Acute encephalopathy following TDAP vaccination

Abstract

A 42-year-old male with a past medical history of hypertension was brought to the emergency department (ED) by his family for evaluation of altered mental status (AMS) that started one day prior to presentation. His symptoms started after he received the Tdap vaccine. He became agitated the evening of administration along with becoming restless. On the day of his presentation to the ED, around 3AM, his wife found him in the bathroom. He reported feeling nauseated and had one episode of vomiting. He was cold, clammy, was sweating profusely and did not reply to any of his wife’s questions. The wife then called the other family members and brought him to the ED for his abnormal behavior. On exam, he was alert but intermittently agitated. He remained non-verbal. His vitals were within normal limits. Neurological examination was limited, as the patient was not following commands. He was moving all his extremities. The remaining aspect of the physical examination was unremarkable. Computed Tomography of the brain was done which showed no acute abnormality. He was admitted for inpatient management of acute encephalopathy. Basic lab workup including complete blood count (CBC) and comprehensive metabolic panel (CMP) was within normal limits. Serum glucose, alcohol and acetaminophen levels were checked which were normal. Urine drug screen panel was negative. His Urinalysis was only positive for 20 ketones. Serum lactate was 2.03 and procalcitonin was normal. On further inquiring, we found out that patient had been diagnosed with influenza B infection 4-5 days before his presentation and had taken a total of 4 doses of Oseltamivir. Neurology was consulted. An MRI of the brain and cervical spine with and without contrast along with a lumbar puncture (LP) was ordered. Later that day, the patient became more agitated and was repeatedly trying to get out of his bed. He still did not speak a word. He was given 2mg of Ativan twice, which calmed him down. Because of his agitation, the procedures were to be performed under general anesthesia. Based on MRI Brain and cervical spine imaging Acute Disseminated Encephalomyelitis (ADEM) was ruled out. Infectious disease was consulted and a plan to start empiric antibiotics with vancomycin, meropenem, and acyclovir. The next day he was s alert and oriented x 3 and was following commands. He underwent lumbar puncture. Cerebrospinal fluid (CSF) was sent for extensive analysis and was initially concerning for a viral process, but meningitis/encephalitis panel came back to be negative. Following normal findings on LP CSF analysis, the patient was discharged home. His symptoms of AMS were suspected to be secondary to the adverse reaction of Tdap vaccination as his symptoms began to appear after receiving the vaccination. According to the wife, the patient had not received any vaccination in the past. The patient had already taken 4 doses of oseltamivir and tolerated it well, hence his AMS seemed less likely secondary to any adverse reaction to Oseltamivir. He was advised not to use Tamiflu or Tdap vaccine in future.

Keywords: encephalopathy, vaccination side effects, ADEM

Case presentation

A 42-year-old male with a past medical history of hypertension was brought to the emergency department (ED) by his family for evaluation of altered mental status (AMS) that started one day prior to presentation. This patient was said to have Tdap vaccine. He became agitated the evening of administration along with becoming restless. On the day of his presentation to the ED, around 3AM, his wife found him in the bathroom. He reported feeling nauseated and had one episode of vomiting. He was cold, clammy, was sweating profusely and did not reply to any of his wife’s questions. The wife then called the other family members and brought him to the ED for his abnormal behavior. On exam, he was alert but intermittently agitated. He remained non-verbal. His vitals were within normal limits. Neurological examination was limited, as the patient was not following commands. He was moving all his extremities. The remaining aspect of the physical examination was unremarkable. Computed Tomography of the brain was done which showed no acute abnormality. He was admitted for inpatient management of acute encephalopathy. Basic lab workup including complete blood count (CBC) and comprehensive metabolic panel (CMP) was within normal limits. Serum glucose, alcohol and acetaminophen levels were checked which were normal. Urine drug screen panel was negative. His Urinalysis was only positive for 20 ketones. Serum lactate was 2.03 and procalcitonin was normal.

On further inquiring, we found out that patient had been diagnosed with influenza B infection 4-5 days before his presentation and had taken a total of 4 doses of Oseltamivir. Neurology was consulted. An
MRI of the brain and cervical spine with and without contrast along with a lumbar puncture (LP) was ordered. Later that day, the patient became more agitated and was repeatedly trying to get out of his bed. He still did not speak a word. He was given 2mg of Ativan twice, which calmed him down. Because of his agitation, the procedures were to be performed under general anesthesia.

Based on MRI Brain and cervical spine imaging Acute Disseminated Encephalomyelitis (ADEM) was ruled out. Infectious disease was consulted and a plan to start empiric antibiotics with vancomycin, meropenem, and acyclovir. The next day he was s alert and oriented x 3 and was following commands. He underwent lumbar puncture. Cerebrospinal fluid (CSF) was sent for extensive analysis and was initially concerning for a viral process, but meningitis/encephalitis panel came back to be negative.

**Investigations**

1. MRI Brain with/without contrast showed no acute intracranial process. Mild cerebral volume loss was noticed.
2. MRI Cervical Spine with/without contrast showed no acute abnormality. It showed subtle posterior central disc protrusion at C4, C5, C6. No significant spinal cord or foraminal narrowing noted.
3. Lumbar Puncture with CSF analysis was done. Meningitis/Encephalitis panel which tested for E.coli, H.influenzae, L.monocytogenes, N.meningitidis, S.agalactiae, S.pneumoniae, Cytomegalovirus, Enterovirus, HSV type 1, HSV type 2, HHV 6, Human parechoirus, Varicella zoster virus, Cryptococcus neoformans came back to be negative.
4. CSF histoplasmosis, blastomycosis, and cryptococcal Ag were negative. No oligoclonal bands were seen. CSF protein was slightly elevated at 55 mg/dL (N=15-45), WBC count was elevated to 23/ul (N=0-5/ul) with 92% lymphocytes.

**Differential diagnosis**

1. Acute Disseminated Encephalomyelitis (ADEM) secondary to vaccination
2. Acute metabolic encephalopathy secondary to an adverse reaction to Tdap vaccination
3. Acute metabolic encephalopathy secondary to an adverse reaction to Oseltamivir
4. Infectious meningoencephalitis

**Treatment**

The patient received only one dose of empirical antibiotics including vancomycin, meropenem, and acyclovir. His condition improved and his antibiotics were stopped the next day.

**Outcome and Followup**

Following normal findings on LP CSF analysis, the patient was discharged home. His symptoms of AMS were suspected to be secondary to the adverse reaction of Tdap vaccination as his symptoms began to appear after receiving the vaccination. According to the wife, the patient had not received any vaccination in the past. The patient had already taken 4 doses of oseltamivir and tolerated it well, hence his AMS seemed less likely secondary to any adverse reaction to Oseltamivir. He was advised not to use Tamiflu or Tdap vaccine in future. This event was reported to Vaccine Adverse reporting system (VARs) as per CDC and the Department of Public Health was also notified.

**Discussion**

American Psychiatric Association has defined Acute Encephalopathy as altered consciousness with a change in cognition and/or with a perceptual disturbance developing over hours or days which is not better explained by a pre-existing or evolving chronic dementia.1

Encephalopathy can be produced by vaccines made from whole, killed organisms like pertussis and influenza because they cause neurological allergic reactions. These reactions result in demyelination and have a frequency of 1 per 100,000 vaccine recipients. Symptoms manifest within 4 days of immunization and are followed by complete recovery. It hasn’t been proven that administration of vaccination results in insidious encephalopathy.2

The demyelinating injuries caused by vaccines include optic neuritis and ADEM and this has been established by several case reports.3–6 The pathogenesis of vaccination induced demyelination remains unclear. There are several ongoing theories suggesting the possible mechanism for this outcome. One theory commonly known as molecular mimicry suggests that vaccine-derived products directly damage myelin membranes. This is an immune-mediated response against vaccine antigens which cross-react with central nervous system myelin proteins resulting in an autoimmune reaction. Immunization leads to an imbalance in the immune regulatory mechanisms and this impedes self-tolerance of host myelin proteins.6

According to a case centered analysis in which 64 million doses of vaccines were given, there is a statistically significant increased risk of ADEM associated with Tdap. This was based on 2 exposed cases with an odds ratio of 15.8 and an estimated excess risk of 1.16 cases of ADEM per million doses of Tdap vaccine.1 Hence proving that Tdap vaccination can cause neurological injuries. In the case presented here, the patient had been receiving oseltamivir for influenza. However, his symptoms manifested after the administration of Tdap vaccine. It is difficult to institute a causal relationship between Tdap and Encephalopathy, the close association of Tdap with the neurological symptoms indicates that Encephalopathy resulted due to the administration of the vaccine. Furthermore, the patient had already received 4 doses of oseltamivir which makes it a less likely cause of encephalopathy. Even though the CSF analysis had a suspicious viral etiology, meningitis and encephalitis panel were negative for any such process. The patient improved after only one dose of antibacterial and antiviral medications further ruling out a viral etiology.

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None.

**Conflicts of interest**

No conflicts of interests have been found.

**References**


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