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Anaphylactic shock to iodinated contrast media: not so rare after all

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To the Editor,

immediate and non-immediate hypersensitivity reactions to iodinated contrast media (ICM) have been reported to occur in a frequency of about 0.5-3% of patients receiving non-ionic ICM (1). Severe reactions occur in 0.04% to 0.22% of intravenous administrations (2). Immediate reactions can be caused by IgE and non-IgE mechanisms. The presence of positive skin tests indicates an IgE-mediated mechanism. Tryptase serum levels increase with the severity of the reaction (1). A recent multicentric prospective study documented allergy in 52.9% of patients with anaphylaxis and in all patients with cardiac arrest (3). IgE-mediated allergic hypersensitivity reactions may have been underreported in the past due to the lack of allergy testing (4).

The main risk factor for developing an immediate hypersensitivity reaction to an ICM is a previous immediate reaction. Other presumed risk factors (asthma, atopy, drug allergy) (5) have shown inconsistent results and therefore cannot be used as a condition for performing ICM allergy work-up (1). In a 2 week period, we had in our hospital 3 anaphylactic shocks to ICM.

Case 1: female, 62 years old, no history of atopy. The patient had indication for ablation of atrial fibrillation and was proposed to have a coronary computed tomography (CT) angiogram (CCTA). During the exam the patient experienced a non-specific discomfort while administering Ultravist® 370 (iopromide), but the exam was completed. Shortly after, the patient became tachycardic, hypotensive and unresponsive to external stimuli, and with generalized erythema. She was treated with intramuscular (IM) adrenaline, hydrocortisone and clemastine, intubated and transferred to the Intensive Care Unit (ICU). Her condition progressively improved and she was discharged 48 hours later.

Case 2: female, 75 years old, history of asthma. The patient also had indication for ablation of atrial fibrillation and was proposed to have a CCTA. Immediately after the administration of iopromide, she became agitated and dyspneic, with central cyanosis and peripheral desaturation. Hydrocortisone and clemastine were administered. The condition evolved into cardiac arrest, and generalized urticaria and angioedema of the tongue, lips and eyelids were observed. Advanced life support was immediately initiated, and intravenous adrenaline was administered, with rapid recovery of spontaneous circulation. She was transferred to the ICU, and was discharged 3 days later.

After these episodes, and although the iopromide administered in these cases had different lot numbers, this ICM was discontinued in the whole hospital and was replaced by Visipaque® 320 (iodixanol).
Case 3: female, 21 years old, history of allergic rhinitis and mild asthma. The patient resorted to the Emergency Room for abdominal pain, and was prescribed an abdominal CT. After the administration of iodixanol, she developed angioedema of the lips and ear lobes, generalized pruritus and erythema, and went into anaphylactic shock. She was promptly treated with IM adrenaline, hydrocortisone and clemastine. The symptoms rapidly improved. She was admitted in the Observation Room for monitoring and discharged after 12 hours.
In the first two reactions tryptase serum levels were found to be extremely elevated. Skin tests with the ICM involved in the reaction were performed 2 months later as recommended by the recent EAACI practice parameters (1): undiluted at 320-370 mg/mL for skin prick tests (SPT) and diluted at 1:10 for intradermal tests (IDT). The SPTs were negative, so we continued with IDT, which were positive in all cases, confirming the IgE-mediated reaction.
All three patients had negative SPTs and IDT to an alternative ICM (iodixanol in the first two and iopromide in the latter). The first patient has already been submitted to a provocation test with iodixanol, which was negative. We performed a protocol that consisted of serial administrations in increasing doses (5 mL, 15 mL, 30 mL, 50 mL), with 45 minutes intervals.
The other two patients are scheduled to have a provocation test with the alternative ICM in the near future. They have a written medical report that states the diagnosis and the need for absolute avoidance of the implicated ICM until completion of the allergy study. The report also emphasizes the need to perform premedication if, in the mean time, an exam with ICM is absolutely required. The premedication protocol we recommend includes the administration of 40 mg prednisolone 12 and 2 hours before the exam and also 10 mg loratadine 2 hours before the exam.
The protocol for ICM administration was precisely the same in all cases and it is nowadays fully automated, so there is no room for human error.
Although the appearance of low-osmolar ICM allowed for a significant reduction in the number of adverse reactions (6) we highlight that severe hypersensitivity reactions continue to occur. These potentially fatal cases reinforce the importance of the awareness for these reactions among radiology and cardiology staff, as well as the existence of acute treatment protocols and even premedication protocols, in cases of increased risk of reaction, in close relation with allergists.

Conflict of interests

The authors declare that they have no conflict of interests.

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