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Case Report

Acute Cerebellitis Associated with Influenza A(H1N1) pdm09 Virus in a Child, Tunisia, 2016

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Abstract

Neurological manifestations attributed to Influenza virus infection are rare in children as well as in adults. Pandemic Influenza Virus A(H1N1)pdm09 was known to be a cause of these manifestations. In this paper, we report a case patient of an acute cerebellitis in a 4-years-old child associated with Influenza A(H1N1)pdm09 virus infection. The subject consulted for ataxia few days after influenza like illness episode. A nasopharyngeal swab sample was collected and analyzed for Influenza viruses by real time Reverse Transcription-Polymerase Chain Reaction (RRT-PCR) using the Center for Disease Control and Prevention protocol. It was positive for Influenza A (Cycle Threshold value=22.26) and subtyped A(H1N1)pdm09. The Luminex technology using "xTAG® RVP fast v2" kit confirmed the result of Influenza virus and reveals the absence of other respiratory viruses. Other virological investigations were undertaken and no other viral agent was detected. Brain medical imagery was normal. The patient recovered rapidly without sequelae. In conclusion, we retain that Influenza viruses remain a possible infectious etiology for patients with neurological signs. These agents should be included in the etiological research of this type of manifestation especially in the presence of respiratory signs and during periods of high Influenza activity.

Keywords: Cerebellar diseases; Child; Humans; Influenzavirus A; Tunisia

Introduction

Since its appearance in April 2009, the Influenza A(H1N1)pdm09 virus has rapidly spread across the globe, causing wide variety of clinical patterns that vary from asymptomatic infections to complicated respiratory infections [1]. Rarely, it was implicated in Central Nervous System manifestations especially among children [2]. The first report describing patients with seizures and encephalopathy due to Influenza A(H1N1)pdm09 was done on July 24, 2009 in Texas, by the US Center for Disease Control and Prevention (CDC) [3].

Case Report

We report a case-patient of an acute cerebellitis in a child associated with Influenza A(H1N1)pdm09 virus infection. The patient was a 4-year-old boy living in Tunis, the capital of Tunisia. He had no notable previous medical history. The onset of the disease occurred in the night of 02 March 2016. The parents of the child consulted immediately the emergency department of Charles Nicolle Hospital in Tunis. The patient suffered from walking difficulties type stumbling, unsteady gait, difficulty maintaining normal upright posture. The interrogation of the parents reveals no notion of slurred speech, vomiting, headache or visual disturbances but unveils Influenza Like Illness (ILI) syndrome one week ago. Respiratory manifestations were fever, runny nose, muscle aches, headaches and cough.

The examination of this patient revealed fever (temperature 38.5°C), cerebellar ataxia, dysdiadochokinesis and hypermetria. There were no behavioral or cognitive changes. Fever was the unique ILI syndrome symptom at the moment of consultation, all others manifestations disappeared. The hospitalization of the child in the pediatric ward was decided for specialized care. The patient was suspected to present herpetic encephalitis and was treated by Acyclovir 500mg/m2/scX3/day. Blood test results showed a red cells count of 4.76 millions/µl, an hemoglobin of 12.9g/dL, a leukocyte count of 5490 elements/µL, percentages of neutrophils was 54% (2960/µL), lymphocytes 34.6% (1900) and monocytes 10.7% (590/µL). Platelets count were 250000/µL. Levels of electrolytes, liver enzymes and C-reactive protein were within reference ranges. A lumbar puncture drained clear and Colorless Cerebrospinal Fluid (CSF) leukocytes were less than 1 elements/µL, red cells were 400/µL and bacteriological culture was negative. Chlorurachia and proteinorachia were within normal range. Glycorachia was slightly increased 4.08 (2.22-3.89) mmol/L. Hemocultures were negative. Viral serology for *Varicella-zoster virus* (VZV), *Herpes simplex virus* (HSV1/2), *Epstein-Barr virus* (EBV), *Cytomegalovirus virus (CMV)* and Mycoplasma pneumonia were negative for the IgM and positive for the IgG which excludes a current infection by these infectious agents. The genome detection by molecular biology of CSF was negative for Human Herpes Virus 6 and 8, Herpes Simplex Viruses 1/2, Varicella Zoster Virus, West Nile virus and Influenza viruses. A nasopharyngeal swab sample was collected and analyzed for Influenza viruses by real time RT-PCR using the CDC Atlanta protocol. It was positive for Influenza A (Cycle Threshold (CT) value = 22.26) and subtyped A(H1N1)pdm09. The Luminex technology using "xTAG® RVP fast v2" kit confirmed the result of Influenza virus and reveals the absence of other respiratory viruses. Brain Magnetic Resonance Imaging (MRI) has objectified no abnormalities. The evolution showed a persistence of the fever for 3 days with a progressive and spontaneous disappearance of the cerebellar syndrome. The duration of hospital stay was 4 days. The patient returned home without any signs of cerebellar ataxia or Influenza confirmed symptoms.

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Discussion

Cerebellitis, or acute cerebellar ataxia, is defined as an inflammation affecting the cerebellar white matter. The most common etiology is an acute systemic viral infection [4]. We report a case of a 4-year-old child that developed cerebellitis a week after an Influenza virus infection episode-characterized by fever, runny nose, muscle aches, headaches and cough- which was diagnosed Influenza A(H1N1)pdm09 detected in a nasopharyngeal sample. The imagery was normal. No other infectious agent was found. Fever was the unique persistent influenza infection symptom at the moment of consultation. He recovered rapidly without sequelae or any respiratory manifestation.

Neurological manifestations associated to seasonal Influenza virus were reported in the literature [2,5]. Influenza A(H1N1)pdm09-associated neurologic complications were present in 4% of patients with a Severe Acute Respiratory Infections (SARI) due to Influenza viruses [6]. The children seem to be more frequently affected than adults [3,6]. Other viruses than Influenza are more incriminated in neurological manifestations among children, such as VZV, HSV (1/2), EBV, CMV, Enterovirus, West-Nile virus [4]. In our case-patient, serological findings and PCR performed on the CSF showed no acute infection with these agents. Influenza A(H1N1)pdm09 RNA was not isolated in CSF, either. Nevertheless, high positivity in nasopharyngeal swab (CT value 22.26) led to consider strong link between Influenza and cerebellitis onset. Similarly, some authors reporting Influenza-associated cerebellitis could not detect Influenza RNA in CSF [7-9]. These findings suppose the absence of the direct effect of virus invasion and replication and suggest that neurologic manifestations such as encephalitis may be an indirect effect of the presence of the virus in the respiratory tract. Indeed, different studies revealed the involvement of metabolites and inflammatory mediators, such as hyper activated cytokine response, in the process of the pathology [10]. Specific physiopathology making disorder leading to acute cerebellitis is not well discussed in literature. However, some other authors reported that Influenza RNA was detected in the CSF of patients with acute cerebellitis which provided clearer diagnosis [11-13].

MRI is an excellent non invasive method to explore cerebellitis cases; it shows various patterns of cerebellar involvement [8]. Nevertheless, in some cases like our and cases from literature, it remains totally normal [9,11]. MRI low sensibility could explain normal or very inconspicuous images in cerebellitis [14,15]. In addition to that, MRI features should be critically related to time of its applying as some authors described delayed MRI abnormalities. For our case, it was performed at the same day of ataxia onset and not proposed later on since studied patient recovered totally without sequalea within few days.

Conclusion

To conclude, for patients presenting neurological signs occurring during or few days after ILI or SARI syndrome, Influenza viruses is a possible infectious etiology and should be taken into consideration especially during flu season and other periods of high influenza activity.

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