



Clinical letter

Intraoperative anaphylactic reaction to gelatin

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Dear Editors,

The incidence of anaphylactic reactions occurring under general anesthesia is about 1 : 10 000–1 : 20 000 [1]. Common triggers include muscle relaxants, antibiotics, and latex. Considering the number of perioperative and intraoperative medications, thorough clarification is warranted [2].

Anaphylactic reactions to gelatin have been reported in conjunction with vaccines (see [3]) and foodstuffs, but they have mainly been reported with adverse anesthesia events related to intravenous administration of plasma expanders.

Gelatins are composed of polypeptides which are derived from animal collagen (e. g., skin, tendons, bones). The collagen is highly hydrolyzed; different cross-linking agents (urea, succinate) are used in polymerization. It is used as a colloidal plasma expander as an alternative to human albumin, dextran, or hydroxyethyl starch to treat hypovolemia, as well as to ensure adequate intraoperative tissue perfusion and hemodynamic status [4].

A multicenter study from the 1970s reported that the incidence of anaphylactic reactions to gelatin-based volume replacement solutions was 0.115 %, and thus significantly higher than the rate for dextran or albumin [5]. Studies from France also showed that gelatin-based preparations had the highest incidence, when compared to other colloidal solutions (0.345 %) [6].

Case report

We describe a 74-year-old woman who had an anaphylactic reaction (fourth degree, based on Ring and Messmer), which occurred about 20 minutes after anesthesia was administered for a scheduled implant exchange of a prosthesis of the right hip in March 2012. As a result, she experienced circulatory arrest and had to be resuscitated. Theophylline, ranitidine, dimetindene, prednisone, and epinephrine were administered intravenously, as was atropine. The surgery was discontinued.

The patient had no known allergies (including to meat), nor did she have a history of atopic disease. She reported avoiding gelatin-based foodstuffs “due to diabetes.”

According to the anesthesia protocol, the following substances were used intraoperatively:

- ▶ *Local anesthetic:* lidocaine 2 %, bupivacaine 0.5 %
- ▶ *Narcotics:* propofol, sufentanil
- ▶ *Muscle relaxant:* rocuronium
- ▶ *Antibiotic:* cefuroxime
- ▶ *Volume replacement:* Gelafundin® 4 % (gelatin polysuccinate, derived from bovine collagen)

In July 2011, the patient had already received an infusion of Gelafundin® during total hip replacement of the right hip, and had tolerated the drug without any complications.

Diagnosis

Serum mast cell tryptase levels were normal. There were specific IgE antibodies (ImmunoCAP®, sandwich ELISA technique, Phadia Sweden) to gelatin (11.40 kU/l; CAP class 3). There was no evidence of sensitization to bovine or porcine sources (< 0.35 kU/l; CAP class 0), or to galactose-alpha-1,3-galactose (α -Gal < 0.35 kU/l; CAP class 0).

The results of a skin-prick test showed a highly positive reaction to Gelafundin® (6/40 mm) with pseudopodia (Figure 1) – three controls (personnel) had negative results. There was no evidence of sensitization to propofol, rocuronium, lidocaine, bupivacaine, cefuroxime, clindamycin,



Figure 1 Skin-prick test.

or latex. The results of intracutaneous testing could not be assessed, as the patient had irritative reactions to all tested antibiotics and local anesthetics. Patch tests yielded no apparent reaction to the above-mentioned substances (including Gelafundin®).

Procedure

The patient was given an "allergy passport" which included the instructions to continue to avoid eating gelatin. In order to determine the clinical relevance of the gelatin sensitization, we would need to perform an oral provocation test under inpatient conditions, but the patient has refused the test. The total hip replacement was subsequently performed without using a gelatin-based colloidal solution. There were no complications.

Conclusion

Colloidal solutions, most often gelatin-based preparations, are possible triggers of intraoperative anaphylaxis [5, 6]. Reactions to gelatins are mainly due to IgE-mediated allergies [3, 7]. In 1999, the alpha-2 chain of bovine type I collagen was identified as an IgE-binding epitope in bovine gelatin-sensitive patients [7]. Previous discussions had focused more on anaphylactoid (non-allergic) reactions with unspecific histamine release [4, 8]. In a 1976 study using healthy volunteers who had *not* been previously treated, elevated histamine blood concentrations were measured – mainly without any associated symptoms – after rapid administration of modified gelatin [8]. Our patient appears to have had an allergic reaction, given the evidence of sensitization based on the results of skin-prick tests and enzyme linked immunosorbent assay (ELISA) results, along with negative skin-prick test results in controls.

In a recent publication, 75 % of patients who were allergic to red meat were found to be sensitive to gelatin. In addition, the pan-allergen galactose-1,3-alpha-galactose (α -Gal) was found to be an important trigger in bovine and porcine allergies related to colloidal solutions containing bovine gelatin; hence α -Gal should be considered as a possible allergen in gelatin allergies [9]. This was not confirmed in our patient; she did not appear to be sensitive to α -Gal, nor did she have a history of meat allergy.

Possible cross-reactivity between vaccine ingredients, containing bovine gelatin (or polygeline as a stabilizer), and gelatin-based colloidal solutions is conceivable [10]. Yet, given that polygeline is rarely used these days, it is unlikely. It is more likely that the patient is sensitive to gelatin, either as a result of foodstuff consumption or the prior operation

which included intraoperative infusion of Gelafundin® in July 2011.

Conflict of interest

None.

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