Editorial

When Giant Cell Myocarditis Affects Only the Atria

Cristina Basso, MD, PhD; Gaetano Thiene, MD, FRCP

In this issue of Circulation, Larsen et al report a new variant of giant cell myocarditis (GCM) with lone involvement of the atria and preserved left ventricular function. The diagnosis was supported not only by histology but also by cardiac magnetic resonance imaging showing atrial dilatation and wall thickening with marked edema, sparing the ventricles. The isolated atrial involvement was implicated as a cause of atrial fibrillation.

The source of the atrial myocardial tissue for histological diagnosis of GCM was endomyocardial biopsy, surgery during maze procedure or valve intervention and bypass grafts, and autopsy. The distinctive histopathologic feature was the observation of giant cells and lymphocytic inflammatory infiltrates associated with cardiomyocyte necrosis, in the absence of caseous or noncaseous granulomas with epithelioid cells.

This peculiar entity was sporadically reported in the past as case reports, which are summarized altogether with the new observations in the form of review of the literature.1 Atrial GCM is a novelty in the field of myocarditis, and the authors should be congratulated for their elegant contribution.

GCM is an ominous life-threatening inflammatory cardiomyopathy with a severe prognosis. GCM is also known with the eponym of Fiedler myocarditis, since Schmorl (as reported by Saphir),11 by reviewing the original hearts of the patients described by Fiedler and reported as isolated interstitial myocarditis, observed the presence of numerous giant cells. When GCM involves the ventricles, as usual, the clinical scenario is often that of cardiogenic shock attributable to abrupt pump failure, leading frequently to death unless averted by urgent intervention with ventricular assistance device or cardiac transplantation. The disease may even recur with a fatal outcome after transplantation.12

Fortunately, the atrial variant of GCM appeared to be benign in this series reported by Larsen et al. All 5 surviving patients, after treatment with corticosteroids and cyclosporine, returned to normal life after 1 to 4 months of follow-up; in 1 patient, who had a postmortem diagnosis, the cause of death was unrelated to GCM.

The study raises some concerns which deserve consideration. Although the authors claim atrial GCM as a distinctive clino-pathological entity, evidence of isolated atrial involvement is given by certainty only in 2 cases; 1 of them has a spectacular cardiac magnetic resonance, demonstrating marked isolated edema of the atrial walls and septum at the onset of the disease and isolated atrial fibrosis after treatment with high-dose corticosteroids and cyclosporine. The remaining cases did not have confirmation by cardiac magnetic resonance or histology that the ventricles were spared. Several patients had comorbidities that can explain atrial dilatation, such as valve and ischemic heart disease.

Only histology and immunohistochemistry investigation were carried out. GCM is known to be usually a noninfective heart muscle disease, most probably an autoimmune disorder, although autoantigens remain poorly defined. However, molecular biology techniques are mandatory in each case of myocarditis for differential diagnosis between infectious and noninfectious forms, particularly with tuberculosis and syphilis. Of note, poorly formed granulomas were identified in 4 of 6 cases and vasculitis in 1, and both features are not typical of GCM. Endomyocardial biopsy should become a molecular biopsy as recommended in the last Consensus Document of the USA and Europe Cardiovascular Pathology Societies.

The description of imaging by cardiac magnetic resonance supports the capabilities of this technique to identify isolated atrial myocarditis as a cause of atrial fibrillation, whether paroxysmal or persistent. Endomyocardial biopsy of the atrial wall has been proven to be effective in giving the final word and might be considered.13

Eight of the 13 cases (62%) of atrial GCM, including those previously reported in the literature, had evidence of rheumatic heart disease. Two types of myocardial lesions are commonly described in rheumatic fever (ie, a nonspecific myocarditis and a specific lesion characterized by granulomas known as Aschoff nodules, the latter undergoing a cycle of development and resolution; in their mature stage, they contain Aschoff cells which are uni- or multinucleated histocytes). The association between GCM and rheumatic fever has been previously emphasized in the literature, suggesting a common pathogenic mechanism. However, in this series the absence of typical histological features of rheumatic disease, such as Aschoff bodies and Anitschkow cells, the presence of abundant giant cells and cardiomyocyte necrosis, as well as the fact that 5 cases lacked a history of rheumatic disease, support the existence of atrial GCM as a distinct separate entity, probably attributable to atrium-specific autoantigens. The association of isolated atrial GCM with mitral and tricuspid valve regurgitation in this series is of note, confirming that the atrial wall surrounding the atrioventricular anulus is an intrinsic part of the atroventricular valve apparatus, contributing to the sphincter annular contraction.

There are many differences between these cases and classical GCM. The mean age of the patients reported by Larsen et al is higher (>65 years) than the usual GCM involving the...
ventricles, which affect young adult population.7,8 Moreover, the adjective fulminant in medicine means rapid fatal outcome (like a bolt). The term fulminant myocarditis17 would not be appropriate to describe a condition with an apparently benign course. This should not be confused with the report of isolated atrial myocarditis as a cause of sudden death in patients with ventricular preexcitation attributable to accessory bypass myocardial fascicles.19 In this setting, the onset of atrial fibrillation may be harmful insofar as the rapid conduction along with the anomalous pathway may transform atrial fibrillation into ventricular fibrillation at risk of abrupt cardiac arrest.

The atrial myocardium is not regularly sampled either at postmortem examination or in the routine surgical pathology practice.19 The report by Larsen et al1 is a lesson for pathologists and cardiac surgeons. Atrial GCM may be more common than generally believed. Atrial cardiomyopathies and histopathology in general may long have been overlooked and underestimated. Atrial wall specimens should routinely be analyzed both in surgical specimens and in cardiac autopsies, to enhance our knowledge about the contribution of atrial pathology to clinical disease.

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None.

References

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