Cellular composition of macrophage infiltration in patients with acute decompensation of ischemic HFrEF depending on the diagnosed human herpes virus type 6

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Topic(s):
Diagnostic Methods

Objective: To determine the cellular composition of macrophage infiltration in patients with acute decompensation of ischemic heart failure (ADHF) depending on the diagnosed human herpes virus type 6 (HHV6) antigen expressions in myocardial tissue.

Methods: This open-label, nonrandomized, single-center, prospective trial was registered at clinicaltrials.gov (#NCT02649517) and included 25 patients (84% men, LVEF of 29.17±9.4%) with ADHF. Inclusion criteria were ADHF, not earlier than 6 months after optimal surgery (PCI or/and CABG) and optimal drug treatment for HF according to ESC guidelines. Invasive coronary angiography was performed in all patients to exclude the progression of coronary atherosclerosis. All patients underwent endomyocardial biopsy with immunohistochemically analysis (IHC) for presence of HHV6. Immunohistochemical criteria of myocarditis were at least 14 leukocytes per sq. mm in the myocardium including up to 4 monocytes and 7 or more CD3+ T lymphocytes per sq. mm. Macrophage infiltration in the heart was assessed by double immunofluorescence. CD68 was a marker for the cells of the macrophage lineage, CD80 was considered as M1-like macrophage and CD163, CD206, stabilin-1 were as M2-like macrophage biomarkers. Each area was evaluated in 5 random fields. The 1 patient who did not have IHC was excluded from the analysis.

Results: After IHC, HHV6 antigen expression were detected in 63% (n=15). There were HHV6-positive myocarditis in 42% (n=10) and HHV6-positive patients without myocarditis - 21% (n=5). HHV6-negative myocarditis was identified in 25% (n=6) cases. HHV6-negative patients without myocarditis were founded in 12% (n=3). Group with HHV6-positive myocarditis had a greater number of CD 45 (19.5 [14.0;31.0] & 14.0 [12.0;21.0], p=0.446) and CD 68 (18.0 [14.0;30.0] & 12.0 [9.0;15.0], p=0.075) cells than group with HHV6-negative myocarditis. The number of CD 68 (18.0 [14.0;30.0] & 12.0 [8.0;14.0], p=0.049) and CD 45 (19.5 [14.0;31.0] & 8.0 [7.0;8.0], p=0.003) significantly were differed between groups with HHV6-positive myocarditis and with HHV6-positive patients without myocarditis. The analysis of macrophage infiltrate in the groups showed differences between groups with HHV6-positive myocarditis and HHV6-negative myocarditis only in the number of CD68+/CD80+ macrophages (57.0 [33.0;68.0] & 85.0 [75.5;110.0], p=0.009). Cellular composition of macrophage infiltration is presented in pic. 1.

Conclusions: The incidence of myocardial HHV6 antigen expression was 63% in patients with ADHF. There were HHV6-positive myocarditis in 42% and carriage of HHV6 in 21% in this study. HHV6-positive myocarditis has been associated with a lot of number of CD 45 and CD 68 in myocardial tissue. The predominance of M2-like macrophages was observed in patients with HHV6-positive myocarditis and carriage of HHV6. There were the largest number of CD 68+/CD 80+ macrophages (M1) were detected in patients with HHV6-negative myocarditis.
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