

A case of anaphylaxis to gelatin included in erythropoietin products

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Recombinant human erythropoietin (EPO) is widely used for the treatment of anemia in patients undergoing chronic dialysis, and is regarded as very safe and effective in the management of these patients. There has been one report of anaphylaxis associated with EPO in which the patient possessed IgE antibody to recombinant EPO.¹ On the basis of this finding, the authors suggested that the anaphylactic reactions were caused by EPO.

In Japan, 2 manufacturers respectively produce 2 different types of EPO products (epoetin- α and epoetin- β). As a stabilizer in the EPO product for injections, human serum albumin (HSA) (2.5 mg/dose for epoetin- α and 1 mg/dose for epoetin- β) was replaced by bovine gelatin (20 mg/dose for epoetin- α and 5 mg/dose for epoetin- β) from 1995 to 1996.

Anaphylactic reactions to measles-mumps-rubella (MMR) vaccines have been reported in association with allergy to egg proteins present in the vaccines, but such reactions have also been described in children who demonstrated no allergy to eggs.² Kelso et al³ reported that a child with anaphylaxis caused by MMR vaccine had IgE antibody to gelatin. Also, in our previous studies^{4,5} we found that most of the children who had systemic immediate-type reactions, including anaphylaxis, to the live virus vaccines had anti-gelatin IgE.

We report here a woman who experienced anaphylaxis to the gelatin stabilizer in the EPO product. To clarify the relationship between the gelatin in the EPO products and the anaphylaxis reaction, we measured the anti-gelatin IgE.

CASE REPORT

A 44-year-old woman had received renal dialysis since 1975. She had also undergone intravenous EPO therapy since 1990 and had demonstrated no allergic reaction to EPO products with HSA.

Abbreviations used

EPO: Erythropoietin
HSA: Human serum albumin
MMR: Measles-mumps-rubella

In October 1995, she first received a new EPO product (epoetin- α) that contained bovine gelatin as a stabilizer. Severe anaphylaxis (hypotension and airway obstruction with cough) began immediately after intravenous injection of the product. She received treatment (administration of dopamine and plasma for hypotension, hydrocortisone, and oxygen therapy) for the symptoms and recovered completely within the day. After recovery, she received a conventional EPO product with HSA and showed no allergic reaction. In January 1996, she again received another EPO product (epoetin- β) with gelatin in another hospital. Immediately, she again showed similar symptoms of anaphylaxis (hypotension, presyncope, and airway obstruction). She received similar treatments for the symptoms and recovered completely by the following morning.

To determine whether the adverse reactions were caused by allergic reactions to bovine gelatin, we measured specific IgE to bovine gelatin. We found that she had antibovine gelatin IgE (13.7 Ua/mL), as determined by the Pharmacia CAP method,² but that she had no anti-EPO IgE, as determined by a fluorometric ELISA.³

DISCUSSION

The patient in this study first received a new EPO product (epoetin- α) that contained gelatin and immediately showed symptoms of severe anaphylaxis. After recovery, she received a conventional EPO product with HSA and had no allergic reaction. When she again received an EPO product with gelatin, she showed similar symptoms of anaphylaxis. We found that she had anti-gelatin IgE. These results suggest that the anaphylaxis to EPO products were associated with hypersensitivity to gelatin included in the products.

In Japan, approximately 100,000 patients undergoing dialysis received EPO products with gelatin from 1995 to 1996. Interestingly, this was the only case in which severe immediate-type reactions to EPO products with gelatin occurred. Thus this appears to be an extremely rare case of hypersensitivity to bovine gelatin in the Japanese adult population.

It is now postulated that most anaphylactic reactions to vaccines are induced by the gelatin contained as a stabilizer.^{2,3,5} We recommend that gelatin-containing EPO

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products, although the number is very few, should be used with the same caution as MMR vaccines.

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