Adenovirus in EV71-associated hand, foot, and mouth disease

Sir—Jane Cardosa and colleagues (Sept 18, p 987) report the discovery of a new fastidious adenovirus among patients with suspected hand, foot, and mouth disease (HFMD) in Sarawak. Subsequent to that outbreak, at least five deaths among young children with almost similar clinical presentations were reported in the Malaysian Peninsula. Enterovirus 71 (EV71) was isolated and identified in all five respectively. In the latter case, the adenovirus was circulating in Sarawak as a new fastidious adenovirus among HFMD. We detected and confirmed adenovirus infection by cell culture and immunofluorescence staining from throat and rectal swab samples in only one patient from Sarawak. However, the adenovirus genome was detected by PCR amplification of the hexon gene in at least six other patients with suspected HFMD, including a patient who succumbed to brainstem encephalomyelitis caused by EV71. From this patient, the amplification product was detected only in Vero cells inoculated with pericardial and cerebrospinal fluid but not in cells inoculated with other tissue materials. Nonetheless, the presence of adenovirus in suspected HFMD patients was confirmed by amplification of Vero cells inoculated with blood from a 10-year-old boy. Amino acid sequence from nucleotide sequencing of amplification products showed that the patient’s adenovirus shared at least 95% identity with the hexon gene of adenovirus 7 and the new subgenus B adenovirus. This finding suggests that perhaps a same adenovirus was circulating in Sarawak and the Malaysian Peninsula during the HFMD outbreak.

Our attempts to propagate the virus or clone the sequence from the initial amplification product of other patients were not successful. However, EV71 was isolated from two of the six suspected adenovirus-positive patients. This includes the fatal infection attributed to EV71 and the HFMD case involving the 10-year-old boy from which EV71 and adenovirus were isolated from rectal swab and blood, respectively. In the latter case, the patient had fever, oral ulcer, and rashes on palms consistent with HFMD. Except for tachycardia and slight pleural effusion, no other overt neurological or cardiopulmonary symptoms were noted and the patient was discharged.

Although there is no specific evidence to associate an adenovirus with the fatal HFMD-associated cases in the Malaysian Peninsula, EV71 was identified in almost all cases, not directly from patients’ tissues but after inoculation of cell cultures mainly suitable for enterovirus isolations. Perhaps the presence of a fastidious adenovirus in the suspected HFMD cases was missed because of use of an unsuitable cell culture system. However, Cardosa and colleagues’ report and our own findings suggest that the potential role of a fastidious adenovirus in EV71-associated HFMD needs to be examined further.

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