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Case Report

VACCINE-INDUCED DEVELOPMENTAL DELAY: A CASE REPORT

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ABSTRACT

Vaccines are weakened or dead microbes injected for the development of an acquired immunity as a preventive measure, also including the use of microbial proteins. The spectrum of adverse events following vaccination has been increasing as well with increasing number of reports detailing the events following immunization. The rate of morbidity and mortality of many communicable diseases has significantly decreased with time with relieve to the quality of life as well as the overall pharma economic cost. In this case report vaccine-induced developmental delay was observed in a child of 16 months of age. The child was born with low birth weight despite which the child was administered with hepatitis B vaccine, poliomyelitis vaccine, and bacillus Calmette-Guerin within 24 h of birth. Consecutive clinical outcomes followed throughout the years, which induced a developmental delay in this child. This case clearly signifies the need for more evidence-based implementation for the management of various diseases at secondary care hospitals.

Keywords: Developmental delay, Febrile seizure, Vaccination, Bacillus Calmette-Guerin, Oral polio vaccine, Hepatitis-B.

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INTRODUCTION

An adverse drug event can be defined as an injury occurring resultant to a drug. In addition, it includes medication errors, adverse drug reactions, allergic reactions, and overdoses [1,2]. Vaccine-induced adverse events usually constitute of anaphylactic reactions and most commonly fever which may result into febrile seizures [3].

A febrile seizure can be defined as a seizure associated with fever resultant above 100.4°F. The prevalence is higher in children aged between 6 months and 5 years, with most of the seizures occurring between 14 and 18 months of age [4]. Recent evidence suggests an increased risk for febrile seizures after vaccinations such as mumps measles rubella and mumps measles rubella varicella and hepatitis B vaccine (HBV) [5]. Usually, febrile seizures resolve once the child reaches the age of 6 years. However, in subjects with positive family history, they may go on to have febrile seizures well beyond this age, even into adult life. This may not necessarily be associated with high temperature, leading to generalized tonic-clonic seizures [4]. A generalized tonic-clonic seizure may attribute for further neurological damage usually affecting the entire brain [6]. The etiologies and pathophysiology may vary depending on the patient and the risk factors (head trauma, central nervous system infections, febrile seizures, developmental history, and medications/toxin exposures) [7]. Recent studies reported that genetic or structural defects are the underlying causes of seizures, which may be activated after vaccination presumably due to the interplay of the innate biology of the body [8].

The latest trends in vaccine safety include that of world health organization. Adverse events following immunization (AEFI) is classified into four categories, namely program-related, vaccine-induced, coincidental, and unknown, where program-related AEFI attribute mostly to the errors in the vaccine itself, dosage forms, and route of administration. Vaccine induced AEFI occurs due to either the effects of vaccine or one of its components or may be due some underlying medical conditions or because of an idiosyncratic reaction.

Anaphylaxis reactions are rare, and the onset of anaphylaxis may occur within minutes with an unpredictable clinical course [9]. In this case report, we present a vaccine-induced developmental delay.

CASE REPORT

A 2-years-old male child presented with complaints of cough since 2 days, and with a history of breathing difficulty. The child weighed about 10 kg and while on examination, the vitals are pulse rate at 116 beats per min, respiratory rate at 36 per min. He was found to be afebrile and cardiovascular system with S1 and S2 +, with positive bilateral air entry, however, with bilateral crept being present in the respiratory system. The child was diagnosed as wheeze associated with lower respiratory tract infection.

On assessing the medical history of the patient, the child was normally delivered with no defects and with no history of familial deformities.

The patient was found to be a known case of generalized tonic-clonic seizures, delayed development and wheeze associated with lower respiratory tract infection was diagnosed since the past 2 weeks. He was treated with injection ampicillin 250 mg intravenous twice daily, injection gentamicin 20 mg Intravenous twice daily, syrup paracetamol 50 ml (25 mg/ml), tablet salbutamol ¼ of 4 mg 3 times a day, salbutamol nebulization 3 times a day, and tablet chlorpheniramine maleate ¼–0-¼ and was discharged with tablet amoxicillin 125 mg 3 times a day for 7 days, tablet zinc ½ (10 mg) once daily for 5 days followed by tablet chlorpheniramine maleate 1 mg twice daily for 3 days.

Assessing further history, it was noted that the child was given HBV, poliomyelitis vaccine (PMV), and bacillus Calmette-Guerin (BCG) within 12 h of birth following which the child developed fever, which was symptomatically controlled. For this, the child got admitted in the neonatal intensive care unit where he developed febrile seizure and was prescribed with tablet sodium valproate 200 mg once daily and tablet clonazepam 0.25 mg twice daily.

At present, the child was found to be afebrile, yet irritable. He was well hydrated, and despite normal cardiovascular sounds, creps were positive for the respiratory system. Respiratory rate was found at 48 beats/min with 84% SpO_2 in room air. On the physical assessments, it was quite evident that the child has a developmental delay. He was not able to utter words and not even able to walk like other children of his age.

The laboratory results suggested anemia with hemoglobin 9.7 g/dL, hematocrit 31.2%, mean cell volume 64.9 m^3, and mean cell hemoglobin at 20.2 pg/cell. The total count was also elevated at 12.8×10^3 cells/mm^3, which indicates infection. The treatment given was as follows, oxygen through face mask at the rate of 5 L/min, injection hydrocortisone 50 mg intravenous twice daily, salbutamol nebulizer for 20 min 3 times a day, injection cefotaxime 500 mg intravenous 3 times a day, injection ranitidine 10 mg intravenous twice daily, tablet sodium valproate 200 mg once daily, and tablet clonazepam 0.25 mg twice daily.

On the 2nd day, bilateral creps were positive, with pulse rate at 122 beats/min, respiratory rate at 30 beats/min and 89% SpO_2. Treatment was followed as injection hydrocortisone 50 mg intravenous twice daily, salbutamol nebulizer Q8H, injection cefotaxime 500 mg intravenous thrice daily, injection ranitidine 10 mg intravenous twice daily, tablet sodium valproate 200 mg once daily, and tablet clonazepam 0.25 mg twice daily. On the 3rd day, the patient presented with complaints of a cough. Injection hydrocortisone was stopped and followed by adding tablet prednisolone 5 mg and tablet azithromycin 250 mg ½ once daily to the therapy. The patient was discharged on the 4th day with tablet sodium valproate 200 mg once daily, tablet clonazepam 0.25 mg twice daily, tablet azithromycin 250 mg ½ once daily for 4 days, tablet cetirizine 5 mg ½ at night time for 4 days, tablet salbutamol ½ at hour of sleep for 4 days, and Budecort 100 mcg 1 puff twice daily for 3 months.

DISCUSSION

With an increasing number of infectious diseases as well as resistant strains, the need for a preventive strategy is a must [10]. However, apart from these active constituents, the vaccine contains one or more of excipients, and once the vaccine enters one's fluid system, a cascade of immunological responses takes place. This pathway defines ones intrinsic reactions to the vaccine for the outcome of a proper response or an anaphylactic reaction [11].

In this case report, the patient despite with low birth weight was given BCG, oral polio vaccine, and HBV within 24 h of birth. A question that arises now is the ultimate fate of the immune system and the biological pathways in low birth weight children. The excipients content of the HBV was aluminum hydroxide gel 0.25 mg, thiomersal 0.025 mg, and phosphate buffer. BCG vaccine being constituted in sodium chloride 1 ml 0.9% w/v and PMV contains kanamycin 20 mcg as a preservative. This brings to light the thiomersal controversy, the removal of thiomersal from vaccines in the United States of America since 2001. Where, once evidence suggested the association between thiomersal and autism while some of the other evidence not supporting the same [12]. However, considering the risk verses benefit, ensuring thiomersal is really associated or not associated to neurological deformities is still controversial. Further requires more evidences and justification.

Furthermore, current recommendations state the need for scheduled vaccinations in preterm and children born with low birth weight [13]. However, this recommendation is feasible only if the child is clinically stable. Quite contrarily, the debate lies in the doses of the vaccine given at the time of birth, that is, HBV and BCG. Still, the implementation of these is restricted in most countries due to the concerns of parents and the health-care providers regarding the biology of immunogenicity and safety of vaccines in these populations [14]. However, the conclusiveness of these finding is a big question keeping in mind the scarcity of evidence in this field. In this case report, the child despite born with low birth weight was given three vaccinations as mentioned above and sequentially developed fever post-vaccination resultant into a febrile seizure. Recurrent febrile seizures led to generalized tonic-clonic seizures not associated with fever. The child suffers from the developmental delay at present. Recent data suggest the interplay of plasma multiplex cytokines and increased level of interleukin-10 and interleukin-1 receptor antagonist as an etiological factor for conversion of febrile seizures into non-febrile seizure [15].

The laboratory values indicated a decreased value of hemoglobin, hematocrit, mean cell volume, mean cell hemoglobin, and a increased value in total white cell count. The treatment that followed indicated for supportive and symptomatic relief. Preventive therapy was initiated later only with an inhaled corticosteroid. Irrational use of antibiotics and corticosteroids was observed in this case, however, with guidelines suggesting antibiotic therapy first-line therapy being the macrolides or amoxicillin followed by preventive measure with inhaled corticosteroids [16].

The long-term use of sodium valproate carries an enormous risk of hepatotoxicity; however, no laboratory tests were done regarding the hepatic abnormality and the laboratory test done was yet not sufficient to rule out many of the complications. In such cases, there is an enormous need of diagnostic protocols [17]. However, in this present scenario, prolonged therapy with sodium valproate yielded acceptable outcome, though the use of add-on therapy with clonazepam indicates the lack of guideline implementation. Laboratory findings and interpretations are necessary in such cases to rule out any forms of complications that need to be addressed.

In addition, it was quite evident the child had a developmental delay (Fig. 1). Developmental delays and autism can be a consequence of vaccine-induced adverse events where the developmental delay is a neurological disorder with huge impact on the quality of life of the patient [18]. Furthermore, the possible association between vaccination and developmental disorders has been subject of great debate resultant doubts and anxiety in the parents seeking the best for their child [19].

This case clearly demonstrates the lack of guideline implementation in the management of respiratory and neurological diseases and furthermore the scarcity of evidence in the sequential vaccination in low birth weight child.

CONCLUSION

This case clearly signifies the need for more evidence-based implementation for the management of various diseases at secondary level hospitals. In addition, further studies are needed to demonstrate the impact of vaccination schedules based on the birth weight of the child and whether thiomersal-containing vaccines should be administered or not. Conclusive guidelines and updated knowledge for physicians are a need of the hour, resultant less incidences of health burden to the general population.

AUTHORS' CONTRIBUTION

Keerthana Chandrasekar-involved in the collection of this case report during the ward rounds and made follow-up of the patient. Tenzin

Fig. 1: Delayed development in the child

Tsundue-involved in the pharmacotherapeutic discussion was conducted and follow-up of the patient. S Ponnusankar - has provided the design to write the case report and summarizing the write-up of the case.

CONFLICTS OF INTEREST

The authors do not report any conflicts of interest.

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