old man was emergently seen and evaluated within 1 h of acute right-sided hemiplegia and dysarthria. The patient had been diagnosed 2 years earlier with seronegative rheumatoid arthritis (RA). Prior treatment of the patient's arthritis included daily low-dose prednisone and weekly methotrexate. He continued this regimen for approximately 18 months, but was lost to follow-up with his rheumatologist 9 months before this acute presentation, and had been off methotrexate during that interval. His past medical history also included gout, diabetes mellitus, hypertension, and chronic kidney disease. The patient developed end-stage renal disease due to diabetes and hypertension; 1 week earlier he had undergone placement of a peritoneal dialysis catheter and had begun peritoneal dialysis.

Physical examination was significant for a previously undocumented grade 2/6 holosystolic systolic murmur at the apex. Splinter hemorrhages could be seen on multiple fingers bilaterally. The patient was afebrile. There were no cutaneous rheumatoid nodules at that time. Neurological examination demonstrated weakness and diminished sensation to light touch in the right upper and lower extremities, right lower facial droop, dysarthria, and right homonymous hemianopsia. The patient's National Institutes of Health stroke scale was determined to be 6, but spontaneous improvement in symptoms precluded the use of fibrinolytic therapy.

Subsequent neurological work-up included a normal non-contrasted head computed tomography scan and carotid Doppler. Magnetic resonance imaging of the brain without contrast revealed an acute left parietal stroke with inferior extension to the parietotemporal junction. Transthoracic echocardiography revealed a large 2.0 × 1.2 cm vegetation on the posterior leaflet of the mitral valve (Figure 1). Culture-negative endocarditis was the working diagnosis. Laboratory data included numerous, consistently negative blood cultures, and negative blood cultures for fungi and acid-fast bacilli. *Brucella* and *Coxiella* antibodies were negative. Erythrocyte sedimentation rate and C-reactive protein were elevated at 99 mm/h and 3.8 mg/dl, respectively. Antinuclear antibodies, anti-histone antibodies, rheumatoid factor, and anti-cyclic citrullinated peptide antibodies were negative.

Given the high risk of further embolization, the patient underwent mitral valve replacement with a mechanical St. Jude valve. Intraoperatively, a severely damaged posterior mitral valve leaflet with areas of calcification was found. No infectious organisms were visualized microscopically. Cultures of the removed tissue were negative for bacteria and fungi. The patient's cardiac histopathology was examined by two separate pathologists at different institutions, both of whom concluded that the mitral valve had central necrosis with palisading histiocytes, fibrosis, calcifications, and giant cells – findings compatible with a rheumatoid nodule (Figure 2) [1]. It was also noted that disruption of the

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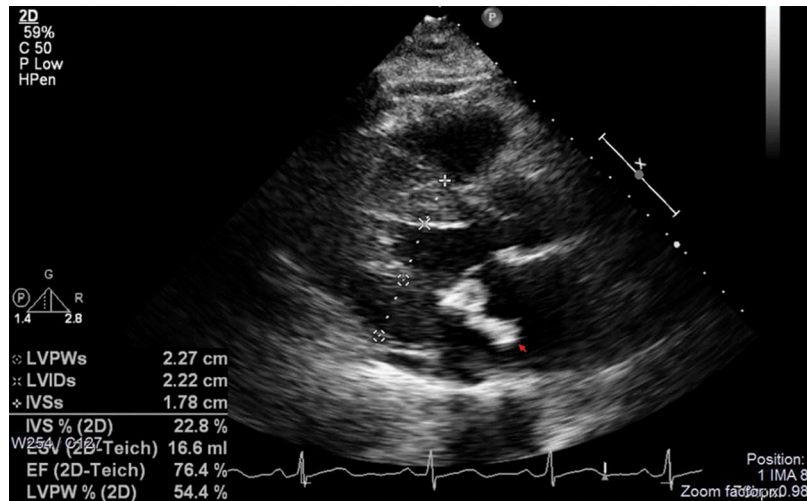


Figure 1. Transthoracic echocardiography revealing a 2.0 × 1.2 cm vegetation on the posterior leaflet of the mitral valve (arrow).

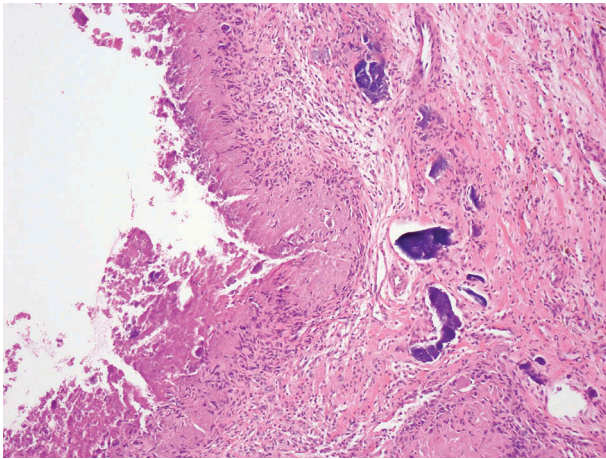


Figure 2. Histopathology of the mitral valve stained with hematoxylin and eosin (10 × magnification), revealing features that are diagnostic for a rheumatoid nodule, including central necrosis, palisading histiocytes, and adjacent fibrosis. The presence of calcium is indicative of underlying valve disease in this patient with end-stage renal disease.

surface without associated thrombus was suggestive that a portion of this rheumatoid nodule had embolized.

The clinical course was complicated by prolonged mechanical ventilation. The patient was finally able to be discharged to a skilled facility after a 23 day hospitalization, where he continued to improve and was ultimately discharged home. The patient again presented to our institution 16 months later with pyogenic arthritis and was found at that time to have two painless cutaneous lesions on his left upper extremity, each measuring 3 × 3 cm. These were compatible with rheumatoid nodules, but were not biopsied.

2. Discussion

Cardiac rheumatoid nodules are a rare but well-documented manifestation of RA. Histologically, the

nodules are indistinguishable from the subcutaneous nodules occurring at pressure sites or over extensor surfaces. Bennett, Zeller, and Bauer [2] first described a pericardial ‘fibrinoid granuloma’ by histological analysis in 1940. Rosenberg and colleagues identified microscopic cardiac rheumatoid nodules in 5% of patients in the following year and subsequent studies confirmed those observations [3–5]. Importantly, these findings occurred predominantly in asymptomatic patients and were post-mortem findings.

Large, clinically symptomatic rheumatoid nodules of the heart have not been widely reported. There are no published series illustrating the clinical presentations of symptomatic cardiac rheumatoid nodules. Table 1 displays a literature search of the reported cases of macroscopic rheumatoid nodules leading to symptomatic disease and medical evaluation [6–12].

The patients’ ages ranged from 41 to 78 years, with roughly equal percentages of men and women. All but one patient had a history of RA, with the majority having had the disease for longer than one decade. The mitral valve was more commonly affected (four cases) than the aortic valve (two cases). The clinical presentations were varied and included embolic phenomena, valvular dysfunction, atrial myxoma, and presumptive infective endocarditis. Echocardiography readily identified the abnormalities, and the descriptive interpretation utilized ‘vegetation’ or ‘tumor’ to describe the lesions. Six of the seven cases recorded the size of the nodules, and all were greater than 1 cm in greatest dimension by echocardiography. Actual identification of the presumed cleavage site of a mitral valve nodule is a unique feature of our case. Figure 1 illustrates the classic histopathology of intracardiac rheumatoid nodules.

The presence of subcutaneous nodules in patients with RA has previously been shown to be

Table 1. Reported cases of cardiac rheumatoid nodules on gross examination.

Clinical report	Age (years), gender	Clinical course of RA	Clinical presentation	Type/size of valvular or endocardial involvement
Suriani et al. (1994) [11]	78, F	10 year history of steroid-dependent RA	Symptomatic aortic stenosis; incidental intracardiac mass at surgery	Nodule on left atrial free wall; 1.2 × 1.0 cm
Webber et al. (1995) [12]	62, F	'Severe, deforming' seropositive RA of unknown duration	Suspected infected atrial myxoma	Pedunculated nodule of the posterior mitral valve annulus; 0.75 × 1.24 cm
Mounet et al. (1997) [10]	65, F	10 year history of seropositive RA	Embolic stroke secondary to intracardiac tumor	Nodule of posterior mitral valve leaflet and ventricular wall; 5 × 2 × 2 cm
Chatzis et al. (1999) [7]	41, M	No previous RA history	Aortic valve endocarditis and embolic stroke	Bicuspid aortic valve; 1 cm nodule
Chand et al. (1999) [6]	74, M	'Long-standing history of nodular, erosive RA'	Symptomatic aortic regurgitation	Grossly apparent nodules on each of the aortic valve leaflets
Kang and Baron (2004) [9]	70, M	20 year history of seropositive RA; cutaneous nodules present	Stroke and peripheral arterial embolism	Pedunculated nodule on posterior mitral valve leaflet; 1.2 × 1.5 cm
Giladi et al. (2008) [8]	56, M	16 year history of seropositive RA without cutaneous nodules	Recurrent TIAs with possible endocarditis	Nodule of anterior mitral valve leaflet; 1.4 × 1.0 cm

RA, rheumatoid arthritis; F, female; M, male; TIA, transient ischemic attack.

associated with systemic manifestations such as pleurisy, interstitial pneumonitis, or Felty's syndrome, but a clear correlation between subcutaneous nodules and intracardiac nodules could not be identified in this case series [13]. Three patients in the case reports had subcutaneous rheumatoid nodules on initial physical examination. Another three patients were explicitly stated to have lacked these nodules, and one report made no mention of their presence or absence.

One of the unusual and surprising features of our case is the seronegativity of the patient's rheumatoid disease in the face of a valvular rheumatoid nodule. Our review identified only one other case of seronegative RA with valvular nodules [7]. The overwhelming majority of these reported cases were seropositive, as such intracardiac lesions often comprise rheumatoid factor among other immune complex deposits.

While intracardiac rheumatoid nodules have been described repeatedly over the past century, the incidence of these macroscopic lesions is being increasingly recognized. Although still an uncommon entity, these often large and clinically relevant nodules should be considered in the differential diagnosis of any rheumatoid patient having vegetation or tumor found on echocardiography in the setting of embolic manifestations.

Disclosure statement

No potential conflict of interest was reported by the authors.

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