

## Gelatin-induced Urticaria and Anaphylaxis after Tick-borne Encephalitis Vaccine

Sir,

Tick-borne encephalitis (TBE) is a rare disease, acquisition of which occurs only in well-known endemic areas, such as south-western Germany, Austria and Switzerland, through the bites of infected ticks. The course of the disease is not trivial: 0.5–2% of cases are fatal, 2.7% have persistent serious paralysis and some 33% a postencephalitic syndrome. Since there is no specific treatment for TBE, immunoprophylaxis is used in endemic areas for controlling this disease. Active immunization has been shown to be effective and safe. Only a few mild side-effects have been reported (1).

Allergic reactions to vaccines occur in approximately 0.001–1% of cases (2) and most important antigens are preservatives, rarely antibiotics, culture media substances from the production process or reagents used for inactivation, stabilizers or absorbents (2). Allergic reactions to vaccines are localized mainly to the application site, whereas the onset of systemic anaphylaxis is extremely rare.

### CASE REPORTS

A 36-year-old woman had received TBE immunizations in March 1997. After the second injection she developed generalized pruritus, angioedema and urticaria within 30 min. All symptoms resolved after taking 10 mg loratadine orally. Previous immunizations with tetanus and diphtheria had been well tolerated. The patient's history revealed the onset of urticaria once in childhood after taking antibiotics (mebacid). Another episode of urticaria lasting several weeks occurred in 1990, after an upper respiratory infection. No type I and type IV allergies were reported and there was no history of rhinoconjunctivitis, asthma or eczema. The family history for atopy was negative.

The second patient was a 29-year-old woman, who developed a generalized urticaria, dyspnea and hypotension a few minutes after the third TBE immunization. The patient immediately received antihistamines and steroids i.v. and the symptoms resolved completely within 1 h. Previous immunizations with tetanus vaccine had been well tolerated. The patient's history revealed no type I allergies or any other diseases.

In both patients, skin prick testing with the single ingredients of the TBE vaccine including the antibiotics tetracycline, neomycin and gentamicin, the preservative formaldehyde and ovalbumin were negative. However, a skin prick test with the complete TBE vaccination solution and haemaccel, which contains gelatin and is used as a preservative in TBE vaccination solution, was positive. The positive skin prick test reaction to TBE vaccine solution and gelatin was greater than the histamine equivalent of 10 mg/ml in both patients. Total IgE was below 100 KU/ml (Pharmacia, Uppsala, Sweden) in each patient and no specific IgE antibodies against ovalbumin were detectable. Anti-IgE against gelatin was detectable in 1 of the 2 patients (0.82 kU/ml, CAP 2, Pharmacia).

### DISCUSSION

We describe here 2 patients with systemic reactions after TBE immunization. Skin prick testing and the detection of specific IgE against gelatin in one of the patients suggests an IgE-mediated anaphylaxis with sensitization against gelatin.

Gelatin is prepared by hydrolysis of collagen from various animal sources, e.g. bovine and porcine bones (3). In

medicine, gelatin solutions are used as plasma expanders, and anaphylactoid reactions have been reported in association with the infusion of such products (4). Some investigators have ascribed these reactions to non-immunological mechanisms (5, 6), whereas others have suggested an IgE-dependent mechanism.

Recently, sensitization towards gelatin was identified as a cause of anaphylactic reactions to vaccines. Kelso et al. (7) showed that anaphylaxis to mumps, measles and rubella (MMR) vaccine was mediated by IgE to gelatin. That gelatin might play an important role in vaccine induced anaphylaxis was also suggested from a study of Sakaguchi et al. (8). These authors detected anti-gelatin IgE in 24 of 26 children, who demonstrated immediate systemic reactions after MMR vaccination. Seven of these 24 children also experienced anaphylactic reactions after ingestion of gelatin-containing foods. In our patients the history of previous anaphylactic reactions was negative and both patients denied any reactions after eating gelatin-containing food, such as "gummy bear" sweets. This might be explained by the fact that different gelatins for human consumption may vary widely in their potential for allergic activity.

### REFERENCES

- Schmeiser-Rieder A, Kunze M. Field study of physicians on the incidence of adverse vaccine effects and vaccine reactions in early summer meningoencephalitis, tetanus and influenza vaccination in general practice. *Wien-Med-Wochenschr* 2000; 148: 214–225.
- ACIP: Update: vaccine side effects, adverse reactions, contraindications, and precautions. Recommendations of the Advisory Committee on Immunization Practices. *MMWR* 1996; 45: 1–35.
- Sattler JM, Horsey PJ. The new generation gelatin. *Anaesthesia* 1987; 42: 998–1004.
- Vervolet D, Fenft M, Dugue P, Arnaud A, Charpin J. Anaphylactic reactions to modified fluid gelatin. *J Allergy Clin Immunol* 1983; 71: 535–540.
- Ring J, Messmer K. Incidence and severity of anaphylactoid reactions to colloid volume substitutes. *Lancet* 1977; 1: 466–469.
- Lorenz W, Doenicke A, Messmer K, Reimann HJ, Thermann M, Lahn W, et al. Histamine release in human subjects by modified gelatin (haemaccel) and dextran; an explanation for anaphylactoid reactions observed under clinical conditions? *Br J Anaesth* 1976; 48: 151–164.
- Kelso JM, Jones RT, Yunginger JW. Anaphylaxis to measles, mumps and rubella vaccine mediated by IgE to gelatin. *J Allergy Clin Immunol* 1993; 91: 867–872.
- Sakaguchi M, Nakayama T, Inouye S. Food allergy to gelatin in children with systemic immediate-type reactions, including anaphylaxis, to vaccines. *J Allergy Clin Immunol* 1996; 98: 1058–1061.

*Accepted February 16, 2000.*

Margitta Worm, W. Sterry and T. Zuberbier  
Klinik für Dermatologie, Venerologie und Allergologie mit Asthma-poliklinik, Campus Charité Mitte, Schumannstr. 20-21, D-10117, Berlin, Germany.  
E-mail: margitta.worm@charite.de