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CASE REPORT

Neurological manifestations of influenza a infection in an adolescent

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Adolescent, Influenza, Encephalitis, Consciousness Disorders.

Abstract

Objective: Neurological complications connected to influenza are rare. We report a case of a 17-year-old teenager with fever and neurological manifestations. **Case Report:** 17-year-old teenager with altered mental status and seizures. Imaging investigation and cerebrospinal fluid analysis did not show relevant alterations. The nasopharyngeal swab was positive for influenza B virus. We assumed a possible case of influenza B encephalitis. **Comments:** Encephalitis associated with influenza infection should be considered when respiratory symptoms and altered mental status are present, if the epidemiological context is appropriate. In influenza encephalopathy, viral invasion of the central nervous system is usually not found and imaging investigation is often normal, constituting a diagnostic challenge.

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INTRODUTION

Influenza infection is usually self-limited and causes mild respiratory symptoms, although it can be associated with multiple complications[1-5]. Neurologic complications associated to influenza have been observed at a rate of 1 to 4 per 1000,000 people per year[2]. It is hard to estimate the real incidence of these complications because there is no uniformity in diagnostic criteria and it is assumed that its incidence is probably underestimated[2-8].

Although both influenza A and B viruses can be associated with neurological complications, most studies focus on complications associated with influenza A[3-5].

The neurological manifestations have a high clinical variability: from febrile seizures to serious neurological conditions[1-7,9-11]. In literature, one of the most frequently described neurologic complication is seizures, followed by encephalopathy[1,2,6,11].

The causality between neurological complications and influenza infection is hard to establish. Imaging evaluation, cerebrospinal fluid (CSF) analysis and electroencephalography are normal in most cases[2,5,7-9].

Cytochemical abnormalities, when present, tend to be limited to mild CSF pleocytosis with predominance of mononuclear leukocytes[5]. Neuroimaging abnormalities have been described including nonspecific T2 sign abnormalities in the splenium and other areas, focal and generalized cerebral edema[2]. Some severe cases exhibit multifocal symmetrical distributed brain lesions of the thalamus cerebral white matter, brainstem, cerebellum, and parenchyma[11].

CASE REPORT

We describe a case of a previously healthy 17-year-old female, with no regular medication. She was observed in an emergency service after three brief episodes of generalized tonic-clonic seizures. Alcohol, illicit substances or medication abuse was denied, as well as recent travel. She referred frontal headache with 4 days of evolution, associated with bilateral ocular pain, photo and phonophobia. Asthenia, dry cough, rhinorrhea, and odynophagia were also mentioned.

On admission, the patient was febrile (38,7°C) and hemodynamically stable, with normal pulse oximetry. She presented a reasonable general state and skin paleness. Pulmonary auscultation was normal. Neurological examination revealed a Glasgow Coma Scale 15 but she was lethargic and bradipsychic. She verbalized with no formal changes of the speech and presented no oculomotor abnormalities. She had a bilateral Bell's phenomenon, suggesting facial diplegia, as well as proximal and distal muscle weakness. There were non-responsive osteotendinous upper limbs reflexes but present in the lower limbs. Meningeal signs were absent. She had no other relevant alterations in physical examination.

Complementary findings included normal complete blood count, biochemistry (including lactate), venous blood gas analysis and negative urine toxicology screen. Nasopharyngeal swab was obtained for virus research (influenza A and B, syncytial respiratory virus). Chest radiography revealed bilateral hilar reinforcement. Cranial computed axial tomography was normal. CSF analysis revealed no pleocytosis or elevated protein levels. RT-PCR testing for influenza was not performed in CSF.

Due to the progressive worsening of the neurological symptoms (decreasing state of consciousness), the patient was admitted to an intensive care unit (ICU). The following differential diagnoses were considered: Miller Fisher variant of Guillain-Barre syndrome, bacterial or viral infection of the central nervous system (CNS). Endovenous acyclovir (10mg/kg), ceftriaxone (2g/day), azithromycin (500mg/day), and immunoglobulin (2g/kg) were initiated.

During her stay in the ICU, the patient had an episode of urinary retention with need for catheterization, and an episode of liquid dysphagia. Electroencephalogram (EEG), cranial and neuroaxis magnetic resonance imaging (MRI) did not reveal abnormal findings.

Approximately 24h later, there was a progressive neurological recovery. Influenza B virus was identified by RT-PCR in the nasopharyngeal swab, without co-infection with other viruses.

The previous medication was suspended and oseltamivir (75mg 12/12h) was taken for five days. Given the favorable clinical evolution, she was discharged at the end of the treatment, with normal neurological examination.

DISCUSSION

The pathogenesis of neurological manifestations associated with influenza remains uncertain[7,9,11,13]. The fact that these viruses are rarely identified in CSF and have no apparent central nervous system tropism support the hypothesis of the existence of more than one pathophysiological mechanism leading to a broad spectrum of neurological manifestations[6]. It is postulated that the immune process preceding neurological manifestations can be divided into two categories. In the first, there is a systemic inflammatory response that causes a deregulation of inflammatory cytokines, which, together with innate immunity, are responsible for acute manifestations (seizures, encephalopathy, acute changes of movement)[6,7]. The second one is an adaptive response of cellular immunity, which is associated with complications such as Guillain-Barre syndrome or transverse myelitis[6].

In this report, we assume a possible case of influenza B encephalitis, which can cause a broad spectrum of clinical manifestations, from mental confusion to comatose state[1,2,9,13]. According to the Consensus Statement of the International Encephalitis Consortium 2013[3] encephalitis is defined as inflammation of the brain parenchyma associated with neurologic dysfunction (Table 1). A possible case of encephalitis is defined by the presence of 1 major criteria and 2 minor criteria[3,10]. Our patient had altered mental status for 24h without any other identified cause (major criteria). In addition, she presented fever and general seizures (minor criteria), as well as laboratory-confirmed influenza B infection. The initial neurologic findings, the

Table 1. Encephalitis criteria.

Major criteria	Altered mental status (defined as decreased or altered level of consciousness, lethargy or personality change) lasting for 24 or more hours without another identified cause
Minor criteria	Fever
	General or partial seizures
	New onset of focal neurologic findings
	CSF leukocyte count ≥5cells/mm^3
	Abnormality of brain parenchyma on neuroimaging suggestive of encephalitis

Source: Adapted from Consensus Statement of the International Encephalitis Consortium 2013[3].

clinical course and the investigation (identification of influenza B in the nasopharyngeal swab, normal CSF analysis, EEG and MRI) excluded other diagnosis: Miller Fisher variant of Guillain-Barre syndrome, bacterial or another viral infection of the CNS.

Of the few cases described in the literature of encephalitis associated with influenza B, we highlight a case of a 16-year-old girl with seizures, confusion, nystagmus, and motor incoordination, beginning 5 days after upper respiratory tract infection. The analysis of the CSF and the CE MRI did not show changes. EEG revealed generalized slow activity without epileptiform activity. Influenza B infection was confirmed by RT-PCR and influenza B-associated encephalopathy was diagnosed[10].

In a retrospective study analyzing the neurological complications associated with influenza in hospitalized children, it was found that encephalopathy is a rare manifestation of this infection and that the majority of patients do not present changes in the CSF or in imaging exams. Of 842 children with influenza infection 153 died due to influenza complications and 6% of these deaths were attributed to encephalopathy[12].

Regarding the treatment, it is not consensual if antiviral therapy prevents the appearance of neurological complications. There are studies showing a reduction in morbidity and mortality due to influenza in patients treated with neuraminidase inhibitors[2,4,5]. Therefore, it is recommended to initiate immediate treatment with oral oseltamivir or inhaled zanamivir, in hospitalized patients with influenza infections. It shows greater efficacy when administered within the first 48 hours of illness[4]. The adamantanes neuraminidase inhibitors (amantadine and rimantadine) aren't recommended because all seasonal influenza viruses are resistant to these agents[4]. Supportive measures are also required[6].

With this case, we intend to alert other clinicians to the fact that when a patient presents with fever and altered mental status or other neurologic manifestations, influenza infection should be considered, if the epidemiological context is appropriate.

REFERENCES

1. Manjunatha N, Math SB, Kulkarni GB, Chaturved SK. The neuropsychiatric aspects of influenza/swine flu: a selective review. Ind Psychiatry J. 2011 Jul;20(2):83-90.
2. Ekstrand JJ. Neurologic complications of influenza. Semin Pediatr Neurol. 2012 Sep;19(3):96-100.
3. Popescu CP, Florescu SA, Lupulescu E, Zaharia M, Tardei G, Lazar M, et al. Neurologic Complications of Influenza B Virus Infection in Adults, Romania. Emerg Infect Dis. 2017 Apr;23(4):574-81.
4. Paules C, Subbarao K. Influenza. Lancet. 2017 Aug;390(10095):697-708.
5. Newland JG, Romero JR, Varman M, Drake C, Holst A, Safranek T, et al. Encephalitis associated with influenza B virus infection in 2 children and a review of the literature. Clin Infect Dis. 2003 Apr;36(7):87-95.
6. Goenka A, Michael BD, Ledger E, Hart IJ, Absoud M, Chow G, et al. Neurological manifestations of influenza infection in children and adults: results of a National British Surveillance Study. Clin Infect Dis. 2014 Mar;58(6):775-84.
7. Gallagher J, Luck RP, Del Vecchio M. Case 1: altered mental status – a state of confusion. Paediatr Child Health. 2010 May/Jun;15(5):263-6.
8. McCullers JA, Facchini S, Chesney PJ, Webster RG. Influenza B virus encephalitis. Clin Infect Dis. 1999 Apr;28(4):898-900.
9. Akins PT, Belko J, Uyeki TM, Axelrod Y, Lee kk, Silverthorn RJ. H1N1 encephalitis with malignant edema and review of neurologic complications from influenza. Neurocrit Care. 2010 Dec;13(3):396-406.
10. Reyes C, Miranda S, Fica A, Navarrete M. Encefalitis por vírus influenza B em um paciente adulto. Reporte de caso. Rev Méd Chile. 2019 Jul;147(7):922-7.
11. Wang GF, Li W, Li K. Acute encephalopathy and encephalitis virus infection. Curr Opin Neurol. 2010 Jun;23(3):305-11.
12. Newland JG, Laurich VM, Rosequist AW, Heydon K, Licht DJ, Keren R, et al. Neurologic complications in children Hospitalized with influenza: characteristics, incidence, and risk factors. J Pediatr. 2007 Mar;150(3):306-10.