Mast Cell Inhibition Attenuates Cardiac Remodeling and Dysfunction during Acute Myocarditis in Rat

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Background: Mast cells are powerful producers of multiple cytokines playing a pivotal role in the pathogenesis of various cardiovascular diseases. We aimed to test the hypothesis that mast cell inhibition will attenuate the inflammatory reaction and associated LV remodeling and dysfunction following acute autoimmune myocarditis.

Methods and Results: Rats (n=30) were immunized with porcine cardiac myosin twice at a 7-day interval to establish experimental autoimmune myocarditis. On day 8, animals were randomized into two groups: a treatment group (n=13) receiving cromolyn sodium (CS) (25mg/kg I.P.) and a control group (n=11) receiving an equivalent volume of normal saline (~0.5ml I.P.) as placebo. Transthoracic echocardiography was performed before day 0 and after 20 days of treatment (day 28), showing that CS reduced LV dilatation compared with the control group (change in LV diastolic area: 8±8 vs. 61±14%, p=0.002; change in LV systolic area: 63±29 vs. 154 ±445, p=0.09) and attenuated LV dysfunction as indicated by fractional area change (-13.48±5.757 vs. -26.29±5.931, p=0.14). Cardiac MRI was performed in a subgroup of animals (treatment n=7; control n=5) before day 0 and after 20 days of treatment (day 28), and confirmed the reduction in LV dilatation in the treatment group. Postmortem morphometric analysis and histological examination of the hearts revealed that CS prevented remodeling and destruction of muscle wall by both preserving wall thickness (LV average wall thickness: 2.2±0.08 vs. 1.9±0.09 mm, p=0.03; LV wall area: 43.7±2.2 vs. 37.1±1.4 mm^2, p=0.02) and preventing fibrosis (% of fibrosis out of LV wall area: 8.9±1 vs. 12.3±1.5, p=0.06).

Conclusions: Our findings suggest that mast cells participate in acute inflammation, fibrosis, and the onset of LV remodeling and dysfunction associated with autoimmune myocarditis. The inhibition of mast cell function could be therapeutic option for prevention of the development fibrosis and dilated cardiomyopathy.