

Case report

Features of hand, foot and mouth disease in neonates

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Abstract

Rationale: Hand, foot and mouth disease (HFMD) is caused by enterovirus. The virus may exist in secretions.

Patient concerns: Five neonates had symptoms of fever and maculopapular rashes involving face, trunk, breech, arms, and legs, especially scattering on palms and feet. Blood, oropharyngeal fluid, urine, and cerebrospinal fluid (CSF) samples were collected and detected for further diagnoses with the consent of the infants' parents. Some of them suffered aseptic meningitis.

Diagnoses: They were diagnosed as HFMD with CSF enterovirus positive.

Interventions: All of them continued breastfeeding. Water bag was used during the pyrogenic stage. Antibiotics were administrated at first and withdrawn as soon as possible.

Outcomes: None of them developed into brainstem encephalitis or pulmonary edema and they all recovered well.

Lessons: HFMD is more common in neonates than it has been thought. Enterovirus may exist in neonatal CSF and cause CSF cell to increase similar to purulent meningitis. Medical history, physical examination, and CSF enterovirus detection are important in making correct diagnosis. Unlike bacterial infection, HFMD is a self-limited disease. Once HFMD is determined and bacterial infection is ruled out, antibiotics should be avoided.

Abbreviations: CRP = C-reactive protein, CSF = cerebrospinal fluid, HFMD = hand, foot and mouth disease, MRI = magnetic resonance imaging, NEUT% = percentage of neutrophils, PCT = procalcitonin, WBC = white blood cell.

Keywords: enterovirus, HFMD, neonate

1. Introduction

Hand, foot and mouth disease (HFMD) is an acute infectious disease caused by enteroviruses, and encounters infants and children before school age mostly, ranging from benign illness to severe life-threatening disease. Thousands of cases have been reported over the past decade worldwide. However, neonatal cases are rare. Two severe cases in newborns were reported in 2014.^[1,2] But the epidemiology and clinical impact of HFMD with neonates are still unknown. Here, we present 5 cases with benign illness.

2. Case presentation

2.1. Case 1

A 10-day-old male infant endured fever and plenty of maculopapular rashes on face, trunk, breech, arms, legs, palms,

and feet for 1 day. He received breastfeeding and was in contact with his brother who was then in a common cold. The laboratory findings revealed white blood cell (WBC) $8.25 \times 10^9/L$, percentage of neutrophils (NEUT%) 75.2%, procalcitonin (PCT) 1.06 ng/dL, C-reactive protein (CRP) 3.82 mg/dL, throat enterovirus negative, CSF cell $42 \times 10^6/L$, CSF enterovirus positive, blood and CSF cultures negative. Antibiotic was administrated when admitted and stopped when the body temperature dropped to normal.

2.2. Case 2

A 16-day-old male infant was confronted with fever and quantity of maculopapular rashes on face, trunk, breech, arms, legs, palms, and feet for 3 days. He was breastfed and in touch with his sister with symptoms of fever previously. The laboratory findings revealed WBC $4.63 \times 10^9/L$, NEUT% 62.8%, PCT 0.52 ng/dL, CRP 7.2 mg/dL, CSF cell $220 \times 10^6/L$, both throat and CSF enterovirus positive, blood and CSF cultures negative. Antibiotic was administrated when admitted and stopped when the CSF turned normal and the cultures came out negative. Cranial magnetic resonance imaging (MRI) was normal.

2.3. Case 3

A 7-day-old male infant endured fever and scattered maculopapular rashes on trunk and between fingers for 1 half day. He was breastfed. His mother got maculopapular rashes on her palms and feet. Then the rashes increased and spread to palms and feet during hospitalization. The laboratory findings revealed WBC $3.82 \times 10^9/L$, NEUT% 46.5%, PCT 0.09 ng/dL, CRP 3.64 mg/dL, throat enterovirus negative, CSF cell $1 \times 10^6/L$, CSF enterovirus positive, blood and CSF cultures negative. Antibiotic was administrated when admitted and stopped when the body temperature dropped to normal.

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2.4. Case 4

A 10-day-old female infant suffered fever and maculopapular rashes of trunk and breech for 1 day. She was breastfed. Her brother suffered a common cold and lived with her. The laboratory findings revealed WBC $17.24 \times 10^9/L$, NEUT% 45%, PCT 0.12 ng/dL, CRP 0.165 mg/dL, throat enterovirus negative, CSF cell $1580 \times 10^6/L$, CSF enterovirus positive, blood and CSF cultures negative. Antibiotic was administered when admitted and stopped when the CSF turned normal and the cultures came out negative. Cranial MRI was normal.

2.5. Case 5

A 18-day-old female infant endured fever and bloating for 1 day. She was breastfed. Her brother got a fever and headache ahead and she contacted with him frequently. Maculopapular rashes emerged and were distributed on face, trunk, breech, arms, legs, palms, and feet during hospitalization. The laboratory finding revealed WBC $7.69 \times 10^9/L$, NEUT% 26.5%, PCT 0.05 ng/dL, CRP 1.51 mg/dL, throat enterovirus negative, CSF cell $3 \times 10^6/L$, CSF enterovirus positive, blood and CSF cultures negative. Antibiotic was administered when admitted and stopped when the body temperature dropped to normal.

3. Discussion

Hand, foot and mouth disease epidemics occurred annually around March and peaked in June or July, and larger epidemics occurred every 2 to 3 years in China.^[3,4] Enterovirus is usually detectable in the oropharyngeal fluid, blood, nasal fluid, stool, and CSF.^[5,6] The disease is characterized by a short lasting fever, mouth ulcers, and vesicles on the hands, feet, or hips.^[7] The cases we reported occurred in the epidemic season, but came from different areas of Zhangzhou City, Fujian Province. Although there was no definite epidemic history, they were more or less in contact with other family members who might be probably in a mild infection. All the 5 cases had symptoms of fever and maculopapular rashes involving face, trunk, breech, arms, and legs, especially scattering on palms and feet without mouth ulcers or vesicles. The enterovirus detection of CSF confirmed enterovirus infection and revealed that the virus existed in the CSF and might caused aseptic meningitis with the CSF cells increasing significantly sometimes. Despite aseptic meningitis, the infants did not display symptoms of seizures, lethargy, poor tone, abnormal nerve reflex, or brain injury on MRI, and did not deteriorate to brainstem encephalitis and pulmonary edema. It is surmised that the antibodies existing in the neonatal blood from maternal blood and breast, which decline with the age growing, might provide protection against the infection.^[8] The WBC, the PCT, and also the CRP, were usually normal or increased slightly, which indicated that the infection was mild and almost impossibly exacerbated.^[9] Although the 5 cases we met were

full-term babies, HFMD also came across preterm babies with an atypical course.^[10] There is no effective antiviral therapy for HFMD and antibiotic is not beneficial. In our unit, all the 5 neonates continued to be breastfed. We put water bag under the occiput when the body temperature was above normal. We did not apply antipyretics, ribavirin, or cortisol during treatment. We gave antibiotics to them at first before the laboratory test came out, because bacterial infection could not be ruled out according to the management of febrile neonates.^[11] Once HFMD was confirmed and no bacterial cultures were obtained, we removed the antibiotics as soon as possible.

4. Conclusions

Hand, foot and mouth disease mostly encounters neonates with complication of aseptic meningitis, which may be misdiagnosed as purulent meningitis. Suspicious exposure to infectious individuals in epidemic season, fever combined with typical aculopapular rashes involving face, trunk, breech, arms and legs, palms, and feet and CSF enterovirus detection may provide clues and support for making correct diagnosis. Identifying neonates with HFMD and separating them from those without the disease can avoid horizontal transmission in neonatal ward.

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