Co-infection of enterovirus 71 and *Staphylococcus aureus* in a 6-month-old male infant

Peng Hu, Jian Wang, Hai Bo Kong, Xue Qi Zhao, Jie Cai, Bo Hu

Department of Pediatrics, the First Affiliated Hospital of Anhui Medical University, Hefei, China

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Corresponding author:
Peng Hu
Department of Pediatrics
the First Affiliated Hospital
of Anhui Medical University
No. 218 Ji-Xi Road
Hefei 230022, PR China
Phone: +86 551 62922058
Fax: +86 551 63633742
E-mail: hupeng28@aliyun.com

Enterovirus 71 (EV71), as a member of the *Picornaviridae* family, is characterized by a single positive-strand genomic RNA known to cause hand, foot, and mouth disease (HFMD) in children. Since the first identification of EV71 infection in California in 1969, periodic epidemics have broken out worldwide [1]. In China, the first EV71 strain was isolated in 1987 by Zheng *et al.* [2]. Generally speaking, EV71 infection follows a benign and self-limiting course with multiple vesicles on the hands, feet and buccal mucosa. However, over the last decade EV71-associated HFMD has posed a great economic and social burden because of more frequent outbreaks with serious complications including neurological involvement, myocarditis and pulmonary edema [3, 4]. Liu *et al.* carried out an epidemiological analysis of an HFMD outbreak in 2010 in Nanchang city, and found that 12 (11%) patients were co-infected with both EV71 and coxsackievirus A16 (CA16) [5]. In the present report, we describe an unusual case of co-infection of EV71 and *Staphylococcus aureus* (SA).

A 6-month-old male infant with a 4-day history of general malaise, fever, poor feeding and skin lesions was admitted to the Department of Pediatrics at the First Affiliated Hospital of Anhui Medical University in June 2012. The birth and past medical history were non-significant, and the family had no history of similar disorders. On admission, his blood pressure was 70/35 mm Hg, heart rate was 132 beats per minute, axillary temperature was 39.2°C, and O_2 saturation (pulse oximetry) was 95%. Physical examination revealed the presence of sporadic pustules and papules on his lower limbs, buccal and perianal mucosa (Figure 1). There was no lymphadenopathy. Cardiac and pulmonary physical examinations were unremarkable. The abdomen showed no clinical signs of peritoneal irritation, masses, or enlarged organs. EV71 was identified from both throat swab and pustular fluid by virus isolation techniques. In addition, two blood cultures from samples obtained at admission were both positive for SA. His initial blood counts were as follows: white blood cell 19.62 × 10^9/l with 63.7% neutrophils, 21.3% lymphocytes, and 8.1% monocytes, hemoglobin 127 g/l, and platelet 361 × 10^9/l. C-reactive protein was 27 mg/l. Serum biochemistry and urinary analysis were normal. Echocardiogram demonstrated no pathologic findings. The patient was diagnosed with co-infection of EV71 and SA, mainly according to the results of the physical examination, virus isolation and blood cultures. He was treated with intravenous acyclovir, immunoglobulin and vancomycin, and bed rest for 14 days. The fever and skin lesions gradually resolved.

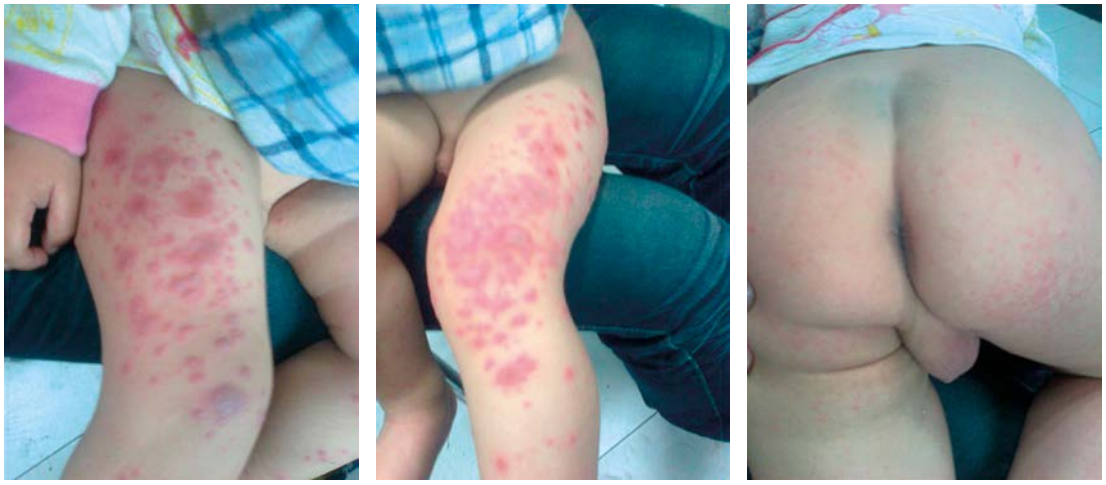

Figure 1. Sporadic pustules and papules on lower limbs and perianal mucosa

The latest large epidemic of EV71-associated HFMD occurred in China in 2008. At the epicenter in Fuyang city, Anhui province, of the 6,049 cases reported between March 1 and May 9, 2008, 3,023 patients were hospitalized, 353 cases were severe and 22 were fatal [6]. The diagnosis of EV71 infection relies mainly on laboratory identification, because not all patients have characteristic skin lesions [7]. The combination of throat swab plus vesicle fluid is most useful, and can increase isolation rates from 49% with throat swab alone, and 48% with vesicle fluid alone, to 67% [8]. EV71 is related to more serious complications. The risk factors contributing to severe HFMD are young male children (≤ 2 years old), general malaise, peak temperature ≥ 38.5°C, atypical physical findings (tachycardia, tachypnea, hypertension, pulmonary hemorrhage and limb movement disorder), leukocytosis and hyperglycemia [9, 10]. Therefore, our case was classified as severe due to the existence of several risk factors, including the fact that the patient was a 6-month-old male, with general malaise, peak temperature ≥ 38.5°C and leukocytosis.

In the present report, we describe for the first time an unusual case of co-infection of EV71 and SA. *Staphylococcus aureus*, a Gram-positive bacterium, is one of the most common causes of both healthcare- and community-acquired infections. A large, multi-center study demonstrated that incidence of SA bacteremia in the United States ranged between 19 and 40 cases per 100,000 with the case fatality rates ranging from 19% to 24% [11]. However, the prevalence of SA infection in China is still unknown. A broad variety of infections, ranging from minor infections of the skin to severe infections such as bloodstream infections and endocarditis, can be caused by SA [12]. In the present case, the chief clinical demonstrations were general malaise, fever, pustules, leukocytosis, elevation of C-reactive protein, and a positive blood culture, which might be attributed, in part, to skin and bloodstream infections. In addition, both cardiac physical examination and echocardiogram were normal in our patient; thus there was no evidence for the existence of endocarditis. Decreased host immunity in this EV71-infected infant may place him at increased risk of SA infection. More persuasively, Furuno *et al.* identified 131 individual episodes of SA bacteremia among HIV-positive patients during the study period between January 1, 2003 and December 31, 2005 [13]. Furthermore, we speculate that individual host genetic factors may also contribute to co-infection of EV71 and SA.

Although the pathogenesis of EV71 infection is still not fully understood, and therapeutic effects of antiviral drugs are controversial, the clinical outcome of our patient was satisfactory after intravenous acyclovir, immunoglobulin and vancomycin, and bed rest for 14 days. Vancomycin is now recommended empirically for SA infection [14]. Besides this, several clinical investigations have also indicated that the use of intravenous immunoglobulin can significantly reduce the acute mortality in patients with either EV71 or SA infection [15, 16].

Conflict of interest

The authors declare no conflict of interest.

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