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Enterovirus 71: The Emerging Threat of Encephalitis in Nepal

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Following the decline of poliovirus, Enterovirus 71 (EV71) has emerged as a major enterovirus, causing outbreaks of hand, foot and mouth disease (HFMD) and neurological complications, particularly among children. EV71 was first identified in the United States in 1969.[1] The virus drew global attention after large outbreaks occurred in Malaysia and Taiwan in 1997. Since then, millions of cases have been reported across the Asia-Pacific region. In Nepal, HFMD has been increasingly recognized since 2016.[2]

EV71 is primarily transmitted via the fecal-oral route, but infection can also occur through respiratory droplets, vesicular fluid, and contaminated surfaces. Humans are the only known natural hosts. After entering the host, the virus initially replicates in lymphoid tissues such as the tonsils and Peyer's patches, before spreading to multiple organs including the central nervous system (CNS). Retrograde axonal spread along cranial or peripheral nerves has been proposed as a mechanism for CNS involvement.

Although, HFMD and CNS infections are the two most recognizable diseases, EV71 infection presents with a broad clinical spectrum. HFMD typically presents as a mild febrile illness with papulovesicular rashes on the palms, soles, and oral mucosa. Of the many enteroviruses that can cause HFMD, Coxsackievirus A16 (CVA16) and EV71 are the most common, with the potential to cause epidemics. CVA16 is not normally associated with neurological disease. EV71, however, is distinctly neurotropic and can cause aseptic meningitis, brainstem encephalitis, acute flaccid paralysis, and neurogenic pulmonary edema.[3] Brainstem encephalitis, frequently followed by pulmonary edema and shock, is a hallmark of severe EV71 infection, often resulting in rapid and fatal cardiorespiratory failure within hours to days. Myoclonic jerks may serve as an early indicator of brainstem involvement and should alert clinicians to possible CNS disease. Other respiratory manifestations in young children include exacerbation of bronchial asthma, bronchiolitis, and pneumonia.

The differential diagnosis of EV71 infection is broad and includes other viral exanthems such as measles, rubella, and varicella; bacterial infections such as meningococcal sepsis and diphtheria; and neurological conditions such as Guillain-Barré syndrome and poliomyelitis. Diagnosis is confirmed by viral isolation or molecular detection by polymerase chain reaction from throat or rectal swabs, cerebrospinal fluid, vesicular fluid, or stool.[1] Magnetic resonance imaging shows characteristic high signal intensities on T2 weighted images in dorsal pons and medulla, midbrain, and dentate nuclei of the cerebellum.

At present, management of EV71 infection remains largely supportive. No specific antiviral therapy is available. Pleconaril, an antiviral tested against other enteroviruses, has not demonstrated efficacy against EV71. Intravenous immunoglobulin (IVIG) may provide benefit due to the presence of neutralizing antibodies and non-specific anti-inflammatory effects. Meticulous fluid management guided by central venous pressure monitoring are essential, especially in cases of brainstem encephalitis or pulmonary edema.

Although several inactivated enterovirus 71 vaccines are now available, effective prevention of EV71 infection still depends on regular hand washing, disinfection of contaminated surfaces, and safe disposal of diapers. During outbreaks, reducing close contact among children, particularly in daycares and schools, can help interrupt transmission. Several Asian countries, including Malaysia, Singapore, Vietnam, Japan, and Taiwan, have declared HFMD a notifiable disease and established surveillance programs for EV71. These measures have proven instrumental in early outbreak

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detection and rapid public health response.

In Nepal, HFMD is being increasingly diagnosed and discussed in clinical practice, although few may be aware of the associated devastating neural illness. Given the potential for fatal consequences, initiating surveillance of EV71 is essential. Integrating screening of enteroviruses into the national Acute Encephalitis Syndrome/Japanese encephalitis surveillance program, could also strengthen understanding and modify control strategy of encephalitis in the country.

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