Original Article

Clinical value of serum KL-6 for lung diseases in patients with polymyositis and dermatomyositis

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Abstract: Objective: To investigate clinical value of serum KL-6 for lung diseases in patients with polymyositis and dermatomyositis. Methods: 77 cases of PM/DM patients, among them 27 cases with interstitial lung disease (ILD), 20 cases with infectious lung disease, 30 cases without lung disease. ELISA method was adopted to measure the KL-6 levels of serum. The association with KL-6 and diagnosis, clinical features, laboratory indexes, treatment, even and prognosis were analyzed. Results: The average values of the KL-6 levels of serum in PM/DM patients with ILD, PM/DM patients with infectious lung disease, and PM/DM patients without lung disease were (1135.33 ± 648.67), (371.85 ± 187.14), (231.00 ± 110.89), respectively. PM/DM patients with ILD had significantly higher median KL-6 levels of serum compared with other two groups, and the difference is statistically significant (P < 0.05), but the difference between PM/DM patients with infectious lung disease and PM/DM patients without lung disease had no statistical significance (P = 0.229); While the 507 U/ml was regarded as positive standard, the sensitivity of KL-6 for PM/DM interstitial lung disease diagnosis was 96.3%, and the specificity was 89.0%; Serum levels of KL-6 were inversely correlated with DLco%, VC%, and TLV% (all P < 0.05). In serum KL-6 increased group, anti-Jo-1 positive rate was higher than normal group (P < 0.05). A follow-up analysis indicated that, KL-6 levels of serum of 10 cases of PM/DM with ILD patients were associated with therapeutic effect (P < 0.05), and KL-6 levels of serum of 5 cases died of PM/DM with ILD patients were significantly higher than those of 22 cases of PM/DM with ILD patients surviving (P < 0.05). Conclusion: KL-6 levels of serum can be used to identify interstitial lung disease and infectious lung disease, and assess clinical response to treatment, and a high level of KL-6 possibly indicates a poor prognosis.

Keywords: Polymyositis, dermatomyositis, KL-6, interstitial lung disease

Introduction

KL-6 is a high molecular weight glycoprotein found in the 1980s [1]. It is mainly secreted by type II epithelial cells of alveoli. Previously regarded as a tumor marker of thymoma and many studies are done on interstitial lung disease recently [2], it has a strong chemotaxis towards fibroblasts and plays an important role in fibrosis in the process of disease [3]. Polymyositis (PM) and dermatomyositis (DM) are a group of systemic autoimmune diseases characterized by inflammation of striated muscle. It is mainly accumulated in skin, gastrointestinal tract, heart, lung and other organs. Interstitial lung disease (ILD) is the most common pulmonary complication with high incidence rate and it is an important factor affecting the prognosis of PM/DM patients [4]. Early diagnosis of ILD and early treatment are the key to stopping the disease changing from ground-glass attenuation into irreversible honeycomb shape. At present, there is no clinically specific serum marker to determine the incidence of ILD, treatment outcome and prognosis. Therefore, this study aims to evaluate the clinical significance of KL-6 in the complication ILD developing from PM/DM through detecting its level.

Objects and methods

Research object

A total of 77 patients with PM/DM who were admitted to our hospital from May, 2015 to May, 2016 were chosen as the research object, including 22 males and 55 females, with age ranging from 17 to 80 years old and an average age of (52 ± 15) years old. Their average dis-
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Table 1. Mean value of serum KL-6 of each group

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of patients</th>
<th>KL-6 (U/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM/DM combined with ILD</td>
<td>27</td>
<td>1135.33 ± 648.67</td>
</tr>
<tr>
<td>PM/DM combined with pulmonary infection</td>
<td>20</td>
<td>371.85 ± 187.14</td>
</tr>
<tr>
<td>PM/DM without lung disease</td>
<td>30</td>
<td>231.00 ± 110.89</td>
</tr>
</tbody>
</table>

Results

Concentration of serum KL-6 in ILD group, pulmonary infection group and the group without lung disease

The mean of KL-6 concentration in each group is shown in Table 1. According to the LSD-t test, it was found that the serum KL-6 level in the ILD group was significantly higher than that in the other two groups and there was statistical significance in the differences (P < 0.05); but there is no statistical significance in the differences between pulmonary infection group and the group without lung disease (P = 0.229). The ROC curve analysis showed that the positive cutoff value of PM/DM patients combined with interstitial lung disease was 507 U/ml, the sensitivity was 96.3%, and the specificity was 89.0%. The ROC curve of KL-6 in the serum of patients with PMD/DM combined with interstitial lung disease is shown in Figure 1.

Correlation between KL-6 levels of serum and clinical feature of patients with PM/DM and laboratory indexes

Further study was conducted on the correlation between KL-6 levels of serum and clinical feature and laboratory indexes for patients with PM/DM. According to Spearman rank correlation analysis, there was significant negative correlation among the KL-6 levels, the proportion of carbon monoxide diffusion capacity to predicted value (DLco%) (r = -0.765, P < 0.01), the proportion of vital capacity to predicted value (VC%) (r = -0.584, P < 0.01) and the proportion of total lung capacity to predicted value (TLC%) (r = -0.635, P < 0.01). However, there is no significant correlation among the KL-6 lev-
els, the proportion of forced expiratory volume in one second to the predicted value (FEV1%), the proportion of forced vital capacity to the predicted value (FVC%), FEV1/FVC, the proportion of residual volume to the predicted value (RV%), ferritin, C-reactive protein, erythrocyte sedimentation rate (ESR), creatine kinase (CK), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), CD3, CD4, CD8 and CD4/CD8 (P > 0.05). In addition, the positive rate of anti-JO-1 antibody in the group with higher serum KL-6 level was higher than that in the normal group (= 4.472, P = 0.034). There is no statistical significance in the differences in anti-JO-1 antibody, other positive antibodies, such as ANA, SSA, SSB, Sm, RNP, RF, etc., and clinical feature, such as cough, dyspnea, dysphagia, myasthenia, arthritis/arthralgia, rash, Reynolds phenomenon etc. between the group with higher serum KL-6 level and the normal group.

**Correlation between serum KL-6 and therapeutic effect**

The treatment situations of 10 patients with PM/DM combined with ILD was followed up and the comparison of serum KL-6 before and after treatment was tested with Wilcoxon test. It showed that the difference between before and after treatment was statistically significant (P < 0.05). The serum KL-6 concentration in the improved group was also lower than that in the deteriorated group, as shown in Figures 2 and 3.

**Effect of serum KL-6 level on prognosis**

Through follow-up visits of the PM/DM patients combined with ILD for 1-13 months, it was found that 5 patients died and the serum KL-6 level in the dead patients (mean: 2663.60 ± 348.49) was significantly higher than that in the surviving patients (mean: 995.14 ± 459.18). There was no statistical significance in the difference between the two groups (t = 7.596, P < 0.05).

**Discussion**

Patients with PM/DM combined with ILD was diagnosed and confirmed mainly based on pulmonary function test, chest radiograph (X or ARCT) or lung biopsy. However, some critically ill patients could not complete pulmonary func-
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Anti-Jo-1 antibody is one of the aminoacyl-tRNA synthetases. According to the study of Taggart [9], the positive rate of anti-JO-1 antibody in PM/DM patients combined with ILD can be as high as 50%-75%. This study showed the positive rate of anti-JO-1 antibody in the group with higher serum KL-6 level is higher than that in the normal group, directly suggesting that KL-6 is correlated with ILD.

It was found through follow-up visits of 10 PM/DM patients combined with ILD that there was an obvious decrease in the serum KL-6 level in the improved group, while there was an obvious increase in the serum KL-6 level in the deteriorated group. There was statistical significance in the difference between before treatment and after treatment and it suggested that regular testing of KL-6 level could effectively reflect treatment effect and facilitate clinical treatment. The studies of Fathi [10] also showed that KL-6 levels of serum can reflect the extent of alveolar damage, and can prompt the outcome of treatment. In addition, it was found through follow-up visits of PM/DM patients combined with ILD for 1-13 months that the serum KL-6 level of 5 dead patients was significantly higher than that of 22 survived patients and about 3 times of that of the survived patients. Therefore, high serum KL-6 level might indicate bad outcome of treatment.

In summary, serum KL-6 can be used as a serum index to indicate whether PM/DM patients have ILD, the outcome of treatment and prognosis and to guide clinical diagnosis and treatment.

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Disclosure of conflict of interest

None.

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