

Anaphylaxis to MMR Vaccine Mediated by IgE Sensitivity to Gelatin

MAJ Charles Kent Miller, MC, USAF* ; MAJ Jun C. Mendoza, MC, USAF† ; COL Christopher A. Coop, MC, USAF‡

ABSTRACT

The measles-mumps-rubella (MMR) vaccine is generally well tolerated, and reports of anaphylaxis to the vaccine are rare. IgE-mediated reactions to vaccines are often caused by additives or residual vaccine components. An inability to obtain proper immunizations can be a disqualifying component to military service. We report a case of anaphylaxis to the MMR vaccine in a new military recruit sensitized to gelatin IgE.

INTRODUCTION

Administration of the measles-mumps-rubella (MMR) vaccination, or proof of this vaccination, is mandatory for new recruits in the military. MMR is a well-tolerated vaccination with rare reports of severe allergic reactions. It is estimated that a severe allergic reaction from any vaccination occurs at a rate of 1.3 per million doses of vaccines given,¹ while rates of anaphylaxis to MMR are even lower.²

Reactions to the MMR vaccine are often caused by additive or residual vaccine components. In addition to MMR viral antigens, the vaccine also contains egg protein, neomycin, sorbitol, and gelatin.³

We report a case of anaphylaxis following MMR vaccination. Laboratory and skin testing results strongly suggest that this reaction was due to an IgE-mediated hypersensitivity reaction to the gelatin component of the vaccine.

CASE REPORT

A 19-year-old male in the United States Air Force Basic Military Training program developed symptoms consistent with an anaphylactic reaction after receiving the MMR vaccine. During in-processing he did not have records of previous immunizations, and a repeat MMR vaccine was recommended. He was given an intramuscular (IM) penicillin injection 15 minutes prior to the MMR vaccine, but had

no immediate symptoms at that time. About 2–3 minutes after getting the MMR vaccine, he developed onset of facial urticaria, periorbital swelling of both eyes with redness and itching, congestion, rhinorrhea, slight cough, and itchy throat.

He was diagnosed with anaphylaxis and promptly treated with an epinephrine 0.3 mg intramuscular (IM) injection and 25 mg of diphenhydramine intravenously. He was then taken to the ER where his symptoms continued to improve over a 6-hour observation period. He was discharged back to training on a 5-day course of prednisone 50 mg daily, diphenhydramine 25 mg every 8 hours as needed, and ranitidine 150 mg twice daily as needed with no further reactions.

He was subsequently referred to the allergy clinic for further investigation to determine if his allergic reaction was from the penicillin injection or from the MMR vaccine.

PAST MEDICAL HISTORY

At 6 years old, this patient reports having a reaction to the varicella vaccine that resulted in tightness of his throat, heaviness of his chest, and vomiting. He did not require medical intervention and his symptoms gradually resolved on their own.

He reports a suspected pork allergy, as he has immediate tightness in his chest after eating large amounts of pork. He also reports a suspected gelatin allergy, as he has immediate tightening in his throat after eating gummy bears as well as hives on his face after using gelatin-containing face creams.

He has never had a reaction to penicillin, but he cannot recall ever taking penicillin in the past. He also has a history of seasonal allergic rhinitis.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses considered included possible IgE-mediated hypersensitivity to MMR vaccine, pork allergy, gelatin allergy, and/or penicillin allergy.

INVESTIGATIONS

The patient's history was consistent with a possible IgE-mediated hypersensitivity to the MMR vaccine and/or the

*Pediatrics, Aviano Air Base, Italy, 31st Medical Group, Via Pedemonte 9, Aviano 33081

†Department of Allergy and Immunology, Wilford Hall Medical Center, 59th Medical Group, 2200 Bergquist Drive Lackland Air Force Base, San Antonio, TX 78236

‡Allergy and Immunology, Wilford Hall Medical Center, 59th Medical Group, 2200 Bergquist Drive Lackland Air Force Base, San Antonio, TX 78236

The views expressed are solely those of the authors and do not reflect the official policy or position of the U.S. Army, U.S. Navy, U.S. Air Force, the Department of Defense, or the U.S. Government. No current conflict of interests to disclose.

doi:10.1093/milmed/usaa058

© The Author(s) 2020. Published by Oxford University Press on behalf of the Association of Military Surgeons of the United States. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.

TABLE I. Initial Serum Lab Results

Varicella Zoster Ab IgG	Immune
Rubella virus Ab IgG	Immune
Rubeola virus Ab IgG	Non-Immune
Mumps virus Ab IgG	Immune
Cat Dander Ab IgE	<0.35 kU/L
Pork Ab IgE	<0.35 kU/L
Gelatin Ab IgE	1.20 kU/L

TABLE II. Administration of Vaccine in Graded Doses

For a vaccine in which the full normal dose volume is 0.5 mL, give the following doses at 15-minute intervals as tolerated ^a	
0.05 mL 1:10 dilution	
0.05 mL full-strength	
0.1 mL full-strength	
0.15 mL full-strength	
0.2 mL full-strength	

^aMust be done under direct medical supervision prepared with emergency medications and equipment to promptly treat an anaphylactic reaction should it occur. Observer for at least 30 minutes afterward.

penicillin IM shot. His past medical history was also concerning for a possible allergy to gelatin and pork. Antibody titers to measles, mumps, and rubella were first obtained to determine if patient still required another MMR vaccine, and serology testing was also obtained to gelatin, pork, and cat (see Table I).

Labs showed patient was rubella immune and mumps immune, but still measles non-immune. His serology testing also showed that he was positive for gelatin but negative for pork. Per Advisory Committee on Immunization Practices (ACIP) guidelines, this patient still required one additional dose of the MMR vaccine, as he was in a postsecondary institution with multiple close contacts.⁴

This patient was informed on the risks and benefits of testing and administration of the MMR vaccine, and he agreed to continue with the procedure.

SKIN TEST/GRADUATED DOSING

Skin prick testing was completed using saline as a negative control, histamine as a positive control, and the MMR vaccine and was initially found to be positive to the MMR vaccine. Per the "Adverse reactions to vaccines practice parameter 2012 update," any patient with a history of a vaccine allergy and positive skin test can still get that vaccine in graduated doses (Table II).⁵ After much discussion, this patient wished to continue with graduated dosing challenge to the MMR vaccine.

Per the practice parameter's graduated dosing protocol, this patient was first given a 0.05 mL injection of the vaccine at 1:10 dilution and was observed for 15 minutes without issues.

He was then given a 0.05 mL injection of the vaccine at full strength, at which time, he developed sudden onset of periorbital swelling of both eyes with redness and itch-

ing, congestion, and sneezing. He denied associated light-headedness, syncope, shortness of breath, wheezing, cough, vomiting, abdominal pain, or diarrhea.

Due to concern for anaphylaxis, he was given one dose of IM epinephrine 0.3 mg, one dose of cetirizine 10 mg orally, and one dose of ranitidine 150 mg orally. 15–20 minutes later, he reported feeling better but continued to have mild left periorbital swelling, so an additional dose of cetirizine 10 mg was given with good response. He was observed for 1 hour and then discharged after complete resolution of his symptoms.

FOLLOW-UP

The results of serology, skin prick testing, and vaccine challenge show that this patient's previous anaphylactic reaction was likely due to the MMR vaccine and not the penicillin shot. Serum IgE testing further suggests that the reaction was due to an IgE-mediated hypersensitivity reaction to the gelatin component in the vaccine.

This patient would still require a second dose of MMR in order to remain in the military. However, he was able to contact his family who helped locate documents that showed he actually did have two previous MMR doses administered in childhood. As he now had three total documented doses of MMR (two from childhood and one during in-processing), no further doses of the vaccine were needed, even if subsequent MMR titers were found to be negative or equivocal.⁵ He also does not need postexposure prophylaxis with immune globulin in the event he has a significant exposure to someone with measles. Doses of vaccine with written documentation of the date of receipt would be valid and considered presumptive evidence of immunity.⁴

This patient was advised that he will need to consult with an allergist before any subsequent dose of any gelatin-containing vaccine is administered. People who have a gelatin allergy typically react to all types of gelatin, whether that gelatin was manufactured from a bovine or porcine source.² This may eventually be a concern in the military should this patient require a yellow fever vaccine, rabies vaccine, or other vaccination that contains high gelatin content.

Further investigation into a possible penicillin allergy was recommended because a penicillin allergy could still not be ruled out as the cause of his first anaphylactic episode. Unfortunately this patient declined and wished to return to training and pursue penicillin testing at his next duty station.

DISCUSSION

Anaphylaxis results from the release of inflammatory mediators from mast cells and basophils which leads to an acute allergic response.⁶ It is a severe systemic allergic reaction with acute onset and potentially fatal implications. Vaccine components including gelatin and serum albumin have been known to cause anaphylaxis in some individuals.^{7,8}

We report a case of a basic military trainee who had an anaphylactic reaction to the MMR vaccine. His history was suggestive of a gelatin sensitivity, and serum testing confirmed positive IgE antibodies to gelatin. Further skin testing, and the resultant second anaphylactic episode, suggests that the patient had an IgE-mediated reaction to a component of the MMR vaccine. The data suggests that the hydrolyzed gelatin added to the vaccine was the cause of his anaphylactic reaction.

REFERENCES

1. McNeil M, Weintraub E, Duffy J et al: Risk of anaphylaxis after vaccination in children and adults. *J Allergy Clin Immunol* 2016; 137(3): 868–78.
2. Pool V, Braun MM, Kelso JM et al: Prevalence of anti-gelatin IgE antibodies in people with anaphylaxis after measles-mumps-rubella vaccine in the United States. *Pediatrics* 2002; 110(6): e71.
3. Kelso JM, Jones RT, Yunginger JW: Anaphylaxis to measles, mumps, and rubella vaccine mediated by IgE to gelatin. *J Allergy Clin Immunol* 1993; 91(4): 867–72.
4. CDC: Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the advisory committee on immunization practices (ACIP). *MMWR* 2013; 62(RR04): 1–34.
5. Kelso JM, Greenhawt M, Li J et al: Adverse reaction to vaccines practice parameter 2012 update. *J Allergy Clin Immunol* 2012; 120(1): 25–43.
6. Castells M: Diagnosis and management of anaphylaxis in precision medicine. *J Allergy Clin Immunol* 2017; 140(2): 321–33.
7. Dumortier B, Nosbaum A, Ponvert C, Nicolas JF, Berard F: Measles-mumps-rubella vaccination of an egg-allergic child sensitized to gelatin. *Arch Pediatr* 2013; 20(8): 867–70.
8. De Silva R, Dasanayake WMDK, Wickramasinha GD et al: Sensitization to bovine serum albumin as a possible cause of allergic reactions to vaccines. *Vaccine* 2017; 35(11): 1494–500.