



Urticaria following varicella vaccine associated with gelatin allergy

Sanford Singer^a, Candice E. Johnson^{c,*}, Rose Mohr^b, Cheryl Holowecky^b

^a*Department of Pediatrics, School of Medicine and MetroHealth Medical Center, Case Western Reserve University, Cleveland, OH, USA*

^b*Department of Otolaryngology, Head and Neck Surgery, School of Medicine and MetroHealth Medical Center, Case Western Reserve University, Cleveland, OH, USA*

^c*Department of Pediatrics, School of Medicine, University of Colorado, Denver, CO, USA*

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Abstract

An uncommon reaction to varicella vaccine has been urticaria. Based on two reports of urticaria believed to be due to gelatin in recipients of measles–mumps–rubella vaccine, we suspected gelatin as the cause of generalized urticaria in two children after varicella vaccination. Intradermal testing with gelatin yielded a wheal and flare reaction in both children. We conclude that children known to be allergic to gelatin should not receive Oka/Merck varicella vaccine (VARIVAX[®]). © 1998 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Varicella vaccine was first licensed in 1995 in the US for use in individuals 12 months or older, after being used in Japan for 20 years. Protective efficacy has been 86% in the first year after vaccination [1]. The incidence in vaccinated children following household exposure is now only 12%, whereas historically, 87% of non-vaccinated children developed varicella [1].

Reported complications of the vaccine have been few, one of them being urticaria [2]. We saw two children in 1996 who developed urticaria after vaccination. We performed intradermal testing to determine the probable cause of the allergic response. Based on reports of urticaria after measles, mumps, rubella vaccine (MMR) [2], we suspected porcine gelatin as the probable allergen in the vaccine.

2. Cases

2.1. Case 1

C.V., a four-year old female, presented to our acute care clinic with urticarial reactions 2 days after having received a dose of varicella vaccine. Within 8 h of receiving the vaccine, the mother reported urticaria and edema over her face, hands and abdomen, along with severe pruritus. There was no airway distress or wheezing. She was treated with 25 mg of diphenhydramine in our clinic and within 2 h was free of the rash and pruritus, which never recurred. Normal laboratory studies included a complete blood count and differential, C3 and C4 levels, anti-nuclear factor, anti-DNA and urinalysis. The mother reported occasional consumption of gelatin desserts without reaction (Figs. 1 and 2).

2.2. Case 2

C.G., a 3-year old male, presented 4 days after having received the varicella vaccine. His mother reported extensive urticaria over his trunk and legs that began

* Corresponding author. Present address: The Child Health Clinic B032, The Children's Hospital, 1056 E. 19th Avenue, Denver, CO 80218, USA. Tel.: +1-303-861-6007; fax: +1-303-764-8072.

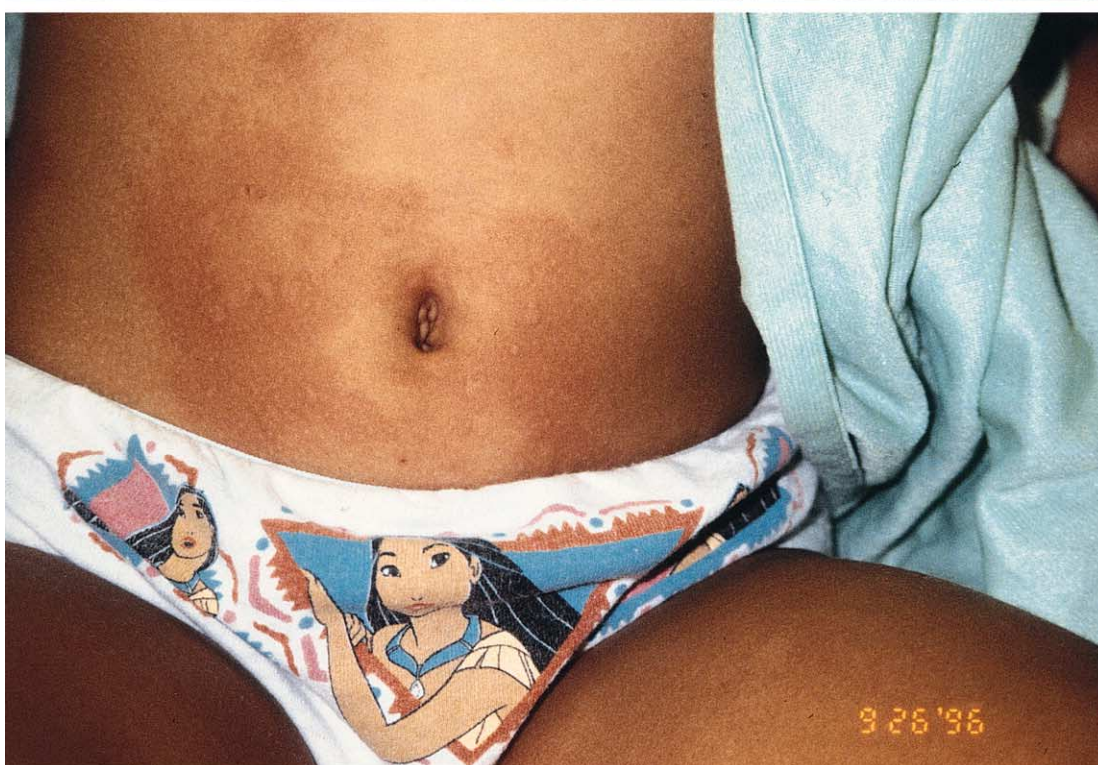


Fig. 1. Case 1 (CV) showing extensive urticaria over her face approximately 48 h after vaccination.

Fig. 2. Case 1 (CV) showing urticaria over the abdomen, 48 h post-vaccination.

on the second day after having received the vaccine. By the time he was seen, the urticaria were less numerous and resolved spontaneously within 1 week. C.G. also had consumed gelatin desserts without problems in the past.

3. Methods

Merck, Sharp and Dohme, the manufacturer of Varivax, supplied us the name of the manufacturer of the porcine gelatin vehicle (Dynagel, Calumet City, IL). They provided a sample of the gelatin product for use in skin testing. Informed consent was obtained from the parents of both children. The children were skin tested for a gelatin allergy. The tests were administered in the Otolaryngology Clinic with resuscitative measures available.

The concentration of the porcine gelatin in the varicella vaccine is 12.5 mg of solute in 0.5 cc. Our test dose consisted of 12.5 mg of porcine gelatin in 0.5 cc sterile water, which was sterilized by autoclaving. An emulsion of lidocaine 2.5% and prilocaine 2.5% was applied to the skin test area 1 h before testing. Control intradermal wheals of 4 mm were made with histamine and albumin saline with phenol (0.4%). Before administering the porcine gelatin in the full vaccine concentration, serial dilutions of 1:25 and 1:5, using the phenolated albumin saline, were administered intradermally. All testing was done intradermally and all wheals were measured after 10 min.

4. Results

Both patients had a positive skin test control to the histamine at the time of testing and a skin test control using phenolated albumin saline was negative. In the first patient, CV, the 4 mm wheal with the porcine gelatin at the vaccine concentration developed a flare reaction and the wheal increased from 4 to 8 mm. In the second patient, the allergic response began with the 1:5 dilution (the 4 mm wheal enlarged to a 7 mm wheal). The vaccine concentration in the second patient gave an immediate response and the initial 4 mm wheal enlarged to a 9 mm wheal.

5. Discussion

Urticarial reactions to varicella vaccine are being reported as occurring several days after vaccination. In a study of 32,947 children at Kaiser Permanente [2],

the rate of hives in children within 21 days of vaccination was 4.75/1000 patient years, compared to none in control children ($p = 0.122$). This is the most common side effect reported. In our hospital we have distributed over 2800 doses of varicella vaccine since early 1995 and have seen 4 cases of urticaria within 1 week of vaccination. Two of these children were skin-tested for gelatin-sensitivity and were positive. No wheezing, anaphylaxis or angioedema has been reported by Kaiser or seen by us [2]. In 1993 Kelso et al. [3] reported the first proven case of anaphylaxis mediated by IgE to gelatin, after receipt of MMR. This was in a 17-year old girl who also developed ear and throat swelling after eating gelatin. Allergy tests for two other vaccine components, eggs and neomycin, were negative. The IgE antibodies of the girl cross-reacted with fish, bovine and porcine gelatin, as well as with unflavored and cherry-flavored gelatin. Sakaguchi et al. [4] studied 26 children who had systemic immediate-type reaction to live measles, mumps and rubella vaccine. 9 had shown anaphylaxis, 10 had shown wheezing and urticaria and 7 had only urticaria. 24 of 26 children had anti-gelatin IgE to both porcine and bovine gelatin, compared to none of 26 control children. 7 of the 24 had allergic reactions to eating gelatin; all 7 had urticaria and three had airway or facial edema. Our two children were not known to be allergic to gelatin, and both had received one dose of MMR with no problems. The occurrence of urticaria following vaccination, coupled with the positive intradermal test results with porcine gelatin at the same concentration as in the vaccine, would dictate caution if a second dose of MMR or varicella vaccine were contemplated in these children. Further studies are needed to determine if gelatin allergy is the cause of all urticaria in varicella vaccine recipients, or if viral antigens may also play a role.

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