

# Novel Swine-Origin Influenza A (H1N1) Viral Encephalitis

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The World Health Organization declared that a new strain of novel swine-origin influenza A (H1N1) virus was responsible for the pandemic infection in June 2009. We report a case of encephalitis diagnosed as the H1N1 virus infection. We describe a 17-year-old patient who had a seizure attack, diagnosed with a H1N1 virus infection via real time reverse-transcriptase polymerase chain reaction (RT-PCR). The H1N1 virus infection can be causative of the encephalitis, as with other influenza virus infections. Careful monitoring is essential for reducing complications.

**Key Words:** H1N1 virus, encephalitis, seizure

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## INTRODUCTION

A novel swine-origin influenza A (H1N1) virus was identified in Mexico and the United States in April 2009 followed the rapid spread of this pathogen all over the world. The H1N1 virus usually causes a febrile respiratory symptoms including fever, cough, sore throat, etc. These symptoms are a self-limited course, but severe complications and death are still increasing.<sup>1</sup> The neurologic complications of this virus have been rarely reported. We herein report a case of encephalitis diagnosed as a H1N1 virus infection.

## CASE REPORT

A 17-year-old male was admitted to our hospital due to a seizure attack on October 30, 2009. He had visited a doctor 2 days before admission because of a cough, sputum, and fever (the highest temperature was 37.7°C), and a nasopharyngeal swab was performed to test for the H1N1 virus. Because there was an exponentially increased number of H1N1-infected patients at that time in Korea, the Center for Disease Control dictated that a patient who had respiratory tract symptoms with a fever should take Oseltamivir (Tamiflu) in advance without confirmation of the disease. He took the Oseltamivir 75 mg twice for a day. The seizure attack happened while he was sleeping at night. When his mother found him, he had a generalized tonic seizure with eyes deviating upward and tongue biting for 5 minutes. Postictal confusion lasted for about 20 minutes until he arrived at the hospital. He did not remember why he was in the hospital and what had happened when he woke up on the next morning.

He was diagnosed with chronic pansinusitis but he recovered without any medications. He did not have a previous seizure attack, or even febrile convulsion.

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There was no family history of epilepsy. His body temperature was 36.9°C at the emergency room and the neurologic examination was normal except for disorientation at the time.

The cerebrospinal fluid (CSF) test revealed a pressure of 7 cmH<sub>2</sub>O, WBC of 15/μL, RBC of 0/μL, protein of 31.3 mg/dL and glucose of 81 mg/dL. The CSF examination for the Epstein-Barr virus, cytomegalovirus, herpes simplex type 1 and 2, bacteria, tuberculosis and fungus provided negative findings for all. The H1N1 influenza virus real time reverse-transcriptase polymerase chain reaction (RT-PCR) via a nasopharyngeal swab was the only positive test. The electroencephalography (EEG) was non-specific. The brain MRI with gadolinium enhancement revealed normal findings except for pansinusitis.

He took Tamiflu 75 mg twice a day for 5 days and was prescribed oxcarbazepine 300 mg twice a day. He was discharged without a recurring seizure attack.

## DISCUSSION

A healthy 17-year-old male was transferred to the emergency room due to a seizure attack. The seizure occurred on the second day of respiratory symptoms with a fever. He was confirmed with the H1N1 virus infection by a real time RT-PCR via a nasopharyngeal swab after 5 days of the symptoms' onset.

In Korea, there have been about 3,600 confirmed cases of H1N1 virus infections up until October 31, 2009. More than half of the patients infected with the H1N1 virus ranged between the ages of 10 and 19 years. This infection has been rapidly spread all over the world, but the symptoms are generally mild and patients mostly recover, although neurologic complications such as a seizure, subsequent postictal mental state, and confusion have been present in four children in the United States.<sup>2</sup>

In this patient, febrile respiratory symptoms, CSF pleocytosis, and the first seizure during his life can be a reliable basis for the diagnosis of encephalitis.<sup>2,3</sup> Furthermore, the seizure occurred on the second day of the febrile respiratory illness which was a confirmed H1N1 virus infection. This is why we regard this case as a neurologic complication of the H1N1 virus.

He did not have a high fever at the time of the seizure attack and he was too old to have a febrile convulsion. We considered it as a case of a co-infectious disease of viral encephalitis, but his clinical symptoms were easily controlled and he rapidly recovered, so the probability of a co-

infectious disease was less likely. The seizure attack could be regarded as a side effect of Oseltamivir. A large amount of Oseltamivir was prescribed to the confirmed or suspicious H1N1 infectious patients, but there was no report about a seizure attack as a side effect of the drug. And CSF pleocytosis cannot be explained by the drug side effects.

We performed CSF real time RT-PCR at laboratories of the Department of Microbiology and Laboratory Medicine, but the results were negative. The previous report of children's encephalitis in the United States shows that CSF PCR were also all negative in the three cases.<sup>2</sup> Even with best efforts for diagnosis, 30-60% of the patients with clinically suspected viral encephalitis remain unconfirmed.<sup>4</sup> Viral culture, serological (immunological) test, and PCR can be available, but many difficulties still exist, including a lack of specialized facilities, derivation of antibodies in the serum and CSF, and false positivity/negativity.<sup>4,5</sup> These results may also be related to the time of sampling CSF, which is critically related to detection.<sup>3</sup> It can be also influenced by the fact that our patient had already taken the antiviral medications.

The number of H1N1 virus infection cases is still increasing substantially with widespread community transmission. To the best of our knowledge, this is the first report of a neurological complication associated with the H1N1 virus in Korea.

Almost all H1N1 virus infections induce mild respiratory symptoms and signs, but severe complications including neurologic problems can occur. Active treatment and careful monitoring should be essential for reducing complications, which is based on the identified pathogenesis up to now.

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