Longitudinally Extensive Transverse Myelitis Following Vaccination With Nasal Attenuated Novel Influenza A(H1N1) Vaccine

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Background: Transverse myelitis has been reported in association with vaccination, including influenza vaccination.

Objective: To describe a case of longitudinally extensive transverse myelitis associated with vaccination with a nasal attenuated novel influenza A(H1N1) vaccine.

Design: Case report.

Setting: Sanford University of South Dakota Hospital.

Patient: A 27-year-old woman with longitudinally extensive transverse myelitis.

Results: Four days following novel influenza A(H1N1) vaccination, the patient developed longitudinally extensive transverse myelitis. Extensive diagnostic evaluation effectively ruled out causes other than vaccination-associated transverse myelitis. Following treatment with corticosteroids and plasmapheresis, the patient made a significant recovery.

Conclusions: Transverse myelitis may be associated with vaccination against novel influenza A(H1N1). Additionally, we believe this to be the first report of longitudinally extensive transverse myelitis associated with any vaccine.

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Widespread vaccination against 2009 novel influenza A(H1N1) has been implemented as a part of US public health policy. Although vaccination has been associated with autoimmune sequelae, relatively few of these complications have been reported in association with the novel influenza A(H1N1) vaccine to date, despite its extensive use.1 Herein we describe a patient who developed longitudinally extensive (LE) transverse myelitis (TM) in association with novel influenza A(H1N1) vaccination.

REPORT OF A CASE

A 27-year-old right-handed woman with a medical history significant only for remote cervical spine fusion and with no family history of autoimmune disorders had a 2-week history of back and lower extremity pain with gradual weakness and paresthesias of the legs, accompanied by urinary retention. This progressed to involve all extremities and ultimately an inability to stand. She reported no prior neurological symptoms or respiratory or gastrointestinal illness preceding the onset of symptoms. She was receiving no medications. Four days prior to the onset of symptoms, she received the attenuated-virus nasal novel influenza A(H1N1) vaccine. Examination revealed mild proximal muscle weakness with mildly diminished sensation of the upper extremities as well as moderate proximal weakness with profound sensory loss in the lower extremities. Sensation was also moderately diminished on the trunk, with a T4 sensory level. There was diffuse hyperreflexia. Plantar response was silent and no clonus was noted.

Magnetic resonance imaging revealed extensive intramedullary nonenhancing T2 hyperintensity extending from the cervical medullary junction throughout the length of the thoracic cord (Figure). Brain magnetic resonance imaging results were normal. Laboratory testing revealed negative results for serum angiotensin-converting enzyme, antinuclear antibody, rheumatoid factor, neuromyelitis optica antibodies, and...
human immunodeficiency virus, Lyme disease, and West Nile virus serologies. Epstein-Barr virus, cytomegalovirus, and mycoplasma IgG results were positive, but their respective IgM results were negative. Sedimentation rate and vitamin B$_12$ levels were normal. Cerebrospinal fluid had a protein concentration of 0.223 g/dL (to convert to grams per liter, multiply by 10.0), a glucose concentration of 41 mg/dL (to convert to millimoles per liter, multiply by 0.0555), and a white blood cell count of 517/µL (to convert to 10$^9$/L, multiply by 0.001) with 98% lymphocytes. Bacterial, fungal, and viral culture results were negative. No oligoclonal bands were present. Following treatment with daily intravenous methylprednisolone (1 g/d) and plasmapheresis both for 5 days followed by slow taper over 6 weeks, symptoms significantly improved.

**COMMENT**

Transverse myelitis is a focal inflammatory demyelinating disorder of the spinal cord, commonly due to an autoimmune process. When the lesion extends more than 3 vertebral segments in length, it is referred to as LETM. The extensive demyelination throughout almost the entire length of the spinal cord in this patient is consistent with a severe case of LETM.

While establishing the diagnosis of TM is reasonably straightforward, determining the exact cause can be challenging. Possible causes include multiple sclerosis, acute disseminated encephalomyelitis, neuromyelitis optica (infectious or parainfectious), and vasculitis with multisystem diseases such as lupus, vascular disease, or postvaccination disease. Idiopathic TM encompasses those cases without other associated causes identified.

The absence of multiple sclerosis–like lesions in the brain, marked cerebrospinal fluid pleocytosis, absence of oligoclonal bands in the cerebrospinal fluid, and the extensive spinal cord lesion all made multiple sclerosis unlikely. The imaging also effectively ruled out acute disseminated encephalomyelitis and vascular lesions. Although LETM correlates commonly with neuromyelitis optica, this case did not meet the diagnostic criteria for that condition. There was no clinical evidence of optic neuritis, and visual evoked potentials were normal. Neuromyelitis optica–IgG antibodies, which have 73% sensitivity, were also negative. The negative serology results coupled with the negative bacterial, viral, and fungal culture results on the cerebrospinal fluid excluded the possibility of an infectious cause. There was no laboratory evidence of vasculitis or connective tissue disease. Having effectively eliminated the most probable causes for this patient’s condition, we attributed it to postvaccination TM following novel influenza A(H1N1) vaccination.

Transverse myelitis is a relatively uncommon condition, and vaccine-associated TM cases are even more scarce. It has been reported to occur following administration of a wide variety of vaccines, including diphtheria and tetanus toxoids and pertussis vaccine, measles, mumps, and rubella virus vaccine, Haemophilus influenzae type B vaccine, oral poliovirus vaccine, Japanese encephalitis virus vaccine, hepatitis B vaccine, cholera vaccine, typhoid vaccine, rabies vaccine, and seasonal influenza virus vaccine. A recent review of the literature found a total of 37 cases of vaccine-associated TM. While a pathogenic causal relationship has been established only for the oral poliovirus vaccine, the temporal relationship of TM with such a wide variety of vaccines suggested to those investigators that a common denominator such as an adjuvant might trigger the syndrome. The 2009 novel influenza A(H1N1) vaccines, however, do not contain an adjuvant. If a common factor between vaccines is the proximal cause of postvaccination TM, it is something other than the adjuvant in this case. Further studies of postvaccination TM, likely in model systems owing to the condition’s rarity, are needed to clarify the risk and its mechanism.

In conclusion, this is a case of a patient with LETM in whom other potential causes have been systematically investigated and eliminated. To our knowledge, this is the first report of TM following novel influenza A(H1N1) vaccination. Additionally, we believe it to be the first report of LETM associated with any vaccine.

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REFERENCEs