Correlation of human cytomegalovirus infection with inflammatory factor secretion and myocardial cell injury in patients with acute myocardial infarction

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ABSTRACT

Objective: To study the correlation of human cytomegalovirus infection (HCMV) with inflammatory factor secretion and myocardial cell injury in patients with acute myocardial infarction. Methods: A total of 80 patients with acute myocardial infarction who were treated in our hospital between September 2015 and September 2017 were selected as the acute myocardial infarction (AMI) group of the research, and 60 healthy volunteers who received physical examination in our hospital during the same period were selected as the control group of the research. The serum was collected to qualitatively determine HCMV, and quantitatively determine the inflammatory factors and myocardial injury indicators. Results: Serum IL-10 and TGF-β1 levels of AMI group were significantly lower than those of control group whereas IL-1β, IL-6, CD62P, CCL21, CK-MB, cMyBP-C, sLOX-1, Caspase-3 and MDA levels were significantly higher than those of control group; serum IL-10 and TGF-β1 levels of AMI group of patients with HCMV infection were lower than those of patients with non-HCMV infection whereas IL-1β, IL-6, CD62P, CCL21, CK-MB, cMyBP-C, sLOX-1, Caspase-3 and MDA levels were higher than those of patients with non-HCMV infection. Conclusion: Cytomegalovirus infection can promote and aggravate the inflammatory factor secretion and myocardial cell injury in patients with acute myocardial infarction.

1. Introduction

Acute myocardial infarction (AMI) is the coronary thrombosis, local vascular occlusion and blood flow disruption developed from coronary atherosclerosis. In recent years, the study on AMI-related factors has shown that human cytomegalovirus (HCMV) infection is involved in the occurrence and development of coronary atherosclerosis. It has been reported that the cytomegalovirus (CMV) infection rate significantly increases in patients with coronary heart disease angina and acute myocardial infarction, but it is still not clear about the specific influencing mechanism of cytomegalovirus infection on the process of coronary atherosclerotic lesions. The excessive activation of the inflammatory response is an important pathological link throughout all lesion stages of coronary heart disease, and cytomegalovirus can also activate the inflammation through the corresponding pattern recognition receptors, so we speculated that the CMV infection in patients with acute myocardial infarction might activate the inflammatory response to participate in the progression of the disease. In this study, we specifically analyzed the correlation of cytomegalovirus infection with inflammatory factor secretion and myocardial cell injury in patients with acute myocardial infarction.

2. General information and research methods

2.1 General case information

A total of 80 patients with acute myocardial infarction who were treated in our hospital between September 2015 and September 2017 were chosen as the AMI group of the study, all patients were diagnosed with acute myocardial infarction by clinical symptoms, signs, electrocardiography and coronary CTA or coronary angiography, and the patients combined with malignant tumor, chronic inflammatory diseases or autoimmune disease and the...
patients with the history of upper respiratory tract infection within previous 1 month were ruled out. 60 healthy volunteers who received physical examination in our hospital during the same period were chosen as the control group of the study. There were 45 males and 35 females in AMI group, and they were 42-65 years old; there were 33 males and 27 females in the control group, and they were 41-63 years old. There was no significant difference in general data between the two groups.

2.2 Research methods

2.2.1 Cytomegalovirus infection test
5-6 mL of cubital venous blood was collected from AMI group after admission, 5-6 mL of cubital venous blood was collected from control group during physical examination, and the blood was centrifuged to separate serum, and the instructions of HCMV-IgM antibody ELISA kit were followed for qualitative detection of HCMV infection.

2.2.2 Serum index detection
Serum specimens separated in section 1.2.1 were taken, and the illustrations of the ELISA kit were referred for quantitative detection of IL-10, TGF-β1, IL-1β, IL-6, CD62P, CCL21, CK-MB, cMyBP-C, sLOX-1, Caspase-3 and MDA contents.

2.3 Statistical methods
Software SPSS 20.0 was used to input data, the difference in measurement data between two groups was analyzed by t test and P<0.05 showed statistical significance in differences.

3. Results

3.1 Serum inflammatory factor levels and their correlation with HCMV infection
Analysis of serum inflammatory factors TGF-β1 (ng/L), IL-10 (ng/L), IL-1β (ng/L), IL-6 (ng/L), CD62P (ng/L) and CCL21 (μg/L) between the two groups of subjects was as follows: serum IL-10 and TGF-β1 levels of AMI group were significantly lower than those of control group whereas IL-1β, IL-6, CD62P and CCL21 levels were significantly higher than those of control group (P<0.05). Analysis of serum inflammatory factors IL-10, TGF-β1, IL-6, CD62P and CCL21 between AMI patients with different HCMV infections was as follows: serum IL-10 and TGF-β1 levels of AMI group of patients with HCMV infection were lower than those of patients with non-HCMV infection whereas IL-1β, IL-6, CD62P and CCL21 levels were higher than those of patients with non-HCMV infection (P<0.05).

3.2 Serum myocardial injury indicator levels and their correlation with HCMV infection
Analysis of serum myocardial injury indicators CK-MB (U/L), cMyBP-C (μg/L), sLOX-1 (μg/L), Caspase-3 (ng/L) and MDA (μmol/L) between the two groups of subjects was as follows: serum CK-MB, cMyBP-C, sLOX-1, Caspase-3 and MDA levels of AMI group were significantly higher than those of control group (P<0.05). Analysis of serum myocardial injury indicators CK-MB, cMyBP-C, sLOX-1, Caspase-3 and MDA levels of AMI group were significantly higher than those of control group (P<0.05).

Table 1
Comparison of serum inflammatory factors between the two groups of subjects.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>IL-10</th>
<th>TGF-β1</th>
<th>IL-1β</th>
<th>IL-6</th>
<th>CD62p</th>
<th>CCL21</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMI group</td>
<td>80</td>
<td>14.75±1.75</td>
<td>22.62±3.52</td>
<td>8.68±0.93</td>
<td>34.27±5.57</td>
<td>49.58±5.58</td>
<td>1.85±0.25</td>
</tr>
<tr>
<td>Control group</td>
<td>60</td>
<td>39.47±5.57</td>
<td>59.67±7.82</td>
<td>3.62±0.52</td>
<td>7.73±0.93</td>
<td>20.12±2.95</td>
<td>0.67±0.08</td>
</tr>
<tr>
<td>t</td>
<td></td>
<td>29.383</td>
<td>25.382</td>
<td>22.374</td>
<td>46.828</td>
<td>26.382</td>
<td>32.855</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 2
Comparison of serum inflammatory factors between AMI patients with different HCMV infections.

<table>
<thead>
<tr>
<th>HCMV infection</th>
<th>n</th>
<th>IL-10</th>
<th>TGF-β1</th>
<th>IL-1β</th>
<th>IL-6</th>
<th>CD62p</th>
<th>CCL21</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>44</td>
<td>9.31±1.05</td>
<td>14.52±1.94</td>
<td>11.93±1.52</td>
<td>49.51±6.72</td>
<td>67.41±7.59</td>
<td>2.52±0.37</td>
</tr>
<tr>
<td>Non-infection</td>
<td>36</td>
<td>20.33±2.85</td>
<td>30.94±5.21</td>
<td>5.22±0.72</td>
<td>20.33±3.42</td>
<td>32.16±3.85</td>
<td>1.21±0.15</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 3
Comparison of serum myocardial injury indicators between the two groups of subjects.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>CK-MB</th>
<th>cMyBP-C</th>
<th>sLOX-1</th>
<th>Caspase-3</th>
<th>MDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMI group</td>
<td>80</td>
<td>62.82±7.72</td>
<td>145.48±17.84</td>
<td>1.74±0.22</td>
<td>84.99±11.32</td>
<td>16.41±2.51</td>
</tr>
<tr>
<td>Control group</td>
<td>60</td>
<td>22.12±2.85</td>
<td>57.58±7.78</td>
<td>0.47±0.06</td>
<td>34.62±5.57</td>
<td>4.52±0.62</td>
</tr>
</tbody>
</table>
sLOX-1, Caspase-3 and MDA between AMI patients with different HCMV infections was as follows: serum CK-MB, cMyBP-C, sLOX-1, Caspase-3 and MDA levels of AMI group of patients with HCMV infection were higher than those of patients with non-HCMV infection (P<0.05).

4. Discussion

Coronary heart disease is one of the most common cardiovascular diseases in our country. In recent years, with the increase of the number of patients with hypertension, hyperlipidemia, diabetes and other metabolic diseases, the incidence of coronary heart disease has been rising year by year. Coronary artery atheromatous plaque formation is the pathological basis of coronary heart disease, the plaque stability reduction and fracture can cause local platelet activation and thrombosis, and severe cases can cause vascular lumen occlusion and lead to acute attack of myocardial infarction. The occurrence of acute myocardial infarction involves multiple pathologic links and multiple risk factors, and the cytomegalovirus infection is closely related to atherosclerosis. CMV is the double-stranded DNA virus of herpesviridae, the host infection can cause the abnormal expression of immediate early genes, early genes and late genes, and can also affect the host immune cells differentiation and change the secretion of various cytokines[4]. Related research on coronary heart disease and cytomegalovirus infection has confirmed that the cytomegalovirus infection rates in patients with angina pectoris and acute myocardial infarction are both increasing, and the CMV infection rate in patients with acute myocardial infarction is higher than that in patients with angina pectoris[5]. It illustrates that the CMV infection is involved in the occurrence and development of coronary atherosclerosis and can cause coronary heart disease progression from angina pectoris to myocardial infarction, but the specific regulatory mechanism of the process is still not completely clear.

Inflammation is an important pathological link in the onset of acute myocardial infarction, plaque rupture, platelet activation, thrombosis, myocardial cell injury and repair, and other links all involve the excessive activation of inflammatory response and the changes in the secretion of pro-inflammatory factors and anti-inflammatory factors[6,7]. Cytomegalovirus infection directly influences the inflammation process, which is specifically characterized by inhibiting regulatory T cell differentiation and reducing anti-inflammatory cytokines IL-10 and TGF-β1 secretion to promote the secretion of IL-1β, IL-6, CD62P, CCL21 and a variety of other pro-inflammatory factors[8,9]. IL-1β has the pro-inflammatory effects such as promoting neutrophil activation, mast cell degranulation and monocyte infiltration[10]; IL-6 has the activity of achieving neutrophil and monocyte chemotaxis, and promoting other adhesion factor and chemokine expression[11]; CD62P and CCL21 are cytokines with direct chemotactic activity, which can promote the infiltration of multiple inflammatory cells in coronary atherosclerotic plaque and local myocardial ischemic area, and amplify inflammation[12]. Analysis of the changes of above serum inflammatory factors in patients with acute myocardial infarction showed that serum IL-10 and TGF-β1 levels of AMI group were significantly lower than those of control group whereas IL-1 β , IL-6, CD62P and CCL21 levels were significantly higher than those of control group. This indicates that the secretion of anti-inflammatory factors decreases and the secretion of pro-inflammatory cytokines increases in the occurrence of acute myocardial infarction. Further analysis of the influence of cytomegalovirus infection on inflammatory factor secretion in the course of acute myocardial infarction showed that serum IL-10 and TGF-β1 levels of AMI group of patients with HCMV infection were lower than those of patients with non-HCMV infection whereas IL-1 β , IL-6, CD62P and CCL21 levels were higher than those of patients with non-HCMV infection. It shows that cytomegalovirus infection in patients with acute myocardial infarction can reduce the secretion of anti-inflammatory factors and increase the secretion of pro-inflammatory cytokines to increase the inflammatory response in the course of myocardial infarction.

Hyperactive inflammatory response after acute myocardial infarction can further aggravate the damage of myocardial cells. First of all, local myocardial ischemia hypoxia after coronary occlusion can directly cause the myocardial cell destruction and damage, and the inflammation cells massively infiltrated in the ischemic myocardium at this time will secrete cytokines to further increase the damage of myocardial cells, and cause the metabolic enzymes and structural proteins to be released from the inside to the outside of the cells[13,14]. CK-MB and cMyBP-C are the metabolic enzyme and structural protein specifically expressed by the myocardial cells respectively, and their serum levels can reflect the degree of myocardial cell damage[15,16]. Secondly, the inflammatory cells excessively infiltrated in myocardial cells can also cause myocardial damage through apoptosis pathway and oxidative stress, LOX-1 is the receptor of ox-LDL, and it can activate Caspase-3 and induce myocardial apoptosis through the downstream Fas pathway after it is activated[17,18]; MDA is the oxidative reaction product of lipid with the oxygen free radicals massively generated in the process of myocardial ischemia hypoxia[19]. Analysis of the changes in above serum myocardial injury indicators in patients with acute myocardial infarction showed that serum CK-MB, cMyBP-C, sLOX-1, Caspase-3 and MDA levels of AMI group were significantly higher than those of control group. This indicates that the myocardial cells are excessively damaged and the oxidative stress and apoptosis are excessively activated during the occurrence
of acute myocardial infarction. Further analysis of the influence of cytomegalovirus infection on myocardial injury degree in the course of acute myocardial infarction showed that serum CK-MB, cMyBP-C, sLOX-1, Caspase-3 and MDA levels of AMI group of patients with HCMV infection were higher than those of patients with non-HCMV infection. This indicates that the cytomegalovirus infection in patients with acute myocardial infarction can aggravate myocardial damage.

The results of the study are summarized as follows: CMV infection in patients with acute myocardial infarction can reduce the secretion of anti-inflammatory factors and increase the secretion of pro-inflammatory factors to aggravate the inflammation in the course of myocardial infarction; meanwhile, cytomegalovirus infection can also aggravate myocardial damage.

References


