Case Report

Diphtheria, pertussis (whooping cough), and tetanus vaccine induced recurrent seizures and acute encephalopathy in a pediatric patient: Possibly due to pertussis fraction

Mahendra K. Patel, Tejas K. Patel, C. B. Tripathi

Department of Pharmacology, Government Medical College, Bhavnagar, Gujarat, India

ABSTRACT

A 5-month-old male patient developed recurrent seizures and acute encephalopathy possibly due to first dose of diphtheria, pertussis (whooping cough), and tetanus (DPT) vaccine used for routine immunization. Postreaction computed tomography (CT) scan of brain, magnetic resonance imaging (MRI) of brain, and electroencephalogram were normal. Pertussis fraction of DPT vaccine is responsible for this reaction. It is suggested that acellular pertussis vaccine should be used instead of whole cell vaccine because it is associated with lower frequency of neurological complications, such as seizures, encephalopathy, and hypotensive episodes. However, acellular pertussis-containing vaccines are currently not affordable in most developing countries.

Key words: Acute encephalopathy, recurrent seizures, whole cell DPT vaccine

INTRODUCTION

Hypersensitivity reaction, hypotensive–hyporesponsive shock and postvaccination encephalopathy are the most dreaded complications associated with diphtheria, pertussis (whooping cough), and tetanus (DPT) vaccine.[1] Occurrence of postvaccination encephalopathy and hypotensive–hyporesponsive shock is a contraindication of further doses of the pertussis component.[1,2] Manifestations that indicate occurrence of encephalopathy include the following: seizures with or without fever occurring within 3 days of immunization and persistent, severe, inconsolable screaming, or crying for 3 or more hours within 48 h of immunization. Usually, these are not associated with permanent sequel.[1,2] Neurological complications are thought to be primary due to the pertussis component of the vaccine and the estimated risk is 1 per 1,70,000 doses administered.[1] Here, we report a case of DPT-induced recurrent seizures and acute encephalopathy in a child possibly due to pertussis fraction.

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CASE REPORT

A 5-month-old male patient weighing 6.78 kg was admitted with a complaint of generalized tonic–clonic seizure for 4–5 times per day for 5 days in pediatric ward of Sir Takhtsinhji General Hospital, Bhavnagar, Gujarat. The patient had an

Address for correspondence:
C.B. Tripathi, Department of Pharmacology, Government Medical College, Bhavnagar – 364 001, Gujarat, India.
E-mail: cbrtripathi@yahoo.co.in

altered sensorium with normal pulse and respiratory rate. Pupil was constricted and poorly reacting to light. Parents revealed the history. The child was vaccinated for the first dose of DPT before 16 days. After 3 days of vaccination, the child developed seizures and admitted to the nearby community health center (CHC) for 9 days. The patient was discharged after the control of seizures and was at home for 3 days without any treatment. Treatment detail is not available on admission at CHC. Reappearance of seizures occurred at home. After that the patient was admitted and treated with phenytoin, methyl prednisolone, and levetiracetam in private hospital at Bhavnagar. Afterward the patient was transferred to our center for further management. There was no history of head injury, trauma, tuberculosis, febrile convulsion, and ear discharge. There was no previous history of seizure before DPT vaccination. Provisional diagnosis as postvaccination encephalopathy was made. Investigations, such as total leukocyte count, differential leukocyte count, red blood cell (RBC) count, packed cell volume, RBC indices, platelet count, erythrocyte sedimentation rate, peripheral smear examination, random blood sugar, liver function tests, renal function tests, and cerebrospinal fluid examination were normal except hemoglobin (10.5 g/dL; reference value: 12.0–18.0 g/dL), LDH (439 IU/L; reference value: 180–360 IU/L), CK-MB (95 IU/L; reference value 18–51 IU/L), and ionized calcium (1.06 mmol/L; reference value: 1.16–1.32 mmol/L). Postreaction CT-scan of brain, MRI of brain and electroencephalogram were normal. The patient was treated with midazolam, phenytoin, levetiracetam, phenobarbitone, and clobazam. After omitting clobazam, clonazepam was added to control seizures at day 5. Acyclovir and methyl prednisolone were started as empirical therapy on the 2nd day of admission. From 7th day onward prednisolone was started. Seizure frequency reduced from 2nd day and last episode occurred on the 13th day. The patient became fully conscious on 8th day. The patient was discharged on 15th day. The patient was followed at 3 months and found without any neurological sequel.

Naranjo's scale showed that the relationship between DPT and acute encephalopathy was probable.[3] According to Brighton criteria for vaccine-induced encephalopathy, the present adverse event was of level 3.[4] According to Modified Schumock and Thornton's criteria, this reaction was definitely preventable and Modified Hartwig and Siegel's scale showed that the reaction was moderately severe.[5,6]

DISCUSSION

Evaluation of vaccination programs requires continuous monitoring of the vaccination coverage, equity of access, incidence and severity of the diseases targeted in the program and also the safety of the vaccination.[7] Adverse event following immunization (AEFI) is defined as a medical incident that takes place after an immunization, causes concern, and is believed to be caused by the immunization.[8] Majority of them are minor and harmless. It is important to note that the benefits of protection afforded by a vaccine always far exceed the small risk of a serious and life-threatening reactions. A few cases of DPT-induced serious neurologic adverse effects were reported from India.[1,2] Pertussis component of the DPT vaccine is mainly responsible for neurologic reactions. It causes neurologic damage: by affecting cellular signaling, catecholaminergic and GABAergic systems and defect in blood–brain barrier due to endotoxin-mediated endothelial damage. Whole cell pertussis vaccine induces the IL-1β production in the hippocampus and hypothalamus of vaccinated animals. This leads to decrease in release of the inhibitory neurotransmitters GABA and adenosine in the hippocampus and induce convulsive activity. Acellular type did not induce the IL-1β production.[9] Association of such severe reactions made the whole-cell pertussis vaccine highly unpopular and withdrawal of it from many countries.[10] Occurrence of neurologic complications is a contraindication for subsequent doses of the whole-cell DPT vaccine and its replacement by the acellular type.[7] Whole-cell pertussis vaccines contain 3000 different proteins, whereas acellular pertussis vaccine (DTaP) contains 2–5 proteins.[10] This may be the reason for less chances of seizures, encephalopathy, and hypotensive episodes with DTaP as compared to whole-cell vaccine.[7,11] An acellular pertussis vaccine (designated as aP) is now available in several countries, including India. It contains purified, inactivated components of *B. pertussis*.[1,2] It is as potent as the whole-cell vaccine. The price of DPT vaccine (Triple Antigen of GlaxoSmithKline) and DTaP vaccine (Boostrix of GlaxoSmithKline) are Rs. 3 and Rs. 699 per dose, respectively. The higher cost may be the reason for inclusion of DPT vaccine instead of DTaP vaccine in Indian national immunization schedule. According to WHO, local and nonserious systemic reactogenicity are more commonly associated with whole-cell pertussis containing vaccines. However, acellular pertussis containing vaccines are unlikely to be currently affordable in most developing countries and there is insufficient marginal benefit to consider changing from whole-cell pertussis-containing vaccine to acellular pertussis-containing vaccine. By 2009, 1 of the 49 least developed countries and 13 of 88 developing countries have adopted acellular pertussis vaccine into their national immunization programs.[12] Indian Academy of Pediatrics (IAP) also endorses the continued use of whole-cell pertussis vaccine.[13] It is suggested that DTaP vaccine can be preferred over DPT vaccine for those who can afford it. This case highlights the importance of the continuous monitoring of vaccine-related adverse events of whole-cell DPT vaccine in countries where it is preferred because of the economic reason.

REFERENCES

1. Gogtay NJ, Kshirsagar NA. Probable DPT induced Generalized Tonic

Clonic seizure. Available from: http://kem.edu/dept/clinical_pharmacology/adverse event_month_case/case_october 2003.htm. [Last cited on 2011 June 17].
2. Kulkarni GS, Patekar MN, Gogtay NJ, Deshmukh CT, Kshirsagar NA. Probable Diphtheria Pertussis Tetanus (DPT) vaccine induced encephalopathy and death. Available from: http://kem.edu/dept/clinical_pharmacology/adverse_event_month_case/case_june2005.htm. [Last cited on 2011 June 17].
3. Naranjo CA, Busto U, Seller EM, Sandor P, Ruiz I, Roberts EA, *et al*. A method for estimating the probability of adverse drug reaction. Clin Pharmacol Ther 1981;30:239-55.
4. Sejvar JJ, Kohl KS, Bilynsky R, Blumberg D, Cvetkovich T, Galama J, *et al*. Encephalitis, myelitis, and acute disseminated encephalomyelitis (ADEM): Case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine 2007;25:5771-92.
5. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm 1992;27:538.
6. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm 1992;49:2229-32.
7. Freitas FR, Sato HK, Aranda CM, Arantes BA, Pacheco MA, Waldman EA. Adverse events following diphtheria, pertussis and tetanus vaccinations and factors associated with severity. Rev Saude Publica 2007;41:1032-41.
8. Vaccine safety and adverse events following immunization. Available from: http://www.who.int/immunization_monitoring/routine/immunization_adverse/en/index.html. [Last cited on 2011 June 20].
9. Donnelly S, Loscher CE, Lynch MA, Mills KH. Whole-cell but not acellular pertussis vaccines induce convulsive activity in mice: Evidence of a role for toxin-induced interleukin-1beta in a new murine model for analysis of neuronal side effects of vaccination. Infect Immun 2001;69:4217-23.
10. Geier DA, Geier MR. An evaluation of serious neurological disorders following immunization: A comparison of whole-cell pertussis and acellular pertussis vaccines. Brain Dev 2004;26:296-300.
11. Diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed DAPTACEL™. Available from: http://www.whale.to/a/p/DAPTACEL.pdf. [Last cited on 2011 June 17].
12. Pertussis vaccines: WHO position paper. Wkly Epidemiol Rec 2010;85:385-400.
13. Immunisation schedule. Available from: http://www.iapindia.org/immunisation/ immunisation- schedule. [Last cited on 2011 June 17].

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