

Injection Site Necrosis and Ulceration Following Vaccination in an Adult Patient

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ABSTRACT

Local adverse reactions to vaccination are typically mild and often quickly resolve. Vaccine adjuvants such as aluminum salts in combination with improper vaccination technique may result in severe local adverse reactions. As far as we know, there is only one prior case of frankly necrotic rapidly progressing vaccine site necrosis, which occurred in a pediatric patient.[1] To our knowledge, this is the first adult case of vaccine site necrosis to be reported. The presumed etiology has been aluminum salt adjuvants and improper vaccination technique. Here we present an adult case of a severe local reaction to a vaccine resulting in necrosis of the epidermis and dermis with central ulceration. Skin appendages were also involved, with necrosis of eccrine coils and hair follicles. This necrotic ulceration was likely due to robust inflammatory response to aluminum salt subcutaneous injection. Correct vaccine placement, needle size, and needle length may reduce adverse local skin reactions.

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INTRODUCTION

Local adverse reactions to vaccines are typically mild and self-limited; severe reactions are very rare. Causes of adverse reactions include reactions to vaccine adjuvants, improper vaccine placement, and inappropriate needle size and length.[2,3] Common local adverse events include erythema and induration, while more severe reactions include abscess formation and necrosis. A single pediatric case of vaccine-associated local necrotizing granulomatous reaction due to subcutaneous injection has previously been reported.[1] We report a case of local epidermal and dermal necrosis and ulceration lacking granulomas in an adult following tetanus-diphtheria-acellular pertussis (Tdap) and pneumococcal polysaccharide (Pneumovax) administration. Skin appendages were also involved, evidenced by hair follicle and eccrine coil necrosis. The Tdap vaccine contains aluminum salt adjuvants, which have been implicated in the pathogenesis of local skin vaccine reactions.

CASE REPORT

A 51-year-old Caucasian female presented with a necrotic ulcer at the site of recent Tdap and Pneumovax vaccination. The patient received both vaccines in her right deltoid 10 days prior to presentation. She had no previous history of local or systemic vaccine reaction. On the evening of vaccination, the patient experienced tenderness, redness, and induration at the vaccination site. The next day bruising developed followed by blistering. A short course of oral doxycycline and a gluteal intramuscular steroid injection provided only mild transient relief.

The blister ruptured on day 4, draining serosanguinous fluid. There was no purulent drainage, but redness persisted at the site. Over the following few days, the eroded blister progressed into a necrotic ulcer with black anesthetic eschar with a surrounding large tender ill-defined indurated erythematous plaque (Figure 1).

The patient applied neomycin to the ulcerated area and covered with a bandage prior to presentation, but this did not provide any relief.

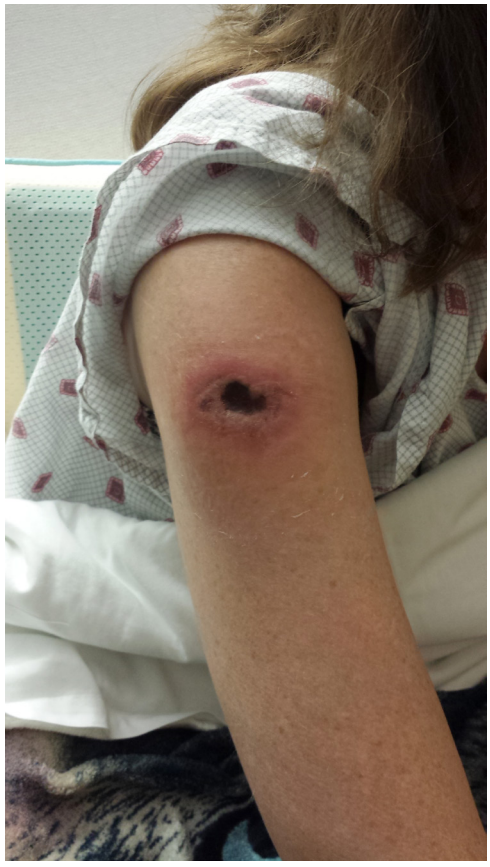
At presentation, she was afebrile and had no leukocytosis. Wound and blood cultures returned negative at 48 hours. Punch biopsy for tissue culture and histological evaluation was performed. Tissue cultures were negative. Dermatopathology results showed nonspecific diffuse and extensive dermal and epidermal necrosis (Figure 2). There was mixed inflammatory cell infiltrate within the dermis with preservation of dermal collagen. Eccrine coils and hair follicles were necrotic. No definitive granulomas were identified. Periodic acid-Schiff, Fite, Gram, silver, and acid-fast stains did not reveal microorganisms.

The patient was counseled to apply Vaseline and Silvadene cream for wound care and ibuprofen as needed for pain.

DISCUSSION

Adjuvants are common in vaccines and are added to optimize the immune response to antigens. Adjuvants are generally considered safe; however adverse events to adjuvant components can occur, especially when injected into subcutaneous fat rather than intramuscularly. Aluminum salts are commonly

FIGURE 1. The patient's site of vaccination in right deltoid exhibiting a grossly necrotic ulcer with black anesthetic eschar with a surrounding large tender ill-defined indurated erythematous plaque.

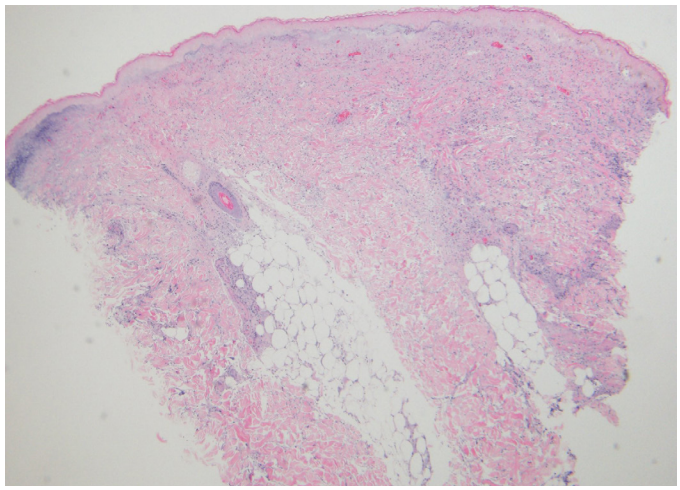


used adjuvants that have been associated with a variety of local adverse reactions including granuloma formation, allergic reaction, and myofasciitis.[2] Granulomatous reactions to aluminum salts have been reported, and while these reactions can result in persistent pruritic nodules, this is considered a benign reaction that is self-resolving.[1,4,5,6] Patients with this local reaction present with mobile subcutaneous nodules. Histological patterns can vary and can include necrobiosis.[4,6] While this reaction pattern is more common than previously suspected, it is still uncommon and the benefits of aluminum salt adjuvants are thought to outweigh the risks.[5]

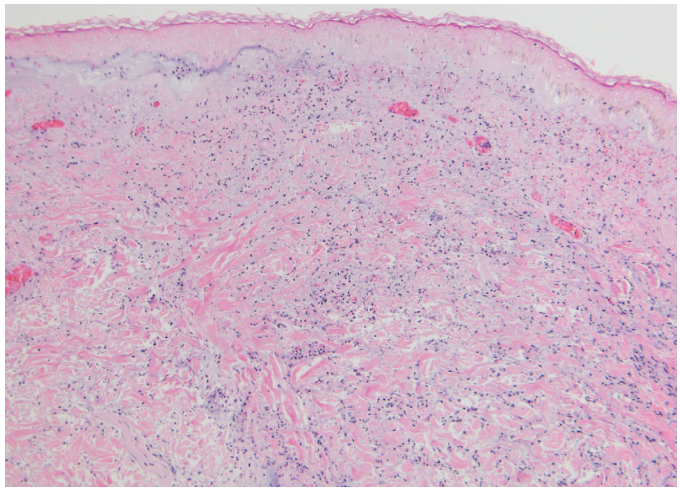
Clinically necrotic and rapidly progressive severe local reactions to vaccines containing aluminum salts are very rare; a single case of a severe necrotic ulcerative reaction to 13-valent pneumococcal conjugate vaccine (PCV13) has been reported in an infant.[1] This case was thought to be due to improper subcutaneous placement of this vaccine rather than a hypersensitivity reaction as this presentation followed his second PCV13 injection; he did not experience adverse reactions to his first or third PCV13 injections.

FIGURE 2. Diffuse necrosis of the epidermis and dermis visible at 4X (A) and 10X (B). Mixed inflammatory cell infiltrate in dermis with necrosis of eccrine coils and hair follicles at 20X (C).

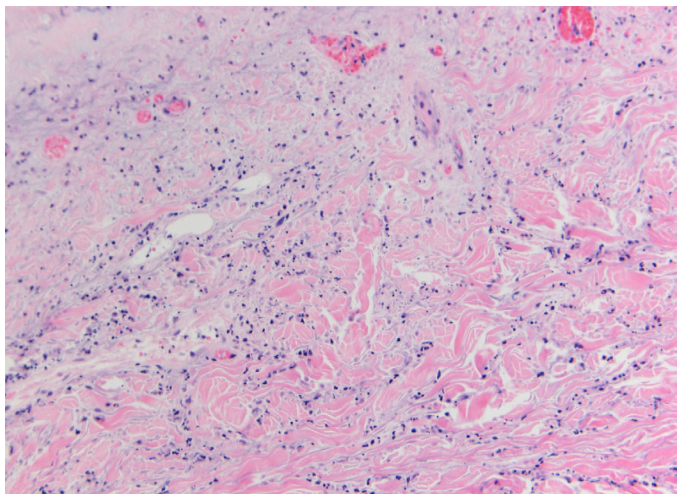
(A)



(B)



(C)



Post-vaccination delayed hypersensitivity reaction to aluminum salts can result in injection site adverse reactions like erythema, subcutaneous nodules, and sterile abscess formation.[7,8] The formation of granulomas in patients with local vaccine reactions has been reported and supports a delayed-type hypersensitivity reaction.[4,5,9] Previous articles have also shown an association between positive aluminum patch tests and post-vaccination subcutaneous nodules.[9,10] Lehman et al describes an infant with recurrent sterile abscesses at vaccination sites who also had a positive aluminum patch test.[11] Further studies are needed to confirm the association between aluminum allergy, delayed hypersensitivity reaction, and formation of persistent nodules following vaccination. Though our patient had frank necrosis rather than an itchy subcutaneous nodule, a delayed type hypersensitivity reaction should be a consideration in the etiology of her ulcer.

Correct vaccine placement and proper needle length and size can minimize vaccine reactions to aluminum salts and improve patient outcomes. Placement of vaccines into subcutaneous tissue rather than deep into muscle can cause irritation and decreases efficacy of the vaccine.[3,12] Frederiksen et al describes a child with an itching granuloma at vaccine injection site on the second shot in a series; however, no granuloma formed when the third shot was carefully placed intramuscularly.[13] A longer needle and larger gauge may facilitate deep intramuscular injection and greater vaccine dispersion, respectively.[3] The blood supply to muscle is larger than subcutaneous tissue, facilitating faster absorption of the vaccine into the circulation. Thus, deep intramuscular injection may reduce local reaction to aluminum salts and improve integration of vaccine components into the blood. Ipp et al demonstrated that a longer needle reduced local redness and swelling in children given the diphtheria, tetanus, pertussis-polio vaccine.[14] A wider bore injects the vaccine over a larger surface area and prevents concentration of vaccine contents in one localized area. Muscles also have fewer pain fibers than the skin and subcutaneous tissue, indicating that intramuscular injection using a longer needle may actually reduce pain at the injection site.[3] To prevent local adverse reactions to aluminum adjuvants, healthcare providers should evaluate each patient prior to vaccination and select an appropriate needle size and gauge to accomplish deep intramuscular injection.

The previous report of necrotizing granulomatous reaction to subcutaneous aluminum salts warrants evaluation for this same condition in our patient.[1] Her current biopsy shows no evidence of granulomatous inflammation, only nonspecific necrosis of the epidermis and dermal appendages. The absence of granulomas in our patient is extremely unique, although it is possible that granulomas were present but missed due to sampling error from the biopsy.

Improper placement and subsequent inflammatory reaction to aluminum salts is the likely cause of our patient's current condition; however, allergic reaction to aluminum or other vaccine components should be considered. The Pneumovax vaccine contains the preservative phenol, a potential allergen. Neomycin is a known contact allergen, and application at the ulcer site may have elicited a delayed-hypersensitivity; however, neomycin-induced granulomatous reaction has not previously been reported. It is also possible that this represented a hypersensitivity reaction to aluminum. However, even in aluminum-allergic patients, proper intramuscular injection reduces local adverse reactions and allows these patients to safely receive aluminum-adjuvant vaccines.[15] Infection was thought to be unlikely given our patient's negative cultures, afebrile state, and normal leukocyte count. It is imperative that healthcare professionals recognize the importance of proper vaccine placement, needle size, and needle length in the placement of vaccines. Proper placement not only reduces adverse local reactions but also improves vaccine efficacy and patients' trust in their healthcare providers.

CONCLUSION

Local necrosis at the site of vaccination is a rare adverse event, with only one case reported to date. Aluminum salt toxicity was thought to be the likely culprit in this case, especially if injected subcutaneously rather than intramuscularly. Proper intramuscular placement and appropriate needle size and length may prevent this severe vaccine reaction and improve patient outcomes.

DISCLOSURES

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Statement of Ethics:

Informed consent was obtained from the patient.

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