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Case report

A pediatric patient with interstitial pneumonia due to enterovirus D68

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ABSTRACT

Enterovirus D68 (EV-D68) infection is associated with upper and lower respiratory tract symptoms such as fever, cough, and wheezing. Pediatric patients with EV-D68 infection easily develop more severe respiratory complications compared to patients infected with other species of enterovirus, and consequently, have a higher rate of hospitalization and admission to intensive care units. Therefore, the clinical picture of respiratory complications associated with EV-D68 infection needs to be elucidated. Here, we report a 4-year-old girl of EV-D68 infection that required artificial respiration management within 24 h from the onset of cold symptoms. The patient was diagnosed with interstitial pneumonia on the basis of chest imaging findings with patchy, funicular and frosted glassy shadows, increased blood markers of surfactant protein-A, surfactant protein-D and sialylated carbohydrate antigen KL-6, and increased neutrophils and lymphocytes in the bronchoalveolar lavage. Steroids showed a remarkable effect in her treatment. Further investigations are needed to confirm the efficacy of steroids for interstitial pneumonia due to EV-D68 infection. As rapid deterioration of respiratory status is observed in EV-D68 infection, the possibility of interstitial pneumonia may be considered.

1. Introduction

Enterovirus D68 (EV-D68) was first detected in the pharynx of four young children hospitalized because of acute lower respiratory tract infections in 1962 [1]. Since the late 2000s, the number of reported patients infected with EV-D68 has increased, leading to the EV-D68 outbreak in North America in 2014 [2]. EV-D68 outbreaks were reported in nations in Europe [3], Asia [4], and the southern Hemisphere [5], and there was an epidemic in the fall of 2015 in Japan [6].

Symptoms include respiratory symptoms such as fever, cough, and wheezing, along with neurological symptoms such as acute flaccid paralysis [7]. The 2014 outbreak of EV-D68 in North America often led to severe respiratory failure that required admission to intensive care units (ICUs) or tracheal intubation [8]. The clinical picture of respiratory complications associated with EV-D68 is still unclear.

We encountered a 4-year-old girl with interstitial pneumonia due to EV-D68, in which respiratory complications became severe within 17 h of the first cold symptoms, requiring artificial respiration management. We considered this case as an important clinical picture of EV-D68 infection and report the details with the agreement from the parents of the patient.

2. Case report

The patient was a 4-year-old girl. She has 3p interstitial deletion (3p−) syndrome and epilepsy (the patient was taking phenobarbital with 9.9 μg/ml of the blood concentration [trough value]). Activities of daily living include walking and simple communication. The patient was hospitalized six times for bronchopneumonia before 1.5 years of age; however, there has been no respiratory infection that required hospitalization since then. There was no bronchial asthma.

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The patient had nasal discharge and fever the day before the hospitalization. Around midnight, her breathing became labored, and the patient was brought to a pediatric emergency medical center near her home. At that time, transcutaneous oxygen saturation was (SpO_2) around 40% (room air), confirming hypoxemia, and the patient was immediately transferred to our hospital for treatment.

At the time of hospitalization, the level of consciousness was E2V2M5 on the Glasgow Coma Scale, temperature was 38.4 °C, heartbeat was 162 bpm, blood pressure was 96/66 mmHg, and SpO_2 was 95% (under administration of 100% oxygen at 5 L/min). Respiratory sounds were coarse crackles in the whole lung field. Exhalation was extended with significant retractive breathing. Cardiac sounds were normal. Blood test results at the time of hospitalization were as follows: white blood cell count, 1400/μl (neutrophil count, 470/μl); hemoglobin level, 8.5 g/dl; platelet count, 224,000/μl; C-reactive protein (CRP), 0.94 mg/dl; endotoxin level < 1.9 pg/ml; and β-D glucan level, 11 pg/ml. Venous blood gas analysis under inhalation of 100% oxygen at 5 L/min yielded the following results: pH 7.121, pCO_2 76.3 mmHg and HCO_3 23.8 mmol/l, which meant respiratory acidosis. No pathogen was detected in bacterial and fungal cultures from the blood or bronchoalveolar lavage (BAL). Chest radiograph and computed tomography (CT) confirmed patchy shadows in both lungs along the bronchial tube, accompanied by air bronchogram (Fig. 1).

The patient's post-hospitalization course is shown in Fig. 2. After being admitted to the ICU, the patient was diagnosed with pneumonia, and treatment (oxygen inhalation, transfusion, and administration of tazobactam/piperacillin and micafungin) was initiated. Due to respiratory distress symptoms and a high level of respiratory acidosis, tracheal intubation was performed 17 h after the onset of the initial symptoms, and artificial respiration management was started. Because CRP levels increased up to 14.6 mg/dl on the second day of hospitalization, the medication was changed to azithromycin and meropenem.

On the seventh day of hospitalization, CRP levels decreased to 2.42 mg/dl. The alveolar-arterial oxygen difference ($AaDO_2$) was 218 mmHg at the beginning of the artificial respiration management, and fluctuated between 210 and 270 mmHg. On the seventh day of hospitalization, the $AaDO_2$ increased to 323 mmHg, while the fraction of inspired oxygen increased to 70% from 45%. When the chest was imaged again, an enhanced reticular shadow was observed in the radiograph, and patchy, funicular and frosted glassy shadows were visible along the bronchial tube by CT (Fig. 1). Blood tests showed surfactant protein-A (SP-A) of 690.9 ng/ml, surfactant protein-D (SP-D) of 929 ng/ml, and sialylated carbohydrate antigen KL-6879 U/ml. BAL leukocyte classification was as follows: 33% neutrophils, 5% eosinophils, 0% basophils, 0% monocytes, 19% lymphocytes, and 43% macrophages, suggesting the increased neutrophils and lymphocytes. The patient was diagnosed with interstitial pneumonia based on the chest imaging findings, increased blood markers of SP-A, SP-D and KL-6, and BAL leukocyte classification. EV-D68 was detected in a polymerase chain reaction (PCR) test and direct sequence analyses of the BAL based on the methods as previously reported [9,10]. Other clinical specimens were not tested for EV-D68 detection. In other tests for pathogenic microorganisms and collagen diseases, there were no abnormal findings (Supplementary Table).

Methylprednisolone (1 mg/kg/day) was initiated on the ninth day of hospitalization. On the 12th day of hospitalization, the $AaDO_2$ decreased and the frosted glassy shadow improved in the chest radiograph and CT images (Fig. 1). On the 15th day of hospitalization, artificial respiration management was discontinued, and on the 16th day of hospitalization, the patient was transferred from the ICU to the pediatric ward. On the 22nd day of hospitalization, administration of oxygen was discontinued. In addition, the medication was changed to oral prednisolone on the 14th day of hospitalization and was discontinued on the 23rd day of hospitalization. On the 34th day, the patient was discharged. There were no neurological symptoms such as muscle weakness during the hospitalization.

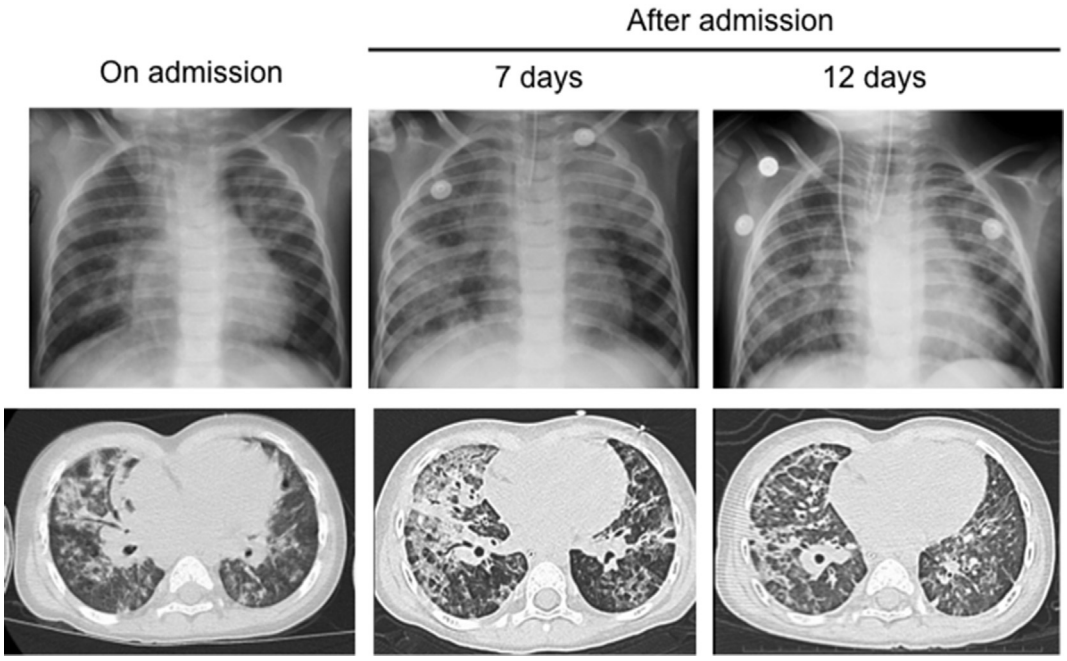

Fig. 1. Chest imaging. Patchy shadows in both lungs along the bronchial tube, accompanied by air bronchogram were prominent on admission. An enhanced reticular shadow was observed in the radiograph, and patchy, funicular and frosted glassy shadows were visible along the bronchial tube by computed tomography on 7 days after admission. On 12 days after admission, the frosted glassy shadow improved. Upper panel: simple chest radiograph, lower panel: computed tomography