Case Report

Delayed-Type Hypersensitivity Reaction to Anthrax Vaccine

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The Anthrax Vaccine Immunization Program is a Department of Defense initiative to protect military personnel against the threat of anthrax. Surveillance for adverse events associated with anthrax vaccination has shown that mild local reactions are not uncommon while systemic reactions are extremely rare. We present a case of a 26-year-old male with delayed-type hypersensitivity after two doses of anthrax vaccine.

Introduction

The anthrax vaccine is given as a series of six shots plus an annual booster as part of the Anthrax Vaccination Program for military personnel. The vaccine is a sterile cell-free filtrate vaccine from an avirulent nonencapsulated strain of *Bacillus anthracis*. Bioport Corporation of Lansing, Michigan manufactures the anthrax vaccine. It contains small amounts of aluminum hydroxide (no more than 2.4 mg per 0.5-mL dose) as an adjuvant. It also contains small amounts of formaldehyde (no more than 0.0037%) and benzethonium chloride (no more than 0.0025%) as preservatives.[1] Medical surveillance by the Department of Defense for adverse events has shown that about 30% of males and 60% of females get small local reactions to the vaccine. This is described as swelling and tenderness at the injection site less than 2.5 cm.[2] Between 1 and 5% of the population get larger local reactions of 2.5 to 12.7 cm. Around 1% of vaccinations produce local reactions larger than 12.7 cm. There has been an extremely low rate of less than 0.2% of systemic reactions. The independent Anthrax Vaccine Expert Committee reviewed 843 Vaccine Adverse Event Reporting System cases in June 2000.[3] Urticaria or other rashes where found in 22 of these cases. Workers at the U.S. Army Medical Research Institute of Infectious Diseases have used the anthrax vaccine since 1973. Under their reporting system, 4% of doses produced a local reaction, which consisted of swelling, erythema, induration, and itching at the injection site.[6] With 0.5% of doses they reported systemic reactions which consisted of fever, chills, malaise, headaches, and muscle and joint aches.

Case Report

A 26-year-old active duty male received his first anthrax immunization in his right arm with no adverse affect. Two weeks later he received the second immunization in the deltoid area of his left arm. He developed a small lump and mild soreness at the injection site and 10 days later noticed a rash distal to the injection site on his left arm. Four weeks after the first immunization, he received a third injection; this time in his right arm. No lump developed but he complained of transient muscle soreness and a similar rash that developed after 3 days at a site distal to the injection on his right arm. He did not complain of pruritus or any systemic symptoms. He was evaluated by dermatology after this second eruption. On physical examination was a pink annular scaly plaque 3.5 × 4.0 cm (Fig.1). This was KOH negative. A 4-mm punch biopsy was performed from the leading edge of this lesion. The microscopic diagnosis revealed focal spongiotic dermatitis. He had a similar resolving eruption on the left arm from his second immunization (Fig. 2). He was given 0.05% halobetasol proprionate ointment to apply twice a day and the lesions resolved within days. He was administered an Allergen Thin-layer Rapid Use Epicutaneous Test and demonstrated no reaction to formaldehyde. We have seen two other patients in the past year with adverse reactions to anthrax immunizations. They both revealed positive allergic reactions to formaldehyde on patch testing. Unlike this case report, these two patients presented with widespread eczematous eruptions after anthrax immunization. Upon referral to the allergist, our 26-year-old patient was given a prick test to which he reacted with 10 mm of induration and 30 mm of erythema to the histamine positive control. He did not react to the water-negative control. He was injected with full-strength anthrax vaccine and a 1:100 and 1:10 dilution. He displayed no immediate response (read at 18 and 31 minutes). On follow-up examination at 48 hours, he displayed 15 mm of induration and 40 mm of erythema to the full-strength anthrax vaccine. The preceding allergy testing strongly suggests a delayed-type hypersensitivity reaction to the anthrax vaccine. The patient complained of a similar pink annular eruption on his right hip developing 10 days after the anthrax prick test. He did not seek medical attention for this eruption and it resolved after several days of treatment with 0.05% halobetasol proprionate ointment. On follow-up examination several weeks later, there was a small annular area of postinflammatory hyperpigmentation on the right hip. The patient was given a medical exemption from the anthrax immunization program and he suffered no further sequela.

Comments

The anthrax immunization program has received considerable press and political attention regarding the safety of the vaccine. Systemic reaction to the anthrax vaccine has been

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This manuscript was received for review in April 2001. The revised manuscript was accepted for publication in September 2001.

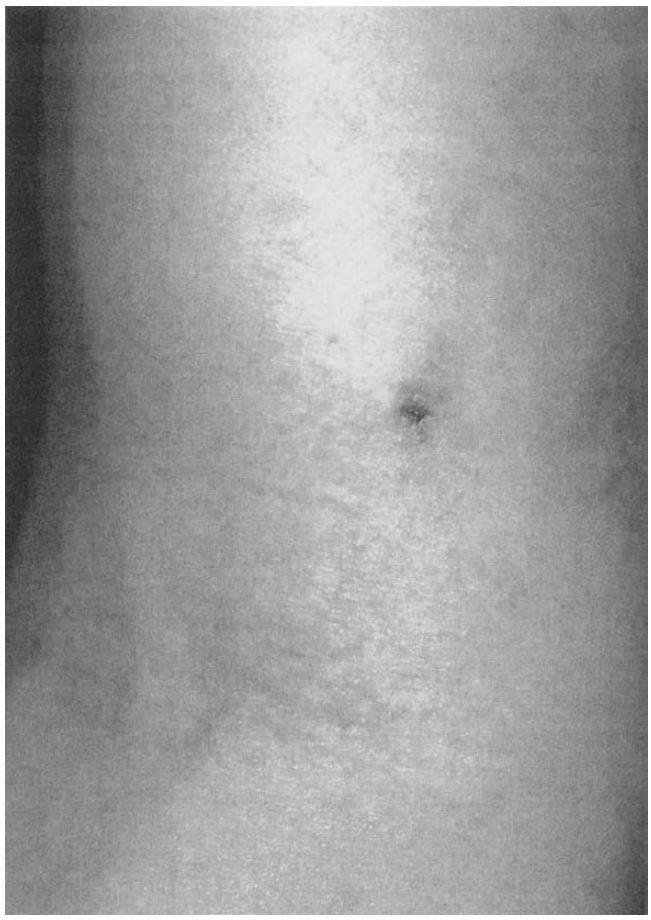

Fig. 1. Right arm.

exceedingly rare. Urticarial reactions and rashes have been an uncommon subset of these systemic reactions. A proposed mechanism of delayed-type hypersensitivity reaction (type IV reaction) was sought for this patient due to the lack of reaction after the first injection of anthrax (sensitization period), delayed cutaneous reaction after the second and third injections (elicitation phase). To our knowledge, this is the first documented case that suggests a delayed-type hypersensitivity reaction to the anthrax vaccine. The authors' recommendation for the Anthrax Immunization Program is for continued surveillance of adverse events, for prompt permanent deferral of the Anthrax Vaccine Immunization Program for those service members who have a severe reaction to the anthrax vaccine, and for increased education of military physicians on the common and unusual presentations of adverse events. Development of protocol for patch and prick testing to all components of the anthrax vaccine may also be useful.

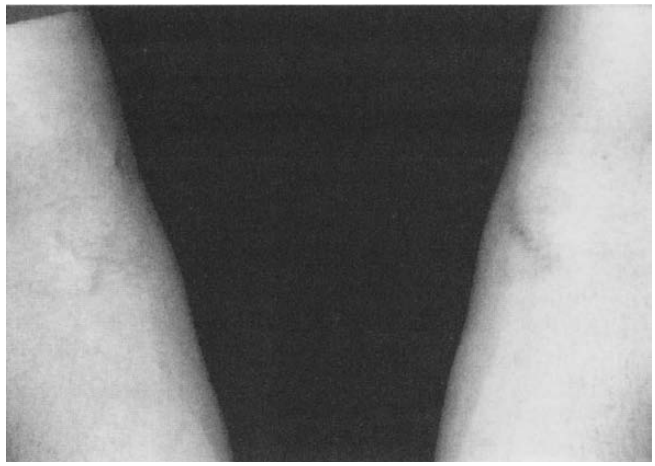

Fig. 2. Both arms.

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