The correlation between the chest X-ray classifications and the pathogens of hand—foot—mouth disease

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Abstract

Objective: To study the correlation between the chest X-ray classifications and different pathogens in patients with hand—foot—mouth disease.

Methods: The images and the results of laboratory examination of patients with HFMD and positive chest X-ray were analyzed retrospectively.

Results: There were 83 cases (21.013%) with positive chest X-ray in this group, including 19 cases of type 1, 19 cases of type 2, 28 cases of type 3, 13 cases of type 4, 4 cases of type 5. The distribution of pathogens had significantly statistical difference between mild and severe HFMD group, critical HFMD group respectively (mild HFMD group VS severe HFMD group, \( \chi^2 = 78.523, P = 0.000 \); mild HFMD group VS critical HFMD group, \( \chi^2 = 30.222, P = 0.000 \)). The distribution of pathogens in different the chest X-ray classifications had no statistical difference (P > 0.05), but the proportion of the EV71 was more than that of CVA16 in type 1 and 2 chest X-ray (P = 0.029 and 0.001).

Conclusions: There was some relativity between clinical grade and pathogens. The severe and critical HFMD were caused mainly by EV71, and the mild HFMD was caused mainly by other pathogens except EV71. There was no significant correlation between chest X-ray classification and pathogens, but in the same chest X-ray classification, the distribution of pathogens was not identical. For the limitations of this study, we will do more research in the future work.

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Keywords: Hand—foot—mouth disease; Chest X-ray classifications; Enterovirus 71

1. Introduction

Hand—foot—mouth disease (HFMD) was a kind of virus disease, which was caused by enterovirus (EV) mainly, including coxsackievirus A2 (CVA2), CVA4, CVA5, CVA6, CVA10, CVA16, CVB1-5, some serotypes echovims (ECHO) and enterovirus 71 (EV71) [1,2]. Clinical symptoms and signs of most HFMD were mild, whose characteristic performances were fever and rashes on hands, feet, mouth and hips of the skin. HFMD was a spontaneous healing disease, so its general prognosis was well. But a few patients complicated by encephalitis, pulmonary infection, myocarditis and other complications, which may cause bad prognosis and even death.

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The purpose of this paper was to study the correlation between the chest X-ray classification and different pathogens and improve the recognition of HFMD chest X-ray.

2. Materials and methods

2.1. Patients

There were 395 inpatients collected in our study during March 2014 to May, whose gender and age were distributed as shown in Table 1. All patients had fever in varying degrees (average temperature 38.78 ± 0.51 °C) and had varying numbers of rashes in hands, feet, hips and mouth. There were 83 inpatients with positive chest X-ray in our study. Those patients had heavy breathing, wheezing or coughing in varying degrees. There were 2 patients with neutropenia, 1 patient with severe pneumonia, and 1 critical patient died.
2.2. Imaging

Chest X-ray was performed using Philips Digital Diagnost Digital Radiography (Philips Healthcare, Eindhoven, Netherlands). If patients were less than 3 years old, they were examined in clinostatism anteroposterior position with the exposure conditions as follows: tube voltage 65 kV, tube current $2.5 \times 3.5 \text{ mAs}$, focus film distance 110 cm. If patients were more than 3 years old, they were examined in standing anteroposterior position with exposure conditions as follows: tube voltage 70 kV, automatic mAs, focus film distance 180 cm.

2.3. Diagnostic criteria

The “hand–foot–mouth disease prevention and control guide (2010 Edition)” was used as the clinical diagnostic and grading criteria, which were as follows:

(1) mild: varying numbers of rashes in hands, feet, hips or mouths, with or without fever;
(2) severe: nervous system involved and brought clinic symptoms (such as poor spirit, somnolence, hyperarousal, deliration, headache and vomiting, limb jitter, myoclonia, nystagmus, ataxia, ocular movement disorder; adynia or acute flaccid paralysis, convulsion) and signs (including meningeal irritation sign, tendon reflexes weakened or disappeared).
(3) critical: one of the following clinic symptoms: The nervous system symptoms: frequent convulsions, coma, hernia cerebri and so on; The respiratory system symptoms: dyspnea, cyanosis, bloody foam sputum, pulmonary rales and so on; The circulation system symptoms: shock and other circulatory insufficiency symptoms.

Imaging diagnostic criteria referred to the classification criteria proposed by Li Xue-qin et al. [3], which were as follows:

(1) Type 1: bronchitis type. The pulmonary interstitial was involved mainly in this type. Those images performed lung marking increased and disordered, and some grid-like or line-like changes, and speckle fuzzy shadows may be visualized among lung-markings;
(2) Type 2: localized lesions type. Only one pulmonary lobe or segment was involved in this type, in which some cloud floccule were visible;
(3) Type 3: localized-wide lesions type. In this type, more than one pulmonary lobes were involved, in which some localized cloud floccule were showed and air bronchogram sign may be visualized in lung consolidation;
(4) Type 4: wide lesions type. In this type, diffuse cloud floccule were visible in both lung fields on chest X-ray. Apart from diffuse cloud floccule, ground-glass, interstitial changes and localized emphysema were displayed by computerized tomography (CT). An example of this type was shown as Fig. 1;
(5) Type 5: pulmonary edema type (neurogenic pulmonary edema). Symmetry patchy opacities were visible in both internal zones of lung fields, which showed 'butterfly' sign that appeared inhomogeneous density from the inside outward gradually fades. Or symmetry patchy opacities were visible in one lung field. An example of this type was shown as Fig. 2.

All patients' throat swab samples were collected and enteroviruses were detected, including EV71, CVA16, and universal nucleic acid of enterovirus.

2.4. Imaging diagnosis and statistical methods

All images were diagnosed by two radiologists with 8 and 13 years experience commonly. The different distribution of pathogens in different HFMD clinical grade or different chest X-ray classifications were all compared by Kruskal–Wallis test. The different distribution of pathogens in the same clinical grade or same chest X-ray classifications were compared by $\chi^2$ test. Dedicated software was used for statistical analysis (SPSS17.0, Chicago).

![Fig. 1. Wide lesions type in a 28-month-old boy with severe HFMD. This chest X-ray shows diffuse cloud floccule in both lung fields.](image)
3. Results

There were 83 cases (21.013%) with positive chest X-ray in this group, including 19 cases of type 1, 19 cases of type 2, 28 cases of type 3, 13 cases of type 4, 4 cases of type 5. There were 10 patients with hilus pulmonis increased. The mild, severe, and critical HFMD patients accounted for 45.570%, 48.607%, and 5.823% in our study respectively, in which the mild, severe, critical HFMD patients with positive chest X-ray accounted for 10.380%, 8.354%, 2.278%, respectively. The distribution of pathogens in different clinical grade was as shown in Table 2 and Fig. 3. After statistical analysis, the distribution of pathogens had significantly statistical difference between mild and severe HFMD group, critical HFMD group respectively (mild HFMD group VS severe HFMD group, \( \chi^2 = 78.523, P = 0.000 \); mild HFMD group VS critical HFMD group, \( \chi^2 = 30.222, P = 0.000 \)), but there was no significantly different distribution of pathogens between critical HFMD group and severe HFMD group (\( \chi^2 = 2.807, P = 0.422 \)). In mild HFMD group, there was significantly statistical difference between the proportion of the EV71 and that of other pathogens (EV71 VS other enteroviruses, \( \chi^2 = 9.870, P = 0.002 \); EV71 VS non-enterovirus, \( \chi^2 = 5.560, P = 0.018 \)), and there was also significantly statistical difference between the proportion of the CVA16 and that of other pathogens (CVA16 VS other enteroviruses, \( \chi^2 = 3.941, P = 0.041 \); CVA16 VS non-enterovirus, \( \chi^2 = 7.565, P = 0.006 \)), but there was no statistical difference between the proportion of EV71 and CVA16, and other enteroviruses and non-enterovirus. In severe and critical HFMD groups, the proportion of the EV71 were much more than that of other pathogens (\( P < 0.05 \)). The distribution of pathogens in different chest X-ray classifications had no statistical difference (\( P > 0.05 \)), but the proportion of the EV71 was more than that of CVA16 in type 1 chest X-ray (\( P = 0.029 \) and 0.001). Those were shown in Table 3, Fig. 4.

Fig. 2. Pulmonary edema in a 34-month-old boy with critical HFMD. The boy presented with frequent convulsions and dyspnea, but the result of his brain CT imaging was normal. A Chest X-ray shows symmetry patchy opacities in internal zones of both lung fields, especially in the right lung fields, in which lung marking and bilateral hilar are showed unclearly. After two days of treatment, B chest X-ray shows symmetry patchy opacities disappeared, and lung marking and bilateral hilar are showed clearly.

Table 2

<table>
<thead>
<tr>
<th>Clinical grade</th>
<th>Pathogens</th>
<th></th>
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<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EV71</td>
<td>CVA16</td>
<td>Other enteroviruses</td>
<td>Non-enterovirus</td>
<td>P (_1)</td>
</tr>
<tr>
<td>Mild</td>
<td>33(4)</td>
<td>36(2)</td>
<td>52(19)</td>
<td>59(16)</td>
<td>0.000</td>
</tr>
<tr>
<td>Severe</td>
<td>114(20)</td>
<td>10(1)</td>
<td>16(6)</td>
<td>52(6)</td>
<td></td>
</tr>
<tr>
<td>Critical</td>
<td>16(6)</td>
<td>0(0)</td>
<td>3(1)</td>
<td>4(2)</td>
<td></td>
</tr>
</tbody>
</table>

P\(_1\) value for comparison between the different distribution of pathogens in HFMD clinical grade (\( \chi^2 = 79.105 \)).
P\(_2\) value for comparison between the distribution pathogens in mild HFMD and that in severe HFMD (\( \chi^2 = 78.523 \)).
P\(_3\) value for comparison between the distribution pathogens in mild HFMD and that in critical HFMD (\( \chi^2 = 30.222 \)).
P\(_4\) value for comparison between the distribution pathogens in critical HFMD and that in severe HFMD (\( \chi^2 = 2.807 \)).

\( \chi^2 \) values for the distribution of pathogens of HFMD with positive chest X-ray.
4. Discussion

According to the data released by the National Health and Family Planning Commission of China, HFMD had been the first number of infectious diseases under class C in 2010 and 2011, and the number of deaths caused by HFMD was within top five\(^4\). HFMD had a high rate of occurrence in the spring and summer, which normally happened in children below 5 years old, especially below 3 years old\(^5,6\), and the children below 3 years old accounted for 76.86% in our study. HFMD was a self-limited disease usually, so most patients would recover without therapy in one week, but some children may be complicated by some symptoms of the nervous system, circulatory system, respiratory system and so on, what’s worse, a few children with severe complications may die in a short time.

The HFMD was caused mainly by enteroviruses, especially the EV71, CVA 16, some serotypes ECHO. As reported in some studies\(^6-9\), EV71 was the dominant viruses in severe HFMD and CVA16 and other enteroviruses were the dominant viruses in mild HFMD, which were similar to our study. In our study, the proportion of enteroviruses was 70.380%, which was the main pathogen for HFMD. In different clinical grade, the dominant virus was not identical. The dominant pathogen was EV71 in severe and critical HFMD. Therefore, when EV71 was positive in HFMD, the doctor should better pay enough attention and take some measures to avoid progressing toward severe and critical HFMD.

According to the study of the distribution of pathogens in different chest X-ray classifications of HFMD, there was no significant correlation between chest X-ray classification and pathogens, but in the same chest X-ray classification, the distribution of pathogens was not identical. In type 1 and 2 groups, EV71 compared with CVA16 was the dominant pathogen (\(P\) values were 0.029 in type 1and 0.001 in type 2). It was worth mentioning that there was no significant difference between EV71 and other pathogens in type 5, but the proportion of EV71 was highest (75%). The possible reasons of those results above were as followed: (1) patients infected different pathogens, which had different biological behaviors, therefore it may cause different pulmonary pathological changes. For example, the number of critical patients in type 5 (pulmonary edema type) was the largest, which may be because the main pathogen of the critical HFMD was EV71, some studies \(^10-12\) showed that the EV71 may cause pulmonary edema, whose the possible mechanism were as followed: ➀EV71 had neuronotropic, caused viremia or invaded the central nervous system directly, made sympathetic fibers excitation and systemic vasoconstriction, so a lot of blood flowed into pulmonary circulation from body circulation. ➁EV71 made a large number of inflammatory factors release excessively, leaded to pulmonary vascular permeability increased. ➂EV71 caused severe myocardial damage and induced cardiorespiratory function failure. All mentioned above may cause neurogenic pulmonary edema and pulmonary hemorrhage finally; (2) Children infected with the same pathogen, but their chest X-ray images showed different features, which may because they complicated by other pathogens (non-HFMD pathogens); (3) Different people’s own immunity were different; (4) When patients visited the hospital, the length of their course was different.

There are some limitations of our study. Firstly, the sample size of this study was only 3 months, and may not be able to cover epidemic character of the HFMD pathogens in a whole year. Secondly, the sample size of the critical patients was not enough, so the analysis of the problem was not comprehensive enough. Thirdly, some children with

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Table 3
The distribution of pathogens in different chest X-ray classifications of HFMD.

<table>
<thead>
<tr>
<th>Chest X-ray classification</th>
<th>Pathogens</th>
<th>(\chi^2)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EV71</td>
<td>CVA16</td>
<td>Other enteroviruses</td>
</tr>
<tr>
<td>Type 1</td>
<td>9(0.300)</td>
<td>2(0.667)</td>
<td>3(0.115)</td>
</tr>
<tr>
<td>Type 2</td>
<td>9(0.300)</td>
<td>0(0.000)</td>
<td>4(0.154)</td>
</tr>
<tr>
<td>Type 3</td>
<td>5(0.167)</td>
<td>1(0.333)</td>
<td>12(0.461)</td>
</tr>
<tr>
<td>Type 4</td>
<td>4(0.133)</td>
<td>0(0.000)</td>
<td>6(0.231)</td>
</tr>
<tr>
<td>Type 5</td>
<td>3(0.100)</td>
<td>0(0.000)</td>
<td>1(0.038)</td>
</tr>
</tbody>
</table>

\(^'(\)\) value for the proportion of the distribution of pathogens in different chest X-ray classifications of HFMD.

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Fig. 4. Histogram of the distribution of pathogens in different chest X-ray classifications of HFMD. In type 1, the proportion of the EV71 was more than that of CVA16. There was no CVA16 in type 2. The distribution of pathogens in other type chest X-ray classifications, including type 3, 4 and 5 had no statistical difference.
pulmonary infection may complicate with the non-HFMD pathogens or they were caused only by the non-HFMD pathogens, which could not be excluded in our study. Forth, during chest X-ray classifying, there may be radiologists' subjective influence.

5. Conclusion

There were some relativity between clinical grade and pathogens. The severe and critical HFMD were caused mainly by EV71, and the mild HFMD was caused mainly by other pathogens except EV71. There was no significant correlation between chest X-ray classification and pathogens, but in the same chest X-ray classification, the distribution of pathogens was not identical. For the limitations of this study, we will do more research in the future work.

References


