

Allergy to tetanus toxoid vaccine

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This paper is dedicated to the memory of Professor Luisa Businco, who shared in its preparation before her death on 1 December 1999.

Key words: reaction; tetanus toxoid; vaccination.

• IGE-MEDIATED hypersensitivity reactions to tetanus toxoid (TT) vaccine are very rare (1/1 000 000) (1); nevertheless, physicians must be prepared to deal with them when administering this agent. We report four cases of IgE-mediated adverse reactions to TT vaccine, as documented by positive serum IgE antibodies to TT and, in two cases also, by a positive skin prick test to TT vaccine components.

Subject 1. Two

hours after
receiving a TT
booster, a 38-
year-old man

without history of allergic disease developed a severe but localized reaction consisting of erythema, swelling, pain, and induration, which spontaneously remitted within 10 days.

Subject 2. As a child, an atopic 19-year-old man experienced local erythema and edema a few minutes after the first administration of the combined diphtheria-tetanus toxoid vaccine (DT). One year later, a few hours after his second DT booster, he developed generalized urticaria, facial angioedema, and fever ($>39.5^{\circ}\text{C}$);

these symptoms responded to oral antihistamines. His most recent DT booster, received as an outpatient, resulted in painful, local erythematous induration and fever ($>39^{\circ}\text{C}$), which resolved after i.m. corticosteroids.

Subject 3. A 6-year-old boy developed local painful edema a few hours after receiving a DT booster. Forty-eight hours later, he experienced a progressive systemic reaction consisting of skin erythema and pruritus, generalized urticaria, facial angioedema, scotoma, and fever ($>40^{\circ}\text{C}$), which remitted after oral corticosteroids.

Subject 4. Three weeks after receiving a TT booster, a 35-year-old woman experienced erythema and pruriginous edema at the injection site. Two months later, a further dose of tetanus vaccine was administered but local painful edema appeared within 24 h, progressively extending to the whole arm and eyelids. Symptoms remitted after administration of i.m. corticosteroids.

The four patients underwent the skin prick test with the components of TT vaccine (TT, merthiolate, aluminum hydroxide – Biocine, Siena, Italy), and measurement of TT-specific serum IgE (Pharmacia CAP System). All of them had positive serum IgE to TT. Subjects 3 and 4 also exhibited a positive skin prick test to TT.

The clinical significance of specific IgE to TT is unclear, since tetanus vaccine may induce specific IgE antibodies even in subjects who do not experience adverse effects after immunization. Fifty percent of 538 24-month-old children developed detectable TT-specific IgE antibodies in response to immunization (2), but no major

systemic or large local clinical reactions were reported after immunization with TT.

Aluminum-containing adjuvants are known to stimulate Th2 responses and increase the production of total and specific IgE antibodies (3). Moreover, aluminum hydroxide, like thimerosal, an organic mercurial compound used as a preservative in TT vaccine, may be sensitizing and cause delayed hypersensitivity reactions (4).

Reaction proneness to TT vaccine correlates with serum antitoxin levels. Among 104 adults with adverse reactions to TT vaccine, 97% had at least four times the minimal protective level of antibodies (i.e., 0.01 IU/ml), and 58% had levels higher than 5 IU/ml (5).

For these reasons, immediate skin test reactivity to TT does not always help to determine the mechanism of adverse reactions to the vaccine, as they may not be IgE-mediated.

In subjects with previous immediate hypersensitivity reactions to TT and in whom tetanus immunization is mandatory because of a risk of tetanus, if the antitoxoid titer (considered to last for about 8 years from the last booster) shows the subject to be immune, further vaccination should not be administered, in order to avoid hyperimmunization and reaction proneness. If the subject proves to be not immune, a graded desensitization protocol may be started (6).

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Four cases of IgE-mediated reactions.

References

1. LEONAR-BELLFILL R, CISTERO-BAHIMA A, CERDA-TRIAS MT, OLIVE-PEREZ A. Tetanus toxoid anaphylaxis. *Ann Pharmacother* 1991;**25**:870.
2. DANNEMAN A, VAN REE R, KULIG M, et al. Specific IgE and IgG4 immune responses to tetanus and diphtheria toxoid in atopic and nonatopic children during the first years of life. *Int Arch Allergy Immunol* 1996;**111**:262–267.
3. RELYVELD EH, BIZZINI B, GUPTA RK. Rational approaches to reduce adverse reactions in man to vaccines containing tetanus and diphtheria toxoids. *Vaccine* 1998;**16**:1016–1023.
4. PATRIZI A, RIZZOLI L, VINCENZI C, TREVISI P, TROSTI A. Sensitization to thimerosal in atopic children. *Contact Dermatitis* 1999;**40**:94–97.
5. LEVINE L, EDSALL G. Tetanus toxoid: what determines reaction proneness? *Infect Dis* 1981;**144**:376.
6. URIEL AJ, BOYTER AC, MACCONNACHIE AM, NATHWANI D. Immunisation against tetanus, in a hypersensitive individual, using a graded dosing regimen. *J Infect* 1995;**30**:83–84.