Severe anaphylactic reaction after primary exposure to an aprotinin test dose in a child with severe milk allergy

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Introduction: Anaphylactic reaction to aprotinin is rarely seen on initial exposure, occurring more often after a previous exposure to the drug(1-4). We report a case of severe anaphylactic reaction following primary exposure to an aprotinin test dose in a child with severe milk allergy. We believe this is the first report of aprotinin anaphylaxis in a patient with bovine product allergy. Cross-sensitization was believed to occur since aprotinin is derived from bovine lung.

Case: A 9 year-old boy with history of severe milk allergy was brought to the operating room for placement of a right ventricular to pulmonary artery conduit, and aortic valve replacement. The patient was born with truncus arteriosus type II and underwent a Rastelli procedure as a neonate. At one year of age he underwent a relief of right ventricular outflow tract obstruction using a bovine pericardial patch. For the present surgery, an aprotinin test dose of 1cc containing 10,000 KIU (kallikrein inactivator units) was given after sternotomy. Immediately after the test dose, the patient developed severe hypotension and increased airway pressures. Systolic blood pressure dropped from 120 to 50 mmHg and remained low for 30 minutes despite resuscitation efforts. He was resuscitated with repeated doses of epinephrine and volume boluses of albumin 5%. Cardiopulmonary bypass was initiated, and the surgery was continued. While on bypass, the patient’s mean arterial pressure initially remained low (range 15-25 mmHg) for about 15 min, then was able to be maintained at acceptable levels (> 40 mmHg). A tryptase level while on bypass was 59.2mcg/L (normal 11.5). The surgery continued uneventfully.

Discussion: Aprotinin is a 58 amino-acid protein extracted from bovine lung. It is immunogenic and severe allergic reactions occur mainly after reexposure. The incidence of aprotinin anaphylaxis with reexposure has been reported as 2.8%(1) to 17%(2). Six months after placement of a bovine patch, the patient developed severe milk allergy, with severe tachycardia, tachypnea, vomiting, and severe lethargy. These symptoms lasted for 2-3 hours and resolved spontaneously. After this incident, immunologic tests confirmed milk allergy. This severe allergy to milk could have been triggered by previous presensitization with the bovine pericardial patch. As aprotinin is a derivative of bovine lung, the patient might also have developed severe anaphylaxis to aprotinin from cross-sensitization. Anaphylactoid reactions cannot be clinically distinguished from true anaphylactic reactions(5). Nevertheless, the severity of the reaction necessitating cardiopulmonary bypass support in response to a small dose of aprotinin, and the high level of tryptase suggest an anaphylactic reaction. Anaphylactic reactions are frequently accompanied by a rise in tryptase levels for several hours(6) and increased concentration of tryptase is a highly sensitive indicator of an anaphylactic reaction(7). Aprotinin is also contained in biologic tissue sealants which are used in open heart surgery(4,5). Tissue sealants have been commercially available in the United States since 1998. Our patient underwent two previous surgeries in 1994 and 1995, prior to their availability. Although not an issue in our present case, one should administer aprotinin with caution in a patient in whom tissue sealant had been previously used.

In conclusion, we present a case of severe anaphylactic reaction after primary exposure to an aprotinin test dose in a child with severe milk allergy and a prior bovine patch. Any allergy to bovine products can result in cross-sensitization and should raise concern of a potential aprotinin reaction. This cross-sensitization between aprotinin and milk, a bovine product, might be similar to the cross-sensitization between protamine and salmon(8). We recommend special attention be given while administering aprotinin to a patient with a bovine product allergy. Safety measures should be taken, including delaying the test dose to a point whereby cardiopulmonary bypass can be instituted rapidly, and avoiding premature priming of the pump.

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