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High prevalence of viral genomes and multiple viral infections in the myocardium of adults with “idiopathic” left ventricular dysfunction

Purpose: For a long time, enteroviruses have been considered to be the most common cause of acute viral myocarditis (MC), with possible transition from Myocarditis to dilated cardiomyopathy (DCM). Recent investigations have shown, however, that other viruses are also frequently encountered in MC patients, suggesting that persistence of various virus species may play a pathogenic role in the transition from MC to DCM. The purpose of this study was to screen endomyocardial biopsies (EMBs) from patients with “idiopathic” DCM for the presence of viral genomes by using polymerase chain reaction (PCR) to assess the frequency of cardiac viral infections that may be involved in the pathogenesis of the disease.

Methods: EMBs were obtained for PCR analysis from 100 consecutive patients (median left ventricular ejection fraction, 35%; range, 5% to 45%). PCR was performed to detect the genomic sequences of enterovirus (EV), adenovirus (ADV), human cytomegalovirus (HCMV), herpes simplex virus, Epstein-Barr virus (EBV), human herpesvirus 6 (HHV-6), parvovirus B19 (PVB19), influenza A and B viruses and Coxella burnetti. Myocardial inflammation was assessed by histological and immunohistological analyses.

Results: Viral genomes could be amplified from EMBs of 85 (85%) of the 100 DCM patients: EV=25 (25%), ADV=5 (6%), PBV=19-10 (12%), HHV/6/7 =10 (12%), EBV=6 (9%), HCMV=6 (7%), including n= 10 cases (10%) with multiple infections. Active or borderline myocarditis according to the Dallas classification did not exist in any case.

Conclusions: Viral genomes were frequently detected in EMBs of patients with systolic left ventricular dysfunction. Our data suggest that myocardial persistence of various viruses, often presenting as multiple infections, play a role in the pathogenesis of DCM far more frequently than suspected so far.

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Late left ventricular systolic dysfunction in patients with acute myocarditis: echocardiographic and cardiac magnetic resonance predictors

Introduction: Myocarditis is usually a benign disease, but sometimes is associated with early significant left ventricular (LV) systolic dysfunction. Little is known about the predictors for late LV dilatation and dysfunction in these patients. Our study aimed to assess global LV systolic function progress from admission to follow-up in patients admitted with acute myocarditis and describe predictors of LV systolic dysfunction at one year follow-up.

Methods: We included 46 patients (pts) with acute myocarditis admitted from 2007 to 2011 in a tertiary center, in whom cardiovascular MRI was performed during hospitalization for myocarditis diagnosis. LV systolic function was assessed by echocardiography using Simpson method at the time of admission and 12-17 months thereafter.

Results: Moderate to severe LV systolic dysfunction (ejection fraction <45%) was present at admission in 10 pts (22%). These pts had higher levels of B-type natriuretic peptide (472 vs 128 pg/ml, p=0.003), of C-reactive peptide (138 vs 64 mg/dl, p=0.008) and troponin I (51 vs 14 ng/ml, p=0.005) than those with normal or mild LV dysfunction. Moderate to severe LV dysfunction was also associated with symptoms of cardiac failure at admission (30% vs 3%, p=0.034), recurrent chest pain during hospitalization (57% vs 37%, p=0.047) and the presence of pericardial effusion (40% vs 13%, p=0.034). MRI predictors of early significant LV failure were the presence of oedema in T2 weight imaging (63% vs 20%, p=0.031) or late gadolinium enhancement (LGE) in 4 or more myocardial segments (100% vs 44%, p=0.038). Moreover, hospitalization time was longer (10±3 vs 6±1 days, p=0.015). At one year follow-up, the only predictor of persistent LV dysfunction was the LV dysfunction at baseline (p=0.039). Oedema, extension or patterns of LGE at admission were not related with late LV systolic dysfunction.

Conclusions: Moderate to severe LV systolic dysfunction at admission in patients with acute myocarditis was the only predictor to late LV dysfunction. Although cardiac MRI parameters were useful in myocarditis diagnosis, they were not associated with prognosis in our population.

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Clozapine-induced myocarditis: characterisation using case-control design
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Purpose: Myocarditis is a hypersensitivity reaction, typically occurring in the third week after commencing clozapine, the most effective treatment available for schizophrenia. The signs and symptoms of myocarditis are notoriously difficult to distinguish from those associated with initiation of clozapine. A case-control design is commonly used to investigate risk factors, we show that it can be used to identify features which assist in the diagnosis of myocarditis.

Methods: Cases and controls were documented from patients’ medical records. Controls were matched by unit at which clozapine was commenced and approximate start date.

Results: 105 cases and 296 controls met entry criteria. Time to onset for cases was 0-33 days, with 82% developing 14-21 days after commencing clozapine. Almost 90% of cases and controls had tachycardia. Eosinophilia developed in 64% of cases and 30% of controls, but onset among cases was delayed 0-8 days after the peak tachycardia. However, 87% of cases had C-reactive protein (CRP) > 50mg/L and CRP could be raised up to 5 days before the rise in tachycardia. Multivariate regression analysis indicated that the risk of myocarditis increased with increasing age (31% per decade; 95% CI 7-66%), increasing rate of clozapine dose titration (26% per 250mg during days 1-9; 95% CI 2-55%) and concomitant sodium valproate (odds ratio 2.59; 95% CI 1.51-4.42).

Conclusion: Comparison of cases and controls permitted identification of the features of myocarditis, and avoided confounding by features associated with introduction of clozapine. Monitoring for myocarditis should use tachycardia and CRP but not eosinophil counts. Clozapine should be introduced by slow dose titration and sodium valproate is best avoided, if clinically feasible.

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Reversible ventricular dysfunction due to granulomatous myocarditis
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Purpose: Myocardial involvement due to Sarcoïdosis and Tuberculosis (TB) can be progressive and results in severe ventricular dysfunction if untreated. This report characterizes a syndrome of myocarditis with granulomatous mediastinal adenopathy, presenting as reversible LV dysfunction.

Methods: Twelve patients with unexplained LV dysfunction in the absence of obstructive CAD with EKG characteristics of granulomatous myocarditis (conduction abnormalities, IQRS and ventricular arrhythmias) were included in this study. All were subjected to CT chest, CMR and or 18FDG PET-CT and paracardiac lymph nodes were sampled. Biopsied nodes showed non-caseating granulomas in all patients. All patients with evidence of TB were treated with anti-tuberculosis therapy, and the rest were treated as sarcoidosis and were followed up.

Results: Predominantly males (10/12) were affected with mean age of 42 (±11.2) yrs. The mean LVEF at presentation was 36.75 (±10.3) % with a mean LV ESD of 42.1 (±6.5) mm and LV EDD of 50.4 (±6.9) mm. Baseline EKG showed IQRS in 5 (41%) patients and conduction abnormalities in 3 (25%) patients. Eight (66%) patients had VT at presentation or on follow up. Node biopsy was positive for M.TB in 8 patients and 18 FDG-PET CT revealed focal nodal uptake in 7 patients. On a mean follow up of 24 months the mean LVEF significantly improved to 55.25 (±9.9) % with normalization of LV function in 7 (58.3%) patients.

Conclusion: Unexplained LV dysfunction in the presence of EKG abnormalities should be evaluated by further imaging to rule out granulomatous myocarditis.