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Spontaneous resolution of diphtheria-tetanus vaccine hypersensitivity in a pediatric population

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Abbreviation: DT, Diphtheria and tetanus.

Diphtheria and tetanus (DT) are two potentially fatal diseases that may be prevented through vaccination (1). Allergy to the DT vaccine is a clinical challenge considering that the regular immunization schedule includes multiple doses of DT-containing vaccine and that boosters are needed throughout life. Although desensitization is an option in these patients, in our experience, it is seldom performed, either because of lack of access to a specialist or for fear of reactions. As a result, vaccination schedule is often interrupted, thereby exposing the patient to the diseases (2, 3).

Little is known of the natural evolution of DT vaccine allergy. In a study by Maryorga and colleagues, four

patients with confirmed anaphylaxis to DT vaccine were re-evaluated after 5 years (4). While specific IgG levels remained high, IgE levels had dropped considerably. Unfortunately, the patients were not rechallenged or skin-tested at follow-up, limiting the clinical interpretation of these results, although they do suggest this allergy can resolve.

To better describe the natural evolution of DT vaccine allergy, we reviewed the charts of patients referred to our institution from 1998 to 2009. Patients whose allergy to the DT component had been confirmed by a positive immediate intradermal skin test were contacted and re-evaluated.

Seventeen such patients were identified, including 11 from new referrals (out of 147) and 6 from follow-up visits. Of these, one passed away from hematologic cancer, and another could not be reached.

Table 1 shows clinical data for the 15 remaining patients. Initial reactions to vaccine included 11 systemic reactions and 4 large local reactions. On re-evaluation, only three patients still had positive skin test to DT toxoids. The remaining patients tolerated vaccination challenges with DT vaccine, except for one patient with needle phobia, for whom vaccination was postponed.

All three patients with persistent allergy had experienced generalized reactions. When compared to those with resolved DT allergy, both mean onset of initial reaction (6.9 vs 9.8 h) and time elapsed between initial reaction and re-evaluation (4.3 vs 8.5 years) appeared shorter (*P*-value of 0.17 and 0.16, respectively).

The rate of positive tests in our cohort [11 of 147 referrals (8%)] was higher than that previously reported by Jacobs and colleagues (<1%) (5). The

difference could be explained by the fact that they studied military recruits with very distant histories of reaction to DT-containing vaccines. The allergy of these adult patients could have resolved in the long period elapsed before their evaluation, which would further support our conclusions.

One limitation to this study is the fact that patients were not challenged upon their initial visit to confirm diagnosis. However, challenge is not usually performed in clinical setting when both history and skin tests are positive.

Also, one could question whether a change in the DT vaccine used for skin testing could have influenced the results. The DT vaccine used for skin testing at the clinic (d2T5, Sanofi Pasteur) has been the same since 1984, well before the evaluation of the eldest subject. The only change in vaccine composition occurred in 2005, when thimerosal was removed. This adjuvant is associated with delayed local reactions and was patch-tested in all four patients with large local reactions, ruling out thimerosal hypersensitivity as a confounding factor.

In conclusion, these results confirm that DT allergy may resolve with time and suggest that patients with early-onset generalized reactions to DT-containing vaccine could take more time to resolve their allergy. Patients with confirmed hypersensitivity to DT vaccine should be re-evaluated periodically to repeat allergy testing and, possibly, resume regular vaccination.

Author's contribution

Philippe Bégin participated in designing the concept, the review of the files from the allergy clinic from 1998 to 2009, and the reassessment of the patients. He analyzed the data and

Table 1 Clinical data of patients

Patient	Age at reaction	Causal vaccine	Symptoms	Initial skin tests†	Age at follow-up* (years)	Follow-up DT skin test	Comments
1	2 months	DPT, Polio, Hib	Generalized urticaria within 24 h	DPT, DT+, Hib–	9 (+9)	Negative	Single-dose challenge with DT tolerated
2	3 months	Penta	Generalized macules and papules within 12 h	Quad, DT, Hib+	15 (+15)	Negative	Single-dose challenge with DT tolerated
3	4 months	DPT	Generalized urticaria within 2 h	DPT, DT+	17 (+16)	Negative	Single-dose challenge with DT tolerated
4	4 months	DPT	Generalized urticaria within 3 h	DPT, DT+	18 (+18)	Negative	Single-dose challenge with DT tolerated
5	6 months	DPT	Generalized urticaria and facial angioedema within 2 h	DPT, DT+	9 (+8)	Negative	Single-dose challenge with DT tolerated
6	18 months	Penta, MMR	Generalized urticaria within 20 h	Penta, DT, MMR+	4.5 (+3)	Positive	Vaccination postponed
7	18 months	Penta, MMR	Generalized urticaria within 1 min	Penta, DT+ MMR, Polio–	5 (+3.5)	Positive	Vaccination postponed
8	4 years	Penta	Generalized urticaria and facial angioedema within 30 min	Quad, DCT, DT+ Polio–	10.5 (+6.5)	Positive	Vaccination postponed
9	5 years	Quad	Generalized urticaria, palpebral angioedema within 8 h	Penta, DT+, Hib, Polio–	11 (+6)	Negative	Single-dose challenge with DT tolerated
10	2 months	DPT, Polio, Hib	Vomiting, crying, and hypotonia within 6 h	Quad, Hib, DT+	5 (+5)	Negative	Single-dose challenge with DT tolerated
11	15 years	DPT	Vomiting, oral angioedema, and respiratory distress with stridor within 5 min	DT+, DPT–	19 (+4)	Negative	Three-step challenge with DT tolerated
12	2 months, 4 months, 6 months	DPT, Hib	Large local reaction after each vaccination	Quad, DT, Hib+, Patch: Neomycin+ Polymixin+	5 (+4.5)	Negative	Single-dose challenge with DT tolerated
13	18 months	Penta	Large local reaction within 14 h (extending to thorax)	Penta, Polio, DT+, Patch: Neomycin+	11 (+9.5)	Negative	Single-dose challenge with DT tolerated
14	2.3 years	Quad, MMR	Large local reaction within 24 h	Quad, DT+, MMR, Patch–	6 (+3.5)	Negative	Single-dose challenge with DT tolerated
15	4.5 years	Penta	Large local reaction within 12 h, extending to whole arm	Penta, Quad, DT+ Patch: aluminum+	8.5 (+4)	Negative	Patient with autism and needle phobia. Challenge postponed to 15 years

DPT, diphtheria, pertussis, and tetanus vaccine; DT, diphtheria and tetanus vaccine; Hib, Haemophilus influenzae B vaccine; Polio, Poliomyelitis vaccine; Quad, DPT and polio vaccine; Penta, DPT, polio, and Hib vaccine; MMR, measles, mumps, and rubella vaccine; n/a, not available.

*Delay between reaction and reevaluation indicated between brackets.

†Intradermal skin tests performed at 1 : 100 dilution; patch-test panel includes formaldehyde, phenoxyethanol, polymixin B, thimerosal, aluminum, and neomycin.

wrote the manuscript. Minh-Quan Vu reviewed all the files from the allergy clinic from 1998 to 2009 and revised the manuscript. Matthieu Picard participated in the reassessment of patients and critically reviewed the manuscript. Dr Louis Paradis participated in designing the concept, supervised the reassessment of patients and the analysis of data, and critically

reviewed the manuscript. Dr Anne Des Roches supervised every aspect of the project, including designing the concept, review of files, reassessment of patients, analysis of the data, and revising the manuscript.

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Conflicts of interest

None of the authors have any conflict of interest to declare.

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