Besides Increasing Surveillance and Waiting for an Effective Vaccine to Emerge in the Future, What Else Can Be Done to Save the Lives of HFMD Victims?

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The recent outbreak of hand, foot and mouth disease (HFMD) has claimed hundreds of lives in Asia. The Chinese Center for Disease Control and Prevention (China CDC) has confirmed that the HFMD outbreak peaked on May 14, 2008. China’s HFMD cases had reached over 60,000 with 40 fatal cases by May 16, 2008 (Xinhua News Agency). As of July 13, 2008, the Centers for Disease Control, R.O.C. Taiwan, (Taiwan CDC) has reported a total of 317 confirmed severe enteroviral cases this year, including 10 deaths.¹ The Center for Disease Control of the United States (US CDC) issued a travelers’ health alert in July to warn people visiting China, Hong Kong, Singapore and Taiwan to take preventive measures including good personal hygiene and safe food and water practices.

In 1998, Taiwan experienced the largest outbreak of enterovirus (EV) 71 recorded in history, with 129,106 cases reported and 405 children with severe complications, 78 of whom died.² The other EV71 outbreaks occurred in 2000 and 2001: there were 291 severe enteroviral cases, 41 of whom died in 2000, and 393 severe enteroviral cases including 58 fatal cases in 2001.³⁴

What is HFMD and Why Is It So Deadly?
HFMD can be caused by EV71 or coxsackievirus A16 (CA16), but the epidemics during which there were many severe and fatal cases were largely caused by EV71, which have been spreading in countries throughout the Asia-Pacific region for more than a decade. Because the virus is mainly spread by contact with the body fluids of infected persons, the increase in population worldwide has ensured frequent outbreaks in many high population density areas. Infection with EV71 can be deadly in immune naïve or compromised individuals, most often affecting young children and infants who have not been previously exposed to the virus.

EV71 was first isolated in California in 1969.⁵ It can cause severe complications, including meningitis, encephalitis, pulmonary edema and poliomyelitis-like paralysis.⁶ There is as yet no effective vaccine to prevent its infection. Medical treatment aims to target the complications rather than the virus itself. Without an effective antiviral treatment, patients must rely on their own immune system to overcome the infection.
Although EV71 infection is often self-limited, it is recognized that the virus can trigger a fulminating neurologic inflammatory response, which may be associated with cardiopulmonary collapse. These severe symptoms can develop in 2–5 days with very limited time allowed for effective treatment even if any is available.

Several candidate compounds have been developed as EV71 vaccines, including formalin-inactivated whole virus vaccine, DNA vaccine and recombinant protein vaccine, but all require further refinement before they can enter clinical trials.

What Can We Do to Save EV71 Victims?

Without an effective antiviral drug, EV71 victims are left with limited options. Vaccines have limited use for individuals who are already infected with EV71 because of the time required for the development of antiviral immunity to control the rapid course of the disease. Recent success in immune cell therapy, however, has opened a new avenue for treating this deadly infection.

Immune cell therapy has proven to be very effective in targeting viral infections, such as in patients undergoing hematopoietic stem cell transplantation to treat Epstein Barr virus (EBV) and cytomegalovirus (CMV). Using a rapid protocol, antigen-specific interferon-γ-producing immune cells can be isolated within 24 hours. The protocol has been used successfully to treat a young bone marrow transplant patient who developed EBV-associated post-transplant lymphoblastoid disease. Only a very small number of antigen-specific immune cells (10³ per kg body weight) are needed for an effective antiviral response in vivo. Therefore, it is conceivable that EV71 antigen-specific immune cells can be isolated from patients (even at low frequencies) or from their healthy haploidentical relatives, and amplified in culture for 24–48 hours. The immune cells could then be infused into the patients and effectively control the disease. There is little to no complication to this approach as the immune cells applied are highly antigen-specific and would be present at a very low concentration.

Such a protocol should be seriously considered for the emergency treatment of severe HFMD victims, as there is no wonder drug available to come to the rescue in the life or death situation of an acute EV71 infection.

References