Scientific Research Publishing

Voice of the Publisher, 2025, 11(1), 83-89
https://www.scirp.org/journal/vp
ISSN Online: 2380-7598
ISSN Print: 2380-7571

Agitation and Behavioral Changes in Children after the Flu Vaccine: Two Case Reports

Abdullah Murat Tuncer

Anka Pedia Child Health Center, Ankara, Türkiye
Email: muratatuncer@gmail.com

How to cite this paper: Murat Tuncer, A. (2025). Agitation and Behavioral Changes in Children after the Flu Vaccine: Two Case Reports. *Voice of the Publisher, 11,* 83-89.
https://doi.org/10.4236/vp.2025.111007

Received: January 6, 2025
Accepted: March 7, 2025
Published: March 10, 2025

Abstract

A 4.5-year-old boy and a 5-year-old girl are presented because they showed behavioral changes after the flu vaccine. Besides the known side effects of the flu vaccine, encephalopathy is rare and not well-known by pediatricians. This case was presented to increase awareness of this issue and inform family physicians and pediatricians about this subject.

Keywords

Vaccine, Flu Vaccine, Side Effects, Behavioral Changes, Encephalopathy

1. Introduction

Flu vaccines are viral vaccines that have been used for many years and whose effectiveness has been shown in various studies. The vaccines currently used are non-living vaccines. There are two commonly used flu vaccines. Glaxo and Merch vaccines are given to those who are at risk. According to WHO, it is especially recommended for those with COPD, asthma, and cardiovascular disease. Apart from this, it is also recommended for children after 6 months. Nonetheless, public tolerance to adverse reactions is minimal, and several reporting systems are in place to monitor adverse events. Accepted limitations of passive surveillance systems such as the Vaccine Adverse Events Reporting System (VAERS) in the USA include under-reporting, reporting of temporal associations or unconfirmed diagnoses, and lack of denominator data and unbiased comparison groups (Sell & Minassian, 2006).

The vaccine has common and rare side effects. Frequent side effects occur primarily as local reactions.

2. Case Report

Case 1. MK is a 4.5-year-old boy. The patient, who has been followed up with

a diagnosis of asthma for 2 years, is the second child of the family. He has been using Flixotide (50 mcg fluticasone propionate) once a day for more than a year due to a crisis that required him to be hospitalized once. He received a flu vaccine for flu protection in September 2023 (Fluarix tetra, Glaxo, Lot No: AFLBA740AF, Exp. Date: 5.24). The day after the vaccination, he had behavioral changes, waking up at night and crying. Play therapy was started by a child psychiatrist, whose consultation was requested due to his waking up at night and wanting to sleep on wet sheets and his aggressive behavior. He had no fever, and the physical and neurological examination findings were completely normal. MRI and other advanced tests were not performed. However, when the approaches recommended by the psychiatrist were not effective, medication was planned to be started, but all symptoms suddenly improved on the 50th day—approaches recommended by the psychiatrist.

Case 2. EJ is a 5-year-old girl. She is being monitored due to recurrent wheezing 3 years ago and is being followed up with a diagnosis of asthma. He has been using Rolastym (Budesonide 80 microgram and formoterol fumarate dihydrate 4,5 microgram) once a day for a year because he had to be hospitalized twice in three years. The flu vaccine was administered in October 2024 (Onfluvac Tetra, Abbot, Lot No: J04, Exp. Date: 4.25). It was observed that immediately after the vaccination, her behavior at school changed; she behaved differently with her friends than before; due to these behaviors, an educational psychologist assisted the patient, and observation began at school. There was no fever and additional neurological findings. There was no neurological deficit. She is sleeping as well. No further examination or laboratory study was considered necessary. This situation was resolved within 59 days without any intervention.

3. Discussion

The development of vaccines against infectious diseases is the most significant medical achievement of the past 100 years. Despite this achievement, parents have been reluctant to immunize their children (Doja, 2008).

Safety is often cited as the primary concern by families who refuse vaccines and, in particular, worries about the risk of neurological disease. The potential for vaccines to cause autism is a significant concern of families, whether through the vaccine itself or the perceived 'mercury toxicity' through thimerosal, a compound used to preserve some vaccines. Considerable evidence suggests no causal effect or association between receipt of vaccinations and autism, which has been reviewed extensively elsewhere (Doja, 2008). The possibility that immunizations may cause seizures or epilepsy is another potential concern, and indeed, febrile seizures have been shown to occur at an increased rate after vaccination.

For the most part, vaccines are safe procedures that prevent communities from suffering outbreaks of deadly diseases like tuberculosis, diseases, and influenza. However, in rare cases, patients suffer injuries like secondary encephalitis as a side-effect of a vaccine. Individual vaccines can produce systemic or neurologic

reactions ranging from minor events, such as pain and erythema at the injection site, to major complications, such as seizures, shock, encephalopathy, or death (Bale, 2004).

Encephalopathy has been described after some antibiotics and vaccines (Kim et al., 2024; Bhattacharyya et al., 2016; Zhou et al., 2003). More than 1100 cases of encephalitis (including brain stem encephalitis) have been reported to the Vaccine Adverse Event Reporting System (VAERS). According to reports published by the Centers for Disease Control (CDC) and the National Center for Biotechnology Information (NCBI), the following vaccines have been linked to encephalitis (Asatryan et al., 2008):

1) MMR vaccine—Measles Mumps and Rubella

2) DTP or DTaP vaccine—Diphtheria, Tetanus, and Pertussis (whooping cough)

3) Influenza (flu) vaccine

4) Varicella or Chicken Pox Vaccine

5) COVID-19 m-RNA vaccines

Some of these vaccines have also been associated with conditions similar to secondary encephalitis, such as acute disseminated encephalomyelitis (ADEM) and measles inclusion body encephalitis. ADEM is a brief but intense inflammation of the brain and spinal cord (Kita et al., 2023).

Side Effects (especially in the pediatric age group between 6 months and 18 years) could be considered as very common, ordinary, uncommon, rare, and infrequent side effects as follows:

1) It is very common, seen in at least 1 in 10 patients. Loss of appetite, restlessness, sleepiness, pain and redness at the injection site, muscle pain, fatigue

2) Common side effects. These are seen in less than 1 in 10 patients. Fever, injection site swelling, nausea, diarrhea, vomiting, abdominal pain, headache, joint pain, chills,

3) Uncommon side effects. Less than 1 in 100 patients. Rash and itching.

4) These are rare side effects in less than 1 in 1000 patients. They include swelling with rash and itching at the injection site.

5) Infrequent side effects. These occur in less than 1 in 10,000 patients and are rarely reported. They include encephalopathy and bleeding due to thrombocytopenia.

Apart from these, neurological findings such as confusion, loss of balance, neuritis, encephalomyelitis, and Guillain-Barre syndrome have been reported (Abdelhady et al., 2023).

Abdelhady and colleagues published an analysis of vaccines related to encephalitis. This analysis extracted demographic data, clinical features, vaccine data, treatment lines, and outcomes associated with COVID-19 m-RNA vaccines. A total of 65 patients from 52 studies were included. AstraZeneca was the most reported vaccine associated with encephalitis (38.5%), followed by Pfizer (33.8%), Moderna (16.9%), and others. Most cases of encephalitis occurred after the first vaccination in 41/65 (66.1%). The mean time between vaccination and symptom

onset was 9.97 ± 7.16 days. The majority of affected individuals experienced a full recovery. This study summarizes the current evidence of reported post-vaccination encephalitis regarding clinical presentation, symptoms onset, management, outcomes, and comorbid conditions; however, it fails to either acknowledge the incidence of occurrence or establish a causal relationship between various COVID-19 vaccines and encephalitis (Abdelhady et al., 2023).

According to the report of The Vaccine Safety Committee in the USA found that the evidence favored the rejection of a causal relation between diphtheria and tetanus toxoids and encephalopathy, infantile spasms, and sudden infant death syndrome, and between conjugate Hib vaccines and susceptibility to Hib (Hemophilus influenza type B) disease. The committee also found that the evidence established causality between diphtheria and tetanus toxoids and anaphylaxis, between measles vaccine and death from measles vaccine-strain viral infection, between measles-mumps-rubella vaccine and thrombocytopenia and anaphylaxis, between oral polio vaccine and poliomyelitis and death from polio vaccine-strain viral infection, and between hepatitis B vaccine and anaphylaxis (Stratton, 1994).

Vaccine Adverse Effects Reporting System (VAERS) found 11 published case reports of hearing loss following the measles, mumps, and Rubella vaccine (MMR). The review of the VAERS reports identified 44 cases of likely idiopathic sensorineural hearing loss after MMR administration (Asatryan, 2008).

Acute mania with psychotic features has been described following mRNA vaccination has been described. It manifested in a 42-year-old man as irritability, sleeplessness, delusions, and finally as amnesia of the whole situation 1 day after receiving the first dose of the BNT162b2 mRNA vaccine (Mouliou & Dardiotis, 2022; Yeşilkaya et al., 2021). Similarly, it manifested in a 57-year-old man as sleeplessness, irritability, and a suicidal attempt some days after receiving the 2nd dose of the BNT162b mRNA vaccine (Mouliou & Dardiotis, 2022; Yeşilkaya et al., 2021). It has also been reported in a 52-year-old woman who experienced a rapid relapse in bipolar mania within a few days of receiving another viral vector COVID-19 vaccine (the 1st dose of the ChAdOx1-S/nCoV-19 vaccine) (Uvais, 2021). Overall, symptom onset in all cases was within 10 days of vaccination, likely suggesting the presence of a high-risk period warranting vigilance (Balasubramanian et al., 2022).

Live virus vaccines may be etiologically related to Reye syndrome. It has been examined, and 404 cases have been reported to the Center for Disease Control. Fifteen of 269 children with Reye syndrome were inoculated with live virus vaccines within 30 days before the onset of illness (Morens et al., 1979).

It is essential to detect the risk groups. Furthermore, the mechanism that could cause psychiatric symptoms might be driven by the vaccine-derived protein antigen, such as in autoimmune psychosis.

Potential mechanisms include the possible molecular mimicry between vaccine antigens and self-antigens or the acceleration of an ongoing autoimmune process caused by vaccines.

In vaccine encephalopathy, many parents cite a lack of family history as a reason why vaccines may be causative in their children's neurological problems. However, because of the high rate of de novo SCN1A mutations, this genetic abnormality likely occurs either in the gametes or very early postfertilization, thus making a family history of seizures extremely unlikely in patients with SCN1A mutations (Claes et al., 2001).

With the increasing use of immune checkpoint inhibitors (ICIs), neurologists encounter more immune-related adverse events (irAEs). Since the mortality rate of encephalitis occurring as an irAE (encephalitis) is as high as 19%, it is as lethal a condition as myocarditis. Vogrig et al. proposed the classification of central nervous system complications associated with autoantibodies. This report is valuable for managing encephalitis, as it shows different features of encephalitis in the usual clinical setting (Vogrig et al., 2020).

Diagnosing encephalitis is difficult, as patients present with a broad range of clinical features. Limbic encephalitis is the most common phenotype of encephalitis; however, unexpected clinical features can be observed, such as those referred to as atypical reactions.

However, these events are infrequent (less than 1 case per million patients), with an incidence up to 617 times lower than those caused by a natural viral infection. Therefore, the benefits of vaccination surpass the potential risks (Irimia et al., 2023).

The important thing here is that especially pediatricians are aware of the issue, inform families, and can intervene quickly when side effects occur, no matter how rare.

Encephalopathy findings such as agitation and hyperactivity have been described after vaccinations and during antibiotics such as azithromycin (Farooq et al., 2011; drugs.com, 2024).

So far, there has been no adequate publication about the interaction of asthma medications and flu vaccine side effects. Since asthma is among the indications for flu vaccination in the childhood age group, most of those who receive the flu vaccine in the pediatric age group have a history of asthma, and many of them use medication. Further studies can reveal whether there is a link between asthma, flu vaccine, and encephalopathy trio.

The physician or pediatrician must know everything about the side effects of the vaccine, antibiotic, or any other medical intervention for treatment or prevention, and the families must be informed.

The paper presented a case report on the effects of the flu vaccine. Two children displayed behavioral changes after receiving the vaccine. Encephalopathy, a shift in brain conditions usually accompanied by behavioral changes, was identified as a potential side effect of the flu vaccine despite its rarity. Pediatricians do not widely recognize this side effect, but the paper aimed to raise awareness among healthcare professionals about these potential side effects.

4. Comment

The paper aimed to inform pediatricians and caregivers of the rare side effects of

flu vaccines. This case report explains these cases and their importance in understanding this potential side effect. Consider patients' medical history and the flu vaccine brand, which may help identify underlying factors, such as the patient's other risk factors for neurological conditions, such as consuming contaminated foods or genetic predispositions. Using many widely tested tests to predict this rare side effect is extremely difficult, expensive, and unethical. However, vaccine providers and manufacturers should be advised to provide information about this temporary side effect.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

References

Abdelhady, M., Husain, M. A., Hawas, Y., Elazb, M. A., Mansour, L. S., Mohamed, M. et al. (2023). Encephalitis Following COVID-19 Vaccination: A Systematic Review. *Vaccines, 11,* Article 576. https://doi.org/10.3390/vaccines11030576

Asatryan, A., Pool, V., Chen, R. T., Kohl, K. S., Davis, R. L., & Iskander, J. K. (2008). Live Attenuated Measles and Mumps Viral Strain-Containing Vaccines and Hearing Loss: Vaccine Adverse Event Reporting System (VAERS), United States, 1990-2003. *Vaccine, 26,* 1166-1172. https://doi.org/10.1016/j.vaccine.2007.12.049

Balasubramanian, I., Faheem, A., Padhy, S. K., & Menon, V. (2022). Psychiatric Adverse Reactions to COVID-19 Vaccines: A Rapid Review of Published Case Reports. *Asian Journal of Psychiatry, 71,* Article 103129. https://doi.org/10.1016/j.ajp.2022.103129

Bale, J. F. (2004). Topical Review: Neurologic Complications of Immunization. *Journal of Child Neurology, 19,* 405-412. https://doi.org/10.1177/088307380401900602

Bhattacharyya, S., Darby, R. R., Raibagkar, P., Gonzalez Castro, L. N., & Berkowitz, A. L. (2016). Antibiotic-Associated Encephalopathy. *Neurology, 86,* 963-971. https://doi.org/10.1212/wnl.0000000000002455

Claes, L., Del-Favero, J., Ceulemans, B., Lagae, L., Van Broeckhoven, C., & De Jonghe, P. (2001). De Novo Mutations in the Sodium-Channel Gene SCN1A Cause Severe Myoclonic Epilepsy of Infancy. *The American Journal of Human Genetics, 68,* 1327-1332. https://doi.org/10.1086/320609

Doja, A. (2008). Genetics and the Myth of Vaccine Encephalopathy. *Paediatrics & Child Health, 13,* 597-599. https://doi.org/10.1093/pch/13.7.597

drugs.com (2024). https://www.drugs.com/sfx/azithromycin-side-effects.html

Farooq, O., Memon, Z., Stojanovski, S. D., & Faden, H. S. (2011). Azithromycin-Induced Agitation and Choreoathetosis. *Pediatric Neurology, 44,* 311-313. https://doi.org/10.1016/j.pediatrneurol.2010.11.014

Irimia, P., Belvís, R., González-García, N. M., Sancho, V., Moreno Loscertales, C., García Rubio, S., & Mur, S. D. (2023). Hashimoto Encephalopathy after Vaccination against SARS-CoV-2. *Neurología, 38,* 599-607.

Kim, J. H., Kim, T., Kim, W., Kim, S., Hong, Y. J., Lim, E. et al. (2024). The Incidence and Predictors of Antibiotic-Associated Encephalopathy: A Multicenter Hospital-Based Study. *Scientific Reports, 14,* Article No. 8747. https://doi.org/10.1038/s41598-024-59555-w

Kita, A., Fuyuno, Y., Matsuura, H., Yamaguchi, Y., Okuhira, K., & Kimoto, S. (2023). Psy-

chiatric Adverse Reaction to COVID-19 Vaccine Booster Presenting as First-Episode Acute Mania with Psychotic Features: A Case Report. *Psychiatry Research Case Reports, 2,* Article 100143. https://doi.org/10.1016/j.psycr.2023.100143

Morens, D. M., Halsey, N. A., Schonberger, L. B., & Baublis, J. V. (1979). Reye Syndrome Associated with Vaccination with Live Virus Vaccines. *Clinical Pediatrics, 18,* 42-44. https://doi.org/10.1177/000992287901800105

Mouliou, D. S., & Dardiotis, E. (2022). Current Evidence in Sars-Cov-2 mRNA Vaccines and Post-Vaccination Adverse Reports: Knowns and Unknowns. *Diagnostics, 12,* Article 1555. https://doi.org/10.3390/diagnostics12071555

Sell, E., & Minassian, B. A. (2006). Demystifying Vaccination-Associated Encephalopathy. *The Lancet Neurology, 5,* 465-466. https://doi.org/10.1016/s1474-4422(06)70452-5

Stratton, K. R. (1994). Adverse Events Associated with Childhood Vaccines Other than Pertussis and Rubella. *Journal of the American Medical Association, 271,* 1602-1605. https://doi.org/10.1001/jama.1994.03510440062034

Uvais, N. A. (2021). Bipolar Mania Following ChAdOx1-S/nCoV-19 Vaccination. *The Primary Care Companion for CNS Disorders, 24,* 21cr03158. https://doi.org/10.4088/pcc.21cr03158

Vogrig, A., Muñiz-Castrillo, S., Joubert, B., Picard, G., Rogemond, V., Marchal, C. et al. (2020). Central Nervous System Complications Associated with Immune Checkpoint Inhibitors. *Journal of Neurology, Neurosurgery & Psychiatry, 91,* 772-778. https://doi.org/10.1136/jnnp-2020-323055

Yesilkaya, U. H., Sen, M., & Tasdemir, B. G. (2021). A Novel Adverse Effect of the BNT162b2 mRNA Vaccine: First Episode of Acute Mania with Psychotic Features. *Brain, Behavior, & Immunity-Health, 18,* Article 100363. https://doi.org/10.1016/j.bbih.2021.100363

Zhou, W., Pool, V., Iskander, J. K., Bullard, R. E. et al. (2003). Surveillance for Safety after Immunization: Vaccine Adverse Event Reporting System (VAERS)—United States, 1991-2001. *MMWR Surveillance Summaries, 52,* 1-24.