

CASE REPORT

Delayed-type hypersensitivity to vaccine aluminum adjuvant causing subcutaneous leg mass and urticaria in a child

Samantha C. Gordon MD¹ | Diana W. Bartenstein BA^{2,3}  | Shahein H. Tajmir MD⁴ |
Johanna S. Song MD, MS² | Elena B. Hawryluk MD, PhD²

¹Department of Pediatrics, Massachusetts General Hospital, Boston, MA, USA

²Department of Dermatology, Harvard Medical School, Massachusetts General Hospital, Boston, MA, USA

³School of Medicine, Tufts University, Boston, MA, USA

⁴Department of Radiology, Harvard Medical School, Massachusetts General Hospital, Boston, MA, USA

Correspondence

Elena B. Hawryluk, MD, PhD, Massachusetts General Hospital, Department of Dermatology, Boston, MA, USA.
Email: ehawryluk@partners.org

Abstract

A 3-year-old girl presented with a 7-month history of a waxing and waning left thigh mass associated with pruritus and erythema at the site of two previous DTaP-HepB-IPV vaccinations. Patch testing was positive to aluminum chloride, supporting a diagnosis of vaccine granuloma secondary to aluminum allergy; her symptoms had been well controlled with antihistamines and topical steroids. Injection site granulomas are a benign but potentially bothersome reaction to aluminum-containing immunizations that can be supportively managed, and we encourage strict adherence to the recommended vaccine schedule in this setting. Patch testing is a sensitive, noninvasive diagnostic tool for patients presenting with this clinical finding, and dermatologist awareness can prevent unnecessary medical examination and provide reassurance.

KEYWORDS

allergy, lumps/bumps, pruritus, therapy-topical, urticaria

1 | REPORT OF A CASE

A 3-year-old girl with a past medical history of acetabular dysplasia presented to dermatology with a 7-month history of a waxing and waning left thigh mass associated with local itching, swelling, and hives. The patient was up to date with the recommended immunization schedule, and medical records revealed DTaP-HepB-IPV injections (GlaxoSmithKline Pediarix: Lots AC21B35788 and AC21B370DA) to her left thigh at 4 and 6 months of age.

On examination, the patient had a firm, mobile, nontender subcutaneous nodule with an overlying hyperpigmented macule and small central urticarial papule on the left lateral thigh (Figure 1). There was one mobile, nontender lymph node in the left inguinal area. Although not part of dermatologic examination, imaging was available from prior evaluations. Ultrasound demonstrated a 1-cm subcutaneous hypoechoic lesion with internal echogenic components and no vascular flow on Doppler, initially thought to be consistent with a lymph node. Repeat ultrasound 2 months later was unchanged. Magnetic resonance imaging demonstrated two enhancing, T1-hypointense

and T2-hyperintense, ill-defined nodular foci in the subcutaneous fat of the left thigh.

Based on literature review, patch testing was performed with pure aluminum (in petroleum, unknown concentration) and aluminum-chloride hexahydrate (in petroleum, 2% concentration). Patient scratching disturbed the pure aluminum patch prematurely. A strong positive, 2+ reaction with erythematous papules and infiltration was observed at the aluminum chloride site 96 hours after patch placement.

Overall, the clinical presentation was consistent with a subcutaneous granuloma from an aluminum allergy. Two aluminum salts were present in her DTaP-HepB-IPV injections, and her 4-month vaccine would have provided sensitization to the 6-month vaccine. The patient was empirically treated with oral cetirizine and desonide cream, which reduced urticarial episodes and minimized pruritus, although continued symptoms were reported at 12-month follow-up, with waxing and waning flares, responsive to treatment. She continues to complete her vaccine schedule, with no specific avoidance of aluminum-containing vaccinations, and has not developed additional reactions despite aluminum-containing injections to other extremities.



FIGURE 1 Left lateral thigh with firm, mobile, nontender subcutaneous nodule with overlying hyperpigmented patch and small central urticarial papule

2 | DISCUSSION

Subcutaneous nodules, sterile abscesses, and contact dermatitis are type IV hypersensitivity reactions that can occur after vaccine administration.¹⁻⁶ Aluminum salts increase the Th2-mediated antibody response to the desired antigen and have been used as adjuvants in vaccines since the 1920s^{1,2} (Table 1). Injection-associated granulomas are a rare side effect of immunizations, with reported frequencies of 0.35%-1.18%.³ Although this reaction is more commonly reported in young children, probably because of their frequent vaccination schedule, adults have presented with similar findings after allergen immunotherapy and human papilloma virus vaccination, which both contain aluminum adjuvants.^{2,4} It has been hypothesized that subcutaneous granuloma formation may occur secondary to unintentional superficial deposition of an intramuscular vaccine.⁷ Such unintentional injection would be expected to occur more commonly in children, who have difficulty remaining still for injections, and could explain the difference in reported frequencies between younger and older patients.

Injection site granulomas classically present as pruritic or tender subcutaneous nodules. Reported secondary changes include localized hyperpigmentation, hypertrichosis, discoloration, and eczema.^{5,6} Although not required for diagnosis, histopathology demonstrates nonencapsulated granulomas that stain positive for aluminum.^{1,3,6} Clinical diagnosis can be challenging, because presentation is often delayed weeks to months and has been reported as late as 8 years after vaccination.^{2,4,5} In our patient, the ultrasound study was helpful to exclude other conditions, such as abscess, and avoided skin biopsy. Imaging results are presented to illustrate the nondiagnostic findings observed in this condition, but we do not believe that extensive imaging is required. Rather, a suggestive history and confirmatory patch testing results are sufficient to confirm the diagnosis. Aluminum patch testing is a sensitive, noninvasive, diagnostic technique for patients with suspected

TABLE 1 Immunizations containing aluminum⁸

Vaccine	Aluminum product
Adenovirus	FD&C Yellow #6 aluminum lake dye
Anthrax (Biothrax)	Aluminum hydroxide
DT (Sanofi)	Aluminum phosphate
DTaP (Daptacel)	Aluminum phosphate
DTaP (Infanrix)	Aluminum hydroxide
DTaP-IPV (Kinrix)	Aluminum hydroxide
DTaP-IPV (Quadracel)	aluminum phosphate
DTaP-HepB-IPV (Pediatrix)	Aluminum hydroxide, aluminum phosphate, aluminum salts
DTaP-IPV/HiB (Pentacel)	Aluminum phosphate
Hib (PedvaxHIB)	Aluminum hydroxyphosphate sulfate
Hep A (Havrix)	Aluminum hydroxide
Hep A (Vaqta)	Amorphous aluminum hydroxyphosphate sulfate
Hep B (Engerix-B)	Aluminum hydroxide
Hep B (Recombivax)	Aluminum sulfate, amorphous aluminum hydroxyphosphate sulfate
Hep A/Hep B (Twinrix)	Aluminum phosphate, aluminum hydroxide
Human Papillomavirus (HPV) (Gardasil)	Amorphous aluminum hydroxyphosphate sulfate
Human Papillomavirus (HPV) (Gardasil 9)	Amorphous aluminum hydroxyphosphate sulfate
Japanese Encephalitis (Ixiaro)	Aluminum hydroxide
Meningococcal (MenB - Bexsero)	Aluminum hydroxide
Pneumococcal (PCV13 - Prevnar 13)	Aluminum phosphate
Td (Tenivac)	Aluminum phosphate
Td (Mass Biologics)	Aluminum phosphate
Tdap (Adacel)	Aluminum phosphate
Tdap (Boostrix)	Aluminum hydroxide

vaccine related reactions, with 77% to 95% of affected patients demonstrating positive contact allergy to aluminum.³ Accurate clinical diagnosis may serve to prevent unnecessary medical investigation and parental anxiety, and we therefore hope to increase awareness of this condition.

When such vaccine granulomas develop, we advise strict adherence to standard immunization schedules despite the local reaction. Most granulomas resolve within months to years, and supportive treatment with antihistamines and low-potency topical steroids can minimize symptoms in the interim.^{3,5} Despite positive patch testing, not all patients will develop additional granulomas when injected with subsequent aluminum-containing vaccines, as seen in our patient.⁵ Vaccine counseling should include granuloma as a possible side effect, and clinicians should provide constructive management approaches for affected patients to achieve their recommended vaccination schedule.

ORCID

Diana W. Bartenstein  <http://orcid.org/0000-0002-8850-9551>

REFERENCES

1. Rosenblatt AE, Stein SL. Cutaneous reactions to vaccinations. *Clin Dermatol*. 2015;33:327-332.
2. Lauren CT, Belsito DV, Morel KD, LaRussa P. Case report of subcutaneous nodules and sterile abscesses due to delayed type hypersensitivity to aluminum-containing vaccines. *Pediatrics*. 2016;138(4):e20141690:e1-e5.
3. Bergfors E, Hermansson G, Nystrom Kronander U, Falk L, Valter L, Trollfors B. How common are long-lasting, intensely itching vaccination granulomas and contact allergy to aluminium induced by currently used pediatric vaccines? A prospective cohort study. *Eur J Pediatr*. 2014;173:1297-1307.
4. Culora GA, Ramsay AD, Theaker JM. Aluminium and injection site reactions. *J Clin Pathol*. 1996;49:844-847.
5. Fawcett HA, Smith NP. Injection-site granuloma due to aluminum. *Arch Dermatol*. 1984;120:1318-1322.
6. Kaaber K, Nielsen AO, Veien NK. Vaccination granulomas and aluminium allergy: course and prognostic factors. *Contact Dermatitis*. 1992;26:304-306.
7. Bergfors E, Trollfors B. Sixty-four children with persistent itching nodules and contact allergy to aluminium after vaccination with aluminium-adsorbed vaccines-prognosis and outcome after booster vaccination. *Eur J Pediatr*. 2013;172:171-177.
8. Centers for Disease Control and Prevention. Vaccine Excipient & Media Summary [on-line]. Available at <https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/excipient-table-2.pdf> Accessed September 6, 2017

How to cite this article: Gordon SC, Bartenstein DW, Tajmir SH, Song JS, Hawryluk EB. Delayed-type hypersensitivity to vaccine aluminum adjuvant causing subcutaneous leg mass and urticaria in a child. *Pediatr Dermatol*. 2018;00:1-3.
<https://doi.org/10.1111/pde.13390>