

TRANSIENT MENINGIOENCEPHALITIS ASSOCIATED WITH ADENOVIRUS INFECTION

To the Editor:

Adenoviruses (AdV) are DNA viruses that typically cause infections involving the upper or lower respiratory tract, gastrointestinal tract, or conjunctiva. Neurological manifestations of AdV infections in immunocompetent children are considered rare, and include meningitis, myelitis, encephalitis and Reye-like syndrome [1]. There are a few case reports describing a distinct entity of AdV-associated-encephalopathy [1,2].

We encountered three male children (mean age 6.5 years, range 4.5–10 years) who presented to the emergency department (ED) with a reduced level of consciousness, convulsions and other signs and symptoms consistent with adenovirus infection, which included tonsillitis (P1 and P3) and conjunctivitis (P2). Physical examination revealed nuchal rigidity in two patients. Lumbar puncture (LP) demonstrated no pleocytosis in P1. In P2 pleocytosis was evident (5 polymorphonuclear cells, 7 lymphocytes and 5 unidentified cells), and in P3 pleocytosis could not be ruled out due to a bloody tap. Toxic screen and brain imaging, including computed tomography (CT) with contrast media and magnetic resonance imaging (MRI), were unremarkable. Electroencephalogram revealed generalized encephalopathy in two children and was unavailable for the third patient. Using polymerase chain reaction (PCR), AdV was identified in the cerebrospinal fluid (CSF) (P2 and P3), sputum (P1 and P3) and blood (P2 and P3). Treatment included antibiotics, acyclovir and dexa-

methasone upon admission. Although the three patients were dramatically ill at presentation in the ED, they all recovered rapidly (3–5 days after admission) with no neurological sequelae.

Most published cases of AdV-related encephalitis occurred in neonates or immunocompromised children, and were typically associated with a fulminant and often fatal course [3]. The current notion is that central nervous system (CNS) involvement due to AdV is rare in the pediatric immunocompetent host [4].

A MEDLINE search of English-language literature for the period 1972–2013 revealed only nine other case reports depicting an acute profound encephalopathy due to AdV that resolves quickly and has no substantial sequelae [1,2]. The most extensive included seven patients, all of whom presented with transient encephalopathy and unremarkable LP results, associated with intercurrent AdV infection [1].

All three patients described here similarly had a stereotypic course of profound encephalopathy and seizures in the presence of intercurrent AdV infection. Patients 2 and 3 had adenovirus viraemia, strongly supporting direct adenoviral involvement of the CNS, although in view of the bloody contamination of the CSF of patient #3, we cannot exclude the possibility that the CSF PCR positivity was a reflection of intercurrent adenovirus viraemia. They all had normal neuroimaging, rapid convalescence, and good neurological outcome.

Due to clinical improvement, the patients were not tested for other viral infections. Moreover, tests for arbovirus infection are not routinely carried out in our institution. Overall, the clinical, laboratory and

imaging studies in our patients support the diagnosis of AdV-related encephalitis.

Evaluation for AdV infections in the ED is not routinely carried out in the setting of pediatric encephalopathy/encephalitis. Finding the etiological agent in cases of acute encephalopathy is important for prognosis and management and to reassure parents if benign entities are documented.

Our findings should increase awareness of this eventually benign and reversible clinical entity. Further studies are needed to assess whether routine evaluation for adenoviral infection should be a part of the encephalopathy and encephalitis investigation algorithm.

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References

1. Straussberg R, Harel L, Levy Y, Amir J. A syndrome of transient encephalopathy associated with adenovirus infection. *Pediatrics* 2001; 107: E69.
2. Kim KS, Gohd RS. Acute encephalopathy in twins due to adenovirus type 7 infection. *Arch Neurol* 1983; 40: 58-9.
3. Schmidt-Hieber M, Schwender J, Heinz WJ, et al. Viral encephalitis after allogeneic stem cell transplantation: a rare complication with distinct characteristics of different causative agents. *Haematologica* 2011; 96: 142-9.
4. Dupuis M, Hull R, Wang H, et al. Molecular detection of viral causes of encephalitis and meningitis in New York State. *J Med Virol* 2011; 83: 2172-81.