

Increased postmortem serum mast cell tryptase in a fatal anaphylactoid reaction to nonionic radiocontrast medium

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Immediate anaphylactoid reactions after the administration of ionic radiocontrast media (RCM) occur in up to 13% of all RCM infusions, and fatalities have been reported in about 1/50,000 procedures.¹ Since the introduction of the newer nonionic RCMs with lower osmolality, adverse reactions have been described in markedly reduced numbers.¹ In the largest prospective study investigating adverse drug reactions to Iopamidol and other lower osmolality RCMs, the prevalence was 3.13%; severe reactions occurred in only 0.04%.² However, deaths associated with the use of lower osmololality RCMs have been reported.¹ The majority of the reactions are considered to be of a nonimmunologic pseudoallergic origin.³ We report a fatal anaphylactoid reaction after the administration of a nonionic RCM and describe the relevant diagnostic procedures.

CASE REPORT

An 81-year-old man in general good health and without a history of heart, lung, or allergic diseases underwent computerized tomography of the eyes to investigate a progredient atrophy of the optical nerve. Shortly after infusion with the nonionic RCM Iopamidol (Solutrast), the patient reported unease. The infusion was interrupted briefly and then restarted. A few minutes later, after the total amount of 100 mL had been infused, he again complained of sweating and nausea. Although the infusion was stopped immediately, frothy sputum appeared in the front of his mouth, and the patient lost consciousness followed by respiratory and cardiac arrest. Immediate resuscitation and intravenous application of dexamethasone and epinephrine was unsuccessful.

METHODS

An autopsy was performed 10 hours after death. Four hours postmortem, serum was taken from venous blood and stored at -80°C after centrifugation. Mast cell tryptase levels were determined by Pharmacia RIACT and UniCAP Tryptase (Pharmacia, Uppsala, Sweden). Serum eosinophil cationic protein (ECP) and myeloper-

Abbreviations used

ECP: Eosinophil cationic protein
RCM: Radiocontrast media

oxidase concentrations were determined by Pharmacia MPO RIA and ECP FEIA ImmunoCAP; total and specific IgE antibody concentrations were determined by FEIA ImmunoCAP (Pharmacia).

In addition, RAST discs were coupled with 2 mL of Iopamidol in 1/10, 1/100, and 1/1000 aqueous dilutions (NaCl 0.9%) onto bromocyanogen bromide-activated filter paper discs. After incubation with 50 µL of the patient's serum and radioactivity labeling with anti-IgE, I¹²⁵-specific binding of IgE to the discs was measured in the Phadebas RAST system (Pharmacia). Binding rates corresponding to less than 0.35 kU/L in comparison with the reference serum was defined as a negative result.

Complement levels were measured by single radial immunodiffusion (Behring, Marburg, Germany); electrolytes and creatinine-kinase were measured by standard laboratory methods. Bacterial or mycological contamination of the RCM and the blood was excluded by microbial assays.

RESULTS

At autopsy, coronary and pulmonary arteries were patent. The right heart chamber was moderately enlarged. The lung was hyperemic and edematous (interstitial and alveolar edema). The most impressive finding was an obstructive edema of the larynx, which especially affected the epiglottis and the aryepiglottical folds.

Serum tryptase levels were highly elevated (338 U/L in RIACT [normal range, <2 U/L] and 621 µg/L in UniCAP tryptase [normal range, <12 µg/L]). Also, ECP was found to be elevated (18 µg/L; normal range, <12 µg/L). Total serum IgE was 185 kU/L, and specific IgE to Timothy grass (CAP class 3) was demonstrated. No specific IgE to the RCM was detectable in Solutrast-coupled paper discs after incubation with the patient's serum; however, positive control sera were lacking. All other parameters analyzed were within normal limits.

DISCUSSION

Establishing the diagnosis of fatal anaphylactoid shock is not always easy because many differential diagnoses have to be considered. In this case, on the basis of the patient's history, the course of events, and especially

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the autopsy, a fatal anaphylactoid reaction to the RCM Iopamidol was identified as the cause of death. This finding demonstrates that, although associated with a reduced rate of adverse reactions, nonionic RCMs also carry a risk of inducing a fatal reaction.

At the autopsy we found an interstitial and alveolar edema combined with a massive laryngeal edema leading to a pronounced upper airway obstruction, which confirmed the diagnosis. Pulmonary edema and visceral congestion have been described in anaphylactoid reactions to RCMs. Laryngeal edema is regarded to be the most characteristic finding of fatal anaphylactoid reactions.⁴

ECP is a marker of eosinophil activation, and increased concentrations have been reported after anaphylactoid reactions. In the serum of this patient, increased ECP concentrations were detected. However, whether this finding can be considered to be a sign for an anaphylactoid event needs further investigation.

Mast cell tryptase can be found after anaphylactoid reactions in the serum of patients with a half-life of about 2 hours. Postmortem increase of serum tryptase has been regarded to be specific for fatal anaphylaxis by some authors.⁵ However, moderately elevated postmortem tryptase concentrations (>2 U/L in tryptase RIACT) in the absence of anaphylaxis have been described by others in 63% of patients.⁶ In 10% of patients, values

exceeding 10 U/L were found, whereas only 1 patient demonstrated a concentration greater than 50 U/L. Thus only high concentrations of mast cell tryptase, as seen in this subject, should be regarded as sufficiently specific for fatal anaphylactoid reactions.

In conclusion, highly elevated concentrations of tryptase can support the diagnosis of a fatal anaphylactoid reaction to an RCM. However, elevated values should be seen only in combination with other relevant clinical information. Differential diagnoses have to be excluded, and further diagnostic procedures still have to be performed.

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