

Allergic Reaction to Rabies Vaccine in a 4-Year-Old Girl during Post-Exposure Rabies Prophylaxis: A Case Report

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Abstract

Adverse events to vaccine or vaccine induced reactions and particularly hypersensitivity post-vaccination reactions to the rabies vaccine, are very rare. Therefore, we wanted to show a case of a four-year-old girl who developed an allergic reaction after a dog and cat bite during rabies post-exposure prophylaxis. Sensitization to some component of the infectious agent of the rabies vaccine, grown on purified chick embryo cells but also on human diploid cells, has been proven. Although, allergic reactions to the rabies vaccine are extremely rare, vaccination can be done following the official WHO guide for pre-exposure and post/exposure prophylaxis in humans.

Keywords: Adverse reactions • Allergy • Allergy testing to rabies vaccines • Rabies post-exposure prophylaxis

Abbreviations: ARs: Adverse Reactions; AEs: Adverse Events; CIPH: Croatian Institute of Public Health; HALMED: Agency for Medicinal Products and Medical Devices of Croatia; HDCV: Human Diploid Cell Vaccine; HRIG: Human Rabies Immune Globulin; PEP: Post-Exposure Prophylaxis; PrEP: Pre-Exposure Prophylaxis; PCECV: Purified Chick Embryo Cells Vaccine; PVRP: Purified Vero Cell Rabies Vaccine; SCH: Srebrnjak Children's Hospital; SPT: Skin Prick Test; VAERS: Vaccine Adverse Event Reporting System

Introduction

Adverse Reactions (ARs) to vaccines are highly varied, ranging from mild, local reactions to fatal anaphylactic reactions [1]. They can be classified depending on the cause: Vaccination-induced reactions, reactions due to errors in storage, manipulation and/or administration of vaccine; and coincidental reactions (no causal relationship with the vaccine). Hypersensitivity reactions may occur depending on the causative agent: reactions due to some component of the infectious agent or additional components; reactions due to adjuvants (aluminium hydroxide), stabilizers (gelatine), preservatives (thiomersal), antibiotics (neomycin) and reactions due to a biological culture medium (chick embryo cells) [1-3].

Case Report

A 4-year-old girl was bitten by a stray dog upon the lower part of the abdomen, right forearm and right upper part of thorax. She was immediately taken to her paediatrician and given an antibiotic therapy. She didn't receive a tetanus shot because she received all proposed vaccines for her age according to the current National immunization schedule. Afterwards she was admitted to the Antirabies Clinic of Public Health Teaching Institute of Brod-Posavina County and received rabies Post-Exposure Prophylaxis (PEP) according to Zagreb 2-1-1 scheme. She received 2 doses of rabies vaccine produced

on Purified Chick Embryo Cells (PCEC)-Rabipur, Novartis (lot: 607011G) in deltoid muscles of her upper arms in a total amount of 2.0 ml. The bites and injuries were afflicted through her clothes and were categorized as category II exposure; therefore she hasn't received Human Rabies Immunoglobulin (HRIG). An immunization schedule was made, and according to it she required two more visits. After 6 days, a second incident occurred. The child was bitten by the cat of the known owner upon her right fist with development of scabs and local oedema. The next day, she had an appointment for the third shot of rabies vaccine. This was postponed by two days due to the development of fever (38.5°C). The day after finishing the PEP schedule, the child developed a suspicious allergic reaction to rabies vaccine. The mother declared that 2 hours after receiving the last shot, her child developed generalized urticaria. She later mentioned that her child also had some adverse reactions after receiving the first two shots of rabies vaccine, with fever (up to 38.5°C) and vomiting.

After receiving the third shot she developed a mild temperature, and after the fourth shot a rash (first on her legs, and later on both arms). The epidemiologist from Slavonski Brod suspected that there was a possible allergic reaction after receiving antirabies vaccines made on purified chick embryo cells (Rabipur), and suggested a detailed examination of possible allergic reactions to rabies vaccine to be made at Clinical Allergy Reference Centre, Srebrnjak Children's Hospital (SCH) in Zagreb. This adverse reaction was officially reported to the Croatian Institute of Public Health (CIPH), HALMED (Agency for Medicinal Products and Medical Devices of Croatia) and Reference Centre for Rabies. From the findings of diagnostic tests performed at SCH, we single out; slightly elevated eosinophils, other laboratory tests including total IgE were practically in the normal range. Skin Prick Test (SPT) to inhaled and nutrient allergens, as well as gelatine and neomycine were negative, but SPT to a vaccine produced on purified chick embryo cells (Rabipur, lot: 631011E, Novartis) was positive, as well as an intradermal test with positive late allergic reaction to Rabipur. The child was also tested with a rabies vaccine from another manufacturer, with vaccine produced on human diploid cells (Sanofi Pasteur, lot N1F685M). SPT was negative but with a positive intradermal test and the appearance of a late allergic reaction.

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Discussion

According to WHO, severe ARs are more often associated with nerve tissue vaccines, in comparison with cell culture vaccines and embryonated egg-based vaccines [2]. Usual Adverse Events (AEs) are fever, headache, dizziness, gastrointestinal symptoms, pruritus, erythematous rash and pain. Systemic allergic reactions are very rare. Kang et al. described an ARs following rabies vaccine in a 10-year-old girl, after being bitten by a stray dog in Bali and prescribed PEP [4]. She developed breathlessness, abdominal cramps, and swelling of lips and eyes 30 minutes after the second dose of rabies vaccine. The last dose of rabies vaccine was given with premedication. Ramezankhani et al. describe ARs to Purified Chick Embryo Cell Vaccine (PCECV) and Purified Vero Cell Rabies Vaccine (PVRV). Most of the reported systemic AEs were headache and fever, but that PCECV vaccination was more associated with fever and itching at the injection site [5]. They concluded that there was no significant difference between PCECV and PVRV vaccine regarding local and systemic ARs. Dobardzic et al., in their study describe how the US Food and Drug Administration (FDA) licensed purified chick embryo cell (PCEC, RabAvert) vaccine against rabies in humans following clinical trials demonstrating safety and efficacy [6]. The Vaccine Adverse Event Reporting System (VAERS) received 336 reports of AEs following vaccination. There were no death reports, but serious events were described in 7%. From a total of 20 serious AEs, just 3 were classified as possible anaphylaxis. Moro et al., in their 25-year review of VAERS in the USA after using rabies Human Diploid Cell Vaccine (HDCV) for PEP [7] reported that out of 1.611 cases of AEs after HDCV, 93 (5.8%) were serious. Among serious reports, four deaths appeared to be unrelated to vaccination. The authors conclude that this 25-year study did not identify new or unexpected AEs after HDCV [7]. There are two vaccines in the Republic of Croatia registered by HALMED Agency for Pre-Exposure (PrEP) and Post-Exposure (PEP) rabies prophylaxis in humans. They are PCECV and HDCV available [8]. HALMED Agency is collecting all AEs regarding therapeutic procedures, including ARs connected to vaccinations. Every AEs regarding vaccination have to be reported to the CIPH, as well. According to the official registry of vaccines AEs from CIPH, there were 63 registered AEs from rabies vaccine produced on PCECV as follows: 29 cases of pyrexia and 10 allergic reactions, 2 anaphylactic reactions, 7 headaches, 6 neurovegetative disorders, 5 local reactions, 2 vomiting with diarrhoea and other rare reactions. There were only 3 cases of ARs from vaccine made on HDCV of rash, and urticaria [9].

Conclusion

This child can receive rabies PEP, but only with vaccines produced on HDCV with caution and premedication. In case of serious AEs with the rabies vaccine we may continue the ordered PEP schedule with other vaccines (e.g. made on human diploid cells). Although allergic reactions to the rabies vaccine are extremely rare, vaccination can be done following the official WHO guide for PrEP and PEP in humans.

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