

CASE REPORT

Possible Association of New-Onset Seizure with the H1N1 Influenza Vaccine

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Since the introduction of the H1N1 influenza vaccine in the wake of the 2009 H1N1 influenza pandemic, many serious and nonserious adverse events related to the vaccine have been reported. We describe a 59-year-old African-American man with severe chronic heart failure and chronic obstructive pulmonary disease who experienced a new-onset, generalized tonic-clonic seizure less than 1 hour after receiving the H1N1 vaccine. He had never experienced any reactions to previous seasonal influenza vaccines. His medical history, physical examination, and targeted investigations revealed no evidence of other potential etiologies for his seizure. After this event, the patient, who was discharged without anticonvulsant therapy, remained seizure free for the next 10 months. Use of the Naranjo adverse drug reaction probability scale indicated a possible relationship (score of 4) between the patient's seizure and the receipt of the H1N1 vaccine. This is the first case report, to our knowledge, to suggest a possible association between the H1N1 influenza vaccine and seizure. The mechanism of the association is unclear. Further case series may clarify the nature of the association.

Key Words: seizure, H1N1 vaccine, influenza.

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With the emergence and rapid spread of the H1N1 influenza virus during the first influenza pandemic this century, it was crucial to develop an effective vaccine to minimize the morbidity and mortality related to this infection. After the licensure of the first 2009 influenza A (H1N1) monovalent vaccine by the United States Food and Drug Administration on September 15, 2009, and its distribution nationwide in October 2009, approximately 124 million doses had been distributed by January 29, 2010.¹ To assess the safety profile of the H1N1 vaccine in the United States, the Centers of Disease Control and Prevention reviewed reports received through the

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Vaccine Adverse Event Reporting System (VAERS) and electronic data from the Vaccine Safety Datalink, a large, population-based database with administrative and diagnostic data.² As of May 29, 2010, VAERS had received 11,180 adverse-event reports concerning patients who had been administered the 2009 monovalent H1N1 vaccine. The vast majority (92.2%) of the events were classified as nonserious, whereas 868 events (7.8%) were considered serious (defined as life-threatening or resulting in death, major disability, abnormal conditions at birth, hospitalization, or extension of an existing hospitalization).³ We report what may be the first published case of new-onset seizure possibly associated with receipt of the H1N1 vaccine.

Case Report

A 59-year-old, African-American man presented for a routine primary care office visit. He received 0.5 ml of the 2009 H1N1 monovalent

inactivated influenza vaccine (Sanofi Pasteur, Lyon, France) intramuscularly right before leaving the office. Forty-five minutes after receiving the vaccine, while being driven home by his wife, the patient developed nausea and lightheadedness that lasted for a few minutes. His wife described rhythmic jerking of all extremities that lasted for 4 minutes, associated with eye rolling, frothy oral secretions, bladder and bowel incontinence, diminished responsiveness, and confusion. The patient's mental status change resolved during an ambulance ride to the emergency department, 90 minutes after receiving the vaccine. His only complaint at that time was headache.

The patient's medical history was significant for hypertension, severe nonischemic cardiomyopathy with an ejection fraction of 20% (probably secondary to remote cocaine abuse and hypertensive cardiomyopathy) and implantable cardioverter-defibrillator placement, severe chronic obstructive pulmonary disease, dyslipidemia, and gastroesophageal reflux disease. No history of head trauma or previous seizures, or family history of epilepsy was reported. He did not drink alcohol, nor did he use tobacco or any illicit drugs. He had achieved abstinence after a remote history of cocaine abuse, which was confirmed by consecutive negative results from drug screening tests in our office.

The patient's drug therapy consisted of aspirin 325 mg/day, lisinopril 20 mg/day, furosemide 40 mg twice/day, spironolactone 25 mg/day, pravastatin 40 mg/day, hydralazine 50 mg 3 times/day, isosorbide mononitrate 20 mg twice/day, ranitidine 150 mg twice/day, and theophylline 200 mg twice/day, in addition to tiotropium bromide and budesonide inhalers. No changes had been made in his drug regimen over the last 3 months; he denied taking any new drugs, nutritional supplements, or herbal remedies. He received the trivalent seasonal influenza vaccine 2 months earlier without incident, as he had done in 2007 and 2008. He had no known drug or food allergies, including eggs.

The patient's physical examination in the emergency department was unremarkable except for scattered end-expiratory wheezing; his vital signs were stable. He was alert, awake, and oriented and had intact extraocular movements and cranial nerves. He had normal power, tone, and reflexes bilaterally; no sensory deficits were appreciated.

Laboratory results showed a complete blood

cell count, basic metabolic panel, thyroid-stimulating hormone level, and cardiac markers all within their normal ranges. Transient elevations were noted in the patient's alanine aminotransferase level, from 68 U/L at baseline to 108 U/L (normal range 0–55 U/L), and aspartate aminotransferase level, from 56 U/L at baseline to 121 U/L (normal range 5–34 U/L). His theophylline level was subtherapeutic at 6.6 mg/dl (therapeutic range 10.0–20.0 mg/dl). Noncontrast computed tomography of the head revealed chronic ischemic changes with no masses, hemorrhage, or acute changes. Electroencephalogram (EEG) showed a well-defined rhythm of 10.5 Hz of medium voltage in the occipital regions and occasional replacement with low-voltage theta activity during drowsiness, consistent with normal drowsy and awake EEG patterns. No urine drug screen was performed at the time of presentation, but a cocaine-induced seizure was not likely based on his long-term, confirmed abstinence. Magnetic resonance imaging was not performed due to the presence of his implanted metal cardioverter-defibrillator. During his hospitalization, the event was reported to the Centers for Disease Control and Prevention through VAERS. He was discharged without antiepileptic drugs and instructed not to operate a motor vehicle for 6 months. The patient remained seizure free for the next 10 months.

Discussion

This patient was brought to the emergency department after experiencing a seizure manifested as tonic-clonic phase followed by postictal confusion and headache. No trigger or correctable metabolic cause was found; neurologic examination, imaging, and EEG results were normal. The patient had no history or risk factors for seizure and had received the H1N1 influenza vaccine 45 minutes before experiencing the new-onset seizure. Use of the Naranjo adverse drug reaction probability scale⁴ indicated that the seizure was a possible (score of 4) adverse drug reaction from the vaccine. It is not clear whether this was an idiosyncratic reaction to the vaccine or just a random association. The mechanism of this association is unknown. In fact, multicenter, randomized controlled trials as well as safety studies of the H1N1 vaccine did not list seizures as an adverse reaction.^{5–7} This is not unexpected; rare adverse reactions may not be detected before widespread distribution of a

vaccine or drug. In one of the trials, solicited local reactions included pain or tenderness, erythema, swelling, induration, and ecchymosis, whereas systemic reactions were fever, headache, malaise, myalgia, and shivering.⁶

To our knowledge, only two other seizures have been reported to VAERS in association with H1N1 influenza vaccines⁸; however, seizures have been reported after receipt of seasonal influenza vaccines. In one study that used VAERS data to evaluate serious adverse events in children after receiving trivalent inactivated influenza vaccine during three influenza seasons, 35 seizures were noted. Twenty-nine of these seizures were thought to be possibly related to the influenza vaccine, although 18 were associated with fever, and five of the patients had experienced previous seizures.⁹

Our patient experienced 59% and 116% increases in his alanine and aspartate aminotransferase levels, respectively, that resolved 4 months later. These are more likely associated with the seizure than with influenza vaccination. Transaminase level elevations have been described after grand mal seizures.¹⁰ There were no changes in liver function tests after influenza vaccination in a series of 58 patients who had cirrhosis or had received liver transplants.¹¹

Conclusion

We present what we believe to be the first published report of a possible association between the receipt of the H1N1 influenza vaccine and new-onset seizure. The mechanism of the association is unclear. Additional case

series may clarify the nature of this association.

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