Diagnostic value of immunoglobulin combined with complement C3 and C4 in mycoplasma pneumonia

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Abstract: Objective: To investigate the diagnostic value of combined detection of immunoglobulin (Ig)M, IgA, IgG and complement C3 and C4 in mycoplasma pneumonia. Methods: From November 2015 to April 2018, 114 patients with mycoplasma pneumonia hospitalized in our hospital were selected and enrolled in the disease group, including 52 mild to moderate mycoplasma pneumonia patients and 62 severe mycoplasma pneumonia patients, and the control group consisted of 80 healthy subjects. The expression levels of Ig and complement C3 and C4 in venous blood of patients in each group were compared, the changes of pulmonary function of patients were detected and recorded, and the correlation between pulmonary function and detection indexes was analyzed. ROC was used to plot the diagnostic value of Ig and complement C3 and C4 combined detection in patients with different severity of mycoplasma pneumonia. Results: The levels of serum IgM, IgG, complement C3 and C4 in the disease group were notably higher than those in the control group, and IgA levels were notably lower than those in the control group, and the above indexes showed statistical difference between severe and mild to moderate mycoplasma pneumonia (P<0.05). Compared with mild to moderate mycoplasma pneumonia group, the predicted values of FEV1/FVC and FEV1% in severe mycoplasma pneumonia group were notably reduced (P<0.05). Correlation between FEV1/FVC and the detection indexes was analyzed by Spearon method. Pulmonary function of patients with mycoplasma pneumonia was negatively correlated with serum IgM, IgG, C3 and C4 levels, and positively correlated with IgA levels. ROC curve showed that detection of IgM, IgA, IgG and complement C3 and C4 and their combination could reveal the severity of mycoplasma pneumonia. Conclusion: The expression of Ig and complement C3 and C4 in patients’ serum has high diagnostic value for mycoplasma pneumonia.

Keywords: Immunoglobulin, complement C3, complement C4, mycoplasma pneumonia, diagnostic value

Introduction

Mycoplasma pneumonia is an acute community-acquired lung inflammation with a high incidence rate in children and young people, accounting for 30% of all pneumonia. It has clinical characteristics such as long course of disease and is easy to be repeated [1, 2]. Chest imaging manifestations of mycoplasma pneumonia are mostly nonspecific and variable. It is difficult to identify mycoplasma, bacterial and viral pneumonia in clinical practice [3, 4]. Typical symptoms of mycoplasma pneumonia include fever, cough, slight phlegm (fatigue, weakness and myalgia) and other non-specific manifestations, among which the most common symptoms and signs are lower respiratory tract fever, cough and rales [5]. If it is not treated in time, it can give rise to serious pulmonary diseases, complicated cardiovascular system and nervous system damage, hematuria, hemolytic anemia and other multi-system multi-organ diseases [6]. At present, the pathogenesis of mycoplasma pneumonia has not been clearly defined, and some scholars have reported that immune dysfunction may become its pathogenic factor [7]. When mycoplasma pneumoniae infection occurs in a patient, the whole body of the patient presents an inflammatory stress state, and the response reaction of the body’s immune system function is regulated by strengthening a series of pathological changes of pro-inflammatory and anti-inflammatory factors [8]. Therefore, early detection of pathogenic microorganisms inducing respiratory tract infection and comprehensive study of the changes of immune function in patients with mycoplasma pneumoniae infection have impor-
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tant significance in clinical analysis of the onset, control and treatment of mycoplasma pneumonia.

Complement and immunoglobulin (Ig) are important substances in the body to complete immunoregulation reactions. Complement is involved in the process of local tissue damage after infection with virus and mycoplasma by intervening inflammatory response and immune response. Ig directly eliminates mycoplasma by participating in the body’s humoral immune response [9, 10]. Relevant reports [11, 12] show that cytomegalovirus antibody detection is generally used for early infection detection, and the detection items mainly include IgM antibody, IgA and IgG antibody, among which IgM antibody exists from the initial infection to the end of infection. IgA has the function of immune barrier in the epithelial tissue of respiratory tract, and can be reflected by the expression of IgG antibody in acute infection. The activation of serum complement C3 and C4 in different pathways can directly affect the immune response of the body [13]. However, the diagnostic value of the combined detection of the above indicators for mycoplasma pneumonia has not been clearly defined. Therefore, in this paper, the diagnostic efficacy of the combined detection of Ig and complement C3 and C4 in patients with mycoplasma pneumonia was reviewed and analyzed, so as to explore a more efficient and accurate diagnostic scheme for mycoplasma pneumonia.

Materials and methods

General data

Totally 114 patients with mycoplasma pneumonia hospitalized in our hospital from November 2015 to April 2018 were selected and enrolled in the disease group. Among them, 52 patients with mild to moderate mycoplasma pneumonia in the disease group were set as the mild to moderate mycoplasma pneumonia group, and 62 patients with severe mycoplasma pneumonia were considered as the severe mycoplasma pneumonia group. And 80 healthy subjects undergoing physical examination were enrolled in the control group.

Inclusion and exclusion criteria

Inclusion criteria: (1) Patients were diagnosed as mycoplasma pneumonia according to their own symptoms, signs, etiology, chest X-ray examination and other results, all of which met the diagnostic criteria for mycoplasma pneumonia [14]. (2) Mycoplasma pneumonia patients with antibody titer ≥ 1:160. (3) Patients met the condition of complete clinical data. Exclusion criteria: (1) Patients with lung diseases other than pneumonia. (2) Patients with congenital heart disease. (3) Patients with hypoxic-ischemic encephalopathy or cerebrovascular disease. The content of this research was approved by the ethics committee of our hospital. All the research subjects were informed of the research process and projects and signed informed consent forms.

Research methods

In this study, the serum complement levels of C3 and C4 were detected by immune scatter turbidity, and the Ig index levels were detected by immunoturbidimetry. American Beckman Kurt IM-MAGE 800 protein analyzer and its supporting reagents were used. Five ml of fasting venous blood was collected from the patient in the morning, and the serum was centrifuged at 1500×g, and stored at -20°C to be tested. Easy One pulmonary function instrument manufactured by NDD (USA) was used to measure the forced expiratory volume in 1 second (FEV1) and FEV1/forced vital capacity (FVC) in patients with mycoplasma pneumonia of different degrees. Each index was tested at least 3 times to optimize the best results.

Outcome measures

(1) The levels of serum complement, IgA, IgM and IgG in each group of patients were compared and observed. (2) The changes of pulmonary function in patients with different pathological changes were compared. (3) Spearson method was used to analyze the correlation of IgM, IgA, IgG, C3 and C4 levels with pulmonary function of patients with mycoplasma pneumonia. (4) The diagnostic significance of combined detection of serum complement, IgA, IgM and IgG levels between healthy persons and patients with mycoplasma pneumonia was analyzed. (5) The diagnostic significance of combined detection of serum complement, IgA, IgM and IgG levels in patients with different pathological change was analyzed.

Statistical analysis

The statistical software SPSS 20.0 was used for data analysis. The measurement data were
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expressed as mean ± standard deviation, and the comparison was conducted by T test. The correlation between FEV1/FVC and each detection index in this paper was detected and analyzed by Spearson method. ROC was used to draw the curve of diagnostic value of Ig and complement C3 and C4 combined detection in mycoplasma pneumonia. Graphpad Prism8 was used to draw the picture in this experiment. P<0.05 was considered statistically significant difference.

Results

Comparison of general data between the two groups

There was no statistically significant difference in gender and age between the two groups (P>0.05). See Table 1 for details.

Comparison of IgM, IgA, IgG, complement C3 and C4 levels in the two groups

The serum levels of IgM (1.61±0.52), IgG (10.87±2.37), complement C3 (2.03±1.12) and C4 (0.45±0.19) in the disease group were significantly higher than those in the control group (IgM (1.16±0.43), IgG (8.82±2.18), complement C3 (1.15±0.65) and C4 (0.31±0.11)), but the level of IgA (0.67±0.39) in the disease group was significantly lower than that in the control group (1.26±0.95), with statistically significant differences (P<0.05). See Table 2 for details.

Comparison of serum IgM, IgA, IgG, complement C3 and C4 levels in patients with different diseases (g/L)

The serum levels of IgM (1.78±0.53), IgG (11.34±2.21), complement C3 (2.11±0.84) and C4 (0.52±0.23) of patients in the severe mycoplasma pneumonia group were significantly higher than those in the mild to moderate mycoplasma pneumonia group (IgM (1.39±0.48), IgG (9.35±2.16), complement C3 (1.69±0.70) and C4 (0.34±0.15)), and IgA level (0.38±0.26) in severe mycoplasma pneumonia group was significantly lower than those in the mild to moderate mycoplasma pneumonia group (0.69±0.44) (P<0.05). See Table 3 for details.

Pulmonary function test results of each group

The predicted values of FEV1/FVC and FEV1% in the severe mycoplasma pneumonia group

Table 1. Comparison of general data between the two groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Control group (n=80)</th>
<th>Disease group (n=114)</th>
<th>X²/t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (case)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>46 (57.50)</td>
<td>67 (58.77)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>34 (42.50)</td>
<td>47 (41.23)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>36.95±26.95</td>
<td>37.32±28.14</td>
<td>0.092</td>
<td>0.927</td>
</tr>
</tbody>
</table>

Table 2. Comparison of IgM, IgA, IgG, complement C3 and C4 Levels in the two groups (g/L)

<table>
<thead>
<tr>
<th>Group</th>
<th>IgM</th>
<th>IgA</th>
<th>IgG</th>
<th>Complement C3</th>
<th>Complement C4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group (n=80)</td>
<td>1.16±0.43</td>
<td>1.26±0.95</td>
<td>8.82±2.18</td>
<td>1.15±0.65</td>
<td>0.31±0.11</td>
</tr>
<tr>
<td>Disease group (n=114)</td>
<td>1.61±0.52</td>
<td>0.67±0.39</td>
<td>10.87±2.37</td>
<td>2.03±1.12</td>
<td>0.45±0.19</td>
</tr>
<tr>
<td>t value</td>
<td>6.362</td>
<td>5.959</td>
<td>6.128</td>
<td>6.318</td>
<td>5.927</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 3. Comparison of serum IgM, IgA, IgG, complement C3 and C4 levels in patients with different diseases (g/L)

<table>
<thead>
<tr>
<th>Group</th>
<th>IgM</th>
<th>IgA</th>
<th>IgG</th>
<th>Complement C3</th>
<th>Complement C4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild to moderate mycoplasma pneumonia group (n=52)</td>
<td>1.39±0.48</td>
<td>0.69±0.44</td>
<td>9.35±2.16</td>
<td>1.69±0.70</td>
<td>0.34±0.15</td>
</tr>
<tr>
<td>Severe mycoplasma pneumonia group (n=62)</td>
<td>1.78±0.53</td>
<td>0.38±0.26</td>
<td>11.34±2.21</td>
<td>2.11±0.84</td>
<td>0.52±0.23</td>
</tr>
<tr>
<td>t value</td>
<td>4.084</td>
<td>4.663</td>
<td>4.838</td>
<td>2.866</td>
<td>4.844</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.005</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
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Table 4. Pulmonary function test results of each group

<table>
<thead>
<tr>
<th>Group</th>
<th>FEV1/FVC (%)</th>
<th>FEV1 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild to moderate mycoplasma pneumonia group (n=52)</td>
<td>75.54±8.73</td>
<td>86.93±9.12</td>
</tr>
<tr>
<td>Severe mycoplasma pneumonia group (n=62)</td>
<td>64.37±9.10</td>
<td>75.64±8.93</td>
</tr>
</tbody>
</table>

were 64.37±9.10 and 75.64±8.93, respectively, which were significantly lower than those in the mild to moderate mycoplasma pneumonia group ((75.54±8.73) and (86.93±9.12), respectively) (P<0.05). As shown in Table 4.

Correlation analysis of levels of IgM, IgA, IgG, complement C3 and C4 with pulmonary function of patients with mycoplasma pneumonia

The changes of the predicted values of FEV1/FVC and FEV1% were consistent with the development trend of lung function. One of FEV1/FVC was selected to represent the development trend of lung function, and Spearson method was applied to detect and analyze the correlation between FEV1/FVC. It was found that the levels of serum IgM, IgG, complement C3 and C4 in patients with mycoplasma pneumonia were negatively correlated with their pulmonary function (r=-0.917, -0.869, -0.852, -0.875, P<0.001), and IgA level was positively correlated with their pulmonary function (r=0.900, P<0.001). More details were shown in Figure 1.

Analysis of diagnostic efficacy of individual and combined detection of each index for patients with mycoplasma pneumonia

AUC of patients with mycoplasma pneumonia detected by IgM was 0.738, with 95% CI of 0.669 to 0.807. AUC of patients with mycoplasma pneumonia detected by IgA was 0.675, with 95% CI of 0.592 to 0.757. AUC of patients with mycoplasma pneumonia detected by IgG was 0.741, with 95% CI of 0.670 to 0.812. AUC of patients with mycoplasma pneumonia detected by complement C3 was 0.781, with 95% CI of 0.717 to 0.845. AUC of patients with mycoplasma pneumonia detected by complement C4 was 0.786, with 95% CI of 0.722 to 0.850. AUC of patients with mycoplasma pneumonia detected by combination of IgM, IgA, IgG and complement C3 and C4 was 0.939, with 95% CI of 0.908 to 0.970. Through comparative analysis of combined detection and individual detection, the AUC of patients with combined detection of various indicators for mycoplasma pneumonia was higher than that of patients with
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of patients with different severity mycoplasma pneumonia detected by complement C3 and C4 were 0.669 and 0.775, respectively, with 95% CI of 0.568 to 0.770 and 0.690 to 0.861, respectively. AUC of patients with mycoplasma pneumonia of different severity detected by IgM, IgA, IgG and complement C3 and C4 was 0.942, with 95% CI of 0.901 to 0.983. More details were shown in Figure 3.

Discussion

Mycoplasma is common in nature and can be colonized in human oral cavity and respiratory tract. Mycoplasma pneumonia is a common pathogen of respiratory tract infection without cell wall [15, 16]. The pathological changes of mycoplasma pneumonia are mostly inflammatory manifestations between bronchioles and interstitium. When mycoplasma proliferates in the body, it can deposit in the lung tissues and the basement membrane of blood vessels in combination with humoral immune factors. A series of immune responses promoted by the body's immune system against mycoplasma invasion stimulate T lymphocytes, monocytes and macrophages to mediate cellular immune responses, release a large amount of toxins to damage epithelial cells, affect ciliary movement of respiratory system, thus damaging the integrity of mucosal surface of respiratory system [17, 18]. The massive release of inflammatory medium covers alveolar capillaries, causing congestion-like edema in capillaries, increasing vascular permeability load, and the severity of exudation and infiltration of inflammatory cells in alveoli also increase [19-21]. Mycoplasma infection not only affects the respiratory system, but also affects the nervous system to a certain extent, which may cause damage to various tissues.
and organs such as encephalitis, cranial nerve inflammation, bacterial meningitis and infectious cerebral infarction [22]. Studies on the pathogenesis of mycoplasma pneumonia have revealed that Ig is an important active substance involved in humoral immune response. After mycoplasma pneumonia infection occurs in the body, IgM, IgA and IgG are secreted and released into the blood by cells due to the induction effect, which changes the antigen structure of the body, leading to damage of the immune function of the body and multiple organs of the body [23, 24]. Complement C3 and C4 are the most common immunologically active substances in the complement activation pathway. Mycoplasma pneumonia infection can activate the body to promote the infiltration and activation of immune cells, and finally trigger autoimmune injury to the body [25]. The role of the above indicators in the body's immune function is elaborated in numerous studies. In order to understand its diagnostic value for mycoplasma pneumonia and in different severity of illness, we conducted experiments to discuss this purpose.

The comparative study of the changes of detection indexes in this experiment between normal subjects and patients with mycoplasma pneumonia showed that the serum IgM, IgG, complement C3 and C4 levels were higher and IgA levels were lower in patients with mycoplasma pneumonia. Mycoplasma pneumonia infection leads to the formation of immune complexes and a series of immune response reactions. It activates complement alteration and lysis (bacteria and cells) and other effects. Cell-mediated antibodies can exhibit cytotoxic effects and have the effect of killing and destroying infected target cells [26]. It has been observed in previous studies [27, 28] that the longer the illness duration and the more severe the disease in patients with mycoplasma, the more severe the lung consolidation. Detection of serum in patients with multiple extrapulmonary complications showed a decrease in Ig A, an increase in IgG, IgM and complement C3 and C4 contents, and the values return to normal at the recovery stage. It is consistent with the results of this study, suggesting that mycoplasma pneumonia influences the expression of Ig and complement through mediating cytotoxicity regulation. Further exploration of the experimental selection of detection indicators in patients with mycoplasma pneumonia of different severity revealed that the levels of serum IgM, IgG and complement C3 and C4 in patients with severe mycoplasma pneumonia were notably higher than those in patients with mild to moderate mycoplasma pneumonia, and IgA levels were notably lower than those in patients with mild to moderate mycoplasma pneumonia. Previous studies have shown that [29] serum Ig levels in patients with mycoplasma pneumonia of different disease courses are different, and there is a significant correlation between malignant transformation of patients' diseases and serum Ig expression. Complement is a key macromolecular substance derived from liver cells to complete humoral immune response. It mainly acts on two aspects in vivo, one is to kill bacteria and viruses by dissolving Ig complexes, the other is to directly neutralize or dissolve viruses, and the total complement content is determined by the amount of virus in vivo [30]. The combined results suggest that Ig and complement C3 and C4 can be used as indicators to judge the severity of inflammatory response of mycoplasma pneumonia. In order to accurately observe the correlation between pulmonary function changes of patients with mycoplasma pneumonia and the detection indexes in the study, the correlation between pulmonary function and various indexes was analyzed, and it was found that the change trend of each index and the deterioration degree of pulmonary function showed similarities. Therefore, we draw pictures of the diagnostic efficiency and combined diagnostic efficiency of each index in mycoplasma pneumonia and draw a conclusion that the condition of patients with mycoplasma pneumonia can be detected under separate detection of each index, and the combined application of detection can improve the diagnostic efficiency and accuracy.

In conclusion, the expression of Ig and complement C3 and C4 in patients' serum has high diagnostic value for mycoplasma pneumonia, and can assist in judging the therapeutic effect of mycoplasma pneumonia patients. At present, in clinical practice, there have been related descriptions on the connection mechanism and diagnostic function between each detection index and mycoplasma pneumonia. In this study, we mainly analyzed the expression changes of each index when pulmonary func-
tion changes to understand the monitoring of each index by different lung function changes at multiple time points, and analyzed the change range of each index in the patient’s body in real time to carry out targeted treatment and further disease judgment for mycoplasma patients. However, there are still some deficiencies in this experiment. Although data statistics and correlation analysis are carried out on pulmonary function, the change of lung function and the trend of each index in mycoplasma pneumonia were not analyzed to reduce errors in this experiment. This is the research direction of our follow-up inquiry to provide a more reliable diagnostic scheme for mycoplasma diagnosis and treatment.

Disclosure of conflict of interest

None.

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References


