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Letter to the Editor

Influenza RNA viral detection in cerebrospinal fluid by PCR in pediatric patients: first report from Cuba

Influenza central nervous system (CNS) disorders are a serious complication of influenza infection, mostly affecting young children.[1] In Cuba, the majority of viral CNS disorders are diagnosed as being caused by enterovirus or herpesvirus infections,[2,3] however the remainder of cases, having predominant early acute respiratory infection symptoms, remain undiagnosed.

In July and August 2005, in the city of Havana, Cuba, eight children died of adenovirus myocarditis during an atypical outbreak of an acute febrile syndrome.[4] In the same period, primary care services detected a spectrum of syndromes, mainly in children – CNS disorders, fever, vomiting and diarrhea, and flu-like illness symptoms – extending the diagnosis of viruses capable of producing them.

The National Influenza Center is involved in investigating CNS disorders in patients with a history of predominant early acute respiratory infection symptoms and cerebrospinal fluid (CSF) samples negative for the genome detection of enteroviruses, herpesviruses, and flaviviruses. Accordingly, 22 pediatric patients were investigated and included in our study; CSF samples and nasopharyngeal swabs were collected.

Viral RNA was extracted from clinical samples using a method described by Casas et al.[5] and tested for respiratory viruses using a previously described multiplex nested reverse transcription polymerase chain reaction (RT-PCR).[6] Isolation was performed in MDCK cell culture, as described in the literature.[7]

The average age of the patients was 5 years, ranging between 5 months and 15 years. Clinical records showed fever (90%), cough (85%), and headache (60%) as the most common symptoms. Other symptoms were vomiting and weakness (45%) and diarrhea (37%).

The most important finding was the detection of three CSF samples positive for influenza virus – one for type A and two for type C; only the patient with CSF positive for influenza A was positive for the virus in the nasopharyngeal swab. The isolation of influenza A from the nasopharyngeal swab was successful; however the virus could not be isolated from any of the CSF samples. Virus isolation from positive CSF is rarely reported,[8] possibly because the virus has disappeared by the time of sampling or because of the low viral load.

A report in the literature has demonstrated that PCR in CSF for other viruses is accurate enough for the diagnosis of viral CNS disorders.[9]

It is not surprising to encounter influenza viruses circulating in Cuba during July and August – the time period of our study – since in tropical zones, seasonal patterns appear to be less pronounced, with year-round detection and isolation of virus.[10] The two hurricanes that hit the island only a few weeks before this situation occurred would also have had an impact.

We could not find any earlier reports of influenza C detection in CSF in the international literature and hence this is the first report from Cuba of the detection of influenza virus genome in CSF. An increased awareness of influenza A, B and C viruses as causes of viral encephalitis is necessary, and studies to determine the incidence, especially during yearly epidemics, should be undertaken.

Conflict of interest

We have no competing interests to declare.

References

1. Amin R, Ford-Jones E, Richardson SE, MacGregor D, Tellier R, Heurter H, et al. Acute childhood encephalitis and encephalopathy associated with influenza: a prospective 11-year review. *Pediatr Infect Dis J* 2008;**27**:390–5.
2. Bello M, Más P, Palomera R, Morier L, Avalos I, Acosta B, et al. Meningoencefalitis virales por enterovirus en Cuba en el período de 1990-1995. *Rev Arg Med Trop* 1997;**29**:176–83.
3. Martínez PA, Díaz R, González D, Oropesa L, González R, Pérez L, et al. The effect of highly active antiretroviral therapy on outcome of central nervous system herpesviruses infection in Cuban human immunodeficiency virus-infected individuals. *J Neurovirol* 2007;**13**:446–51.
4. Valdés O, Acosta B, Piñón A, Savón C, Goyenechea Hernandez A, Gonzales G. First report on fatal myocarditis associated with adenovirus infection in Cuba. *J Med Virol* 2008;**80**:1756–61.
5. Casas I, Powell L, Klapper PE, Cleator GM. New method for the extraction of viral RNA and DNA from cerebrospinal fluid for use in the polymerase chain reaction assay. *J Virol Methods* 1995;**53**:25–36.
6. Coiras MT, Perez-Brena P, Garcia ML, Casas I. Simultaneous detection of influenza A, B, and C viruses, respiratory syncytial virus, and adenoviruses in clinical samples by multiplex reverse transcription nested-PCR assay. *J Med Virol* 2003;**69**:132–44.
7. Youil R, Su Q, Toner TJ, Szymkowiak C, Kwan WS, Rubin B, et al. Comparative study of influenza virus replication in Vero and MDCK cell lines. *J Virol Methods* 2004;**120**:23–31.
8. Okabe N, Yamashita K, Taniguchi K, Inouye S. Influenza surveillance system of Japan and acute encephalitis and encephalopathy in the influenza season. *Pediatr Int* 2000;**42**:187–91.
9. Jeffery KJ, Read SJ, Peto TE, Mayon-White RT, Bangham CR. Diagnosis of viral infections of the central nervous system: clinical interpretation of PCR results. *Lancet* 1997;**349**:313–7.
10. Girard M, Cherian T, Pervikov Y, Kieny MP. A review of vaccine research and development: human acute respiratory infections. *Vaccine* 2005;**23**:5708–24.

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