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Case Report

Gadolinium-based contrast agent anaphylaxis, a unique presentation of acute abdominal pain

Abstract

Gadolinium-based contrast agents (GBCAs) for magnetic resonance imaging have emerged as safe and well-tolerated agents with minimal adverse effects over the past 3 decades. Hypersensitivity reactions to GBCAs including skin and/or mucocutaneous involvement and occasionally respiratory reactions occur approximately in 0.1% of the cases. Severe adverse events including GBCA-induced anaphylaxis are extremely rare, occurring in 0.004%–0.01% of the cases. We report a severe case of GBCA-induced anaphylaxis who presented with a sudden onset of severe abdominal pain shortly after receiving a dose of GBCA. The patient later became hypotensive and in shock status requiring epinephrine administration. Emergency physicians and radiology staff administering these compounds need to be aware of the potential harm and anaphylactic shock from GBCA.

Over the past 30 years, magnetic resonance imaging (MRI) has emerged as a safe alternative modality to computed tomographic scans in patients, particularly in patients with allergic reactions to computed tomography iodinated contrast media [1]. More than 34 million MRI studies are performed each year, with approximately half of them with the use of intravenous contrast [2]. MRI contrast media have been recognized as having excellent safety profiles with minimal adverse effects. Commercially available MRI contrast agents can be classified into 2 main groups: paramagnetic and superparamagnetic. Most of the contrast agents belong to the first group, containing either gadolinium or manganese, among them gadolinium being predominantly used worldwide [3]. Gadolinium-based contrast agents (GBCAs) are characterized further based on ionic state, the chelating ligand, and pharmacokinetics [2].

Common extravasation upon intravenous administration, nephrogenic systemic fibrosis, allergic reactions, and nephrotoxicity are among the known risks of GBCA injections [4,5,6,7,8].

These adverse effects are mainly categorized into 3 different major events including toxic reactions to contrast, type I hypersensitivity allergic reactions, and nonspecific reactions such as dizziness or syncope [10,11]. The incidence of acute adverse effects after injection of MRI contrast media ranges from 0.17% to 2.4% [9].

A 48-year-old woman with a history of chronic abdominal pain and Raynaud disease presented to an outpatient radiology center for a magnetic resonance cholangiopancreatography. After the administration of the GBCA, the patient developed severe diffuse abdominal pain and diaphoresis, prompting emergency medicine services call and transfer to the emergency department (ED). En route, emergency medicine services vitals included a blood pressure (BP) of 90/60 and heart rate of 85. On arrival to the ED, the patient was found to be further hypotensive at 72/46 with a heart rate of 95 and a shock index of 1.3. She was

transferred to a medical resuscitation bay where she continued to complain about severe abdominal pain and nausea, dramatically different from her baseline abdominal pain. The patient also noted new diffuse pruritus. On physical examination, repeat vital signs were notable for a sustainable hypotension of 69/50 and a pulse of 98 with a newly developed maculopapular rash all over her body. A significantly prolonged capillary refill time of 5–6 seconds was noticed at her digits and extremities. Despite the severe abdominal pain, her abdomen was soft, with moderate tenderness at the suprapubic region but nondistended and with no evidence of acute abdomen.

The patient received an epinephrine dose of 0.5 mg (1:1000 concentration) intramuscularly in her lateral thigh twice, methylprednisolone 125 mg, diphenhydramine 50 mg, and famotidine 20 mg intravenously. Over the next 20 minutes, the patient's blood pressure improved to 110/69, her urticarial rash resolved, and her abdominal pain improved from 10 of 10 to her baseline level of 2 of 10. The patient was then observed in the ED for an additional 4 hours and discharged home without any complications. Upon further questioning, the patient reported an allergic reaction of unknown severity to an intravenous pyelogram with contrast more than 15 years ago without any significant sequela.

This patient's presentation with abdominal pain, acute onset of a diffuse maculopapular rash, and hypotension that occurred within minutes of receiving an injection of GBCA is consistent with anaphylaxis. As defined by the National Institute of Allergy and Infectious Disease, and the Food Allergy and Anaphylaxis Network, anaphylaxis is highly likely when 1 of these 3 criteria is met: (1) an acute onset of illness (minutes to hours) with an involvement of skin and/or mucosal tissue *and at least 1 of the following*—respiratory compromise, hypotension, or associated symptoms of end-organ dysfunction; (2) 2 or more of the following occur rapidly (minutes to hours) *after a likely allergen exposure* for that patient—*involvement of skin mucosal tissue, respiratory compromise, hypotension or associated symptoms of end-organ dysfunction or persistent gastrointestinal symptoms*; and (3) reduced BP *after exposure to a known allergen* for that patient with a systolic BP of less than 90 mm Hg or greater than 30% decrease from patient's baseline [13]. This case report is notable for presenting a unique example of anaphylactic shock to GBCA. Although “persistent gastrointestinal symptoms” are part of the criteria for diagnosing anaphylaxis, this case report is a vivid example of acute and initially isolated severe abdominal pain as the presenting symptom for anaphylaxis in the setting of allergen exposure.

As previously mentioned, GBCAs are well tolerated, with hypersensitivity reactions occurring approximately 0.1% of the time. Although there are a variety of hypersensitivity reactions caused by GBCA injections, the most common symptoms are urticaria, respiratory symptoms, and other mucocutaneous manifestations [5]. There are several factors

that increase a patient's risk of experiencing an immediate GBCA hypersensitivity reaction. Patients who have experienced prior immediate hypersensitivity reactions to MRI contrast media and/or iodinated-contrast media are 30% more likely to experience a recurrence upon a subsequent injection [5]. In addition, patients are at a higher risk of experiencing adverse reactions if they have features of atopy (asthma, dermatitis, urticaria), multiple allergies, or prior major anaphylactic response or if they underwent multiple prior exposures to GBCAs [6]. GBCA-induced adverse events are seen more frequently in outpatient settings than in inpatient settings [12]. Adverse events are more common in female patients, but sex is not indicative of the severity of the reactions [12]. Age is also not a determining factor of allergic reaction occurrences or their severities.

GBCA-induced anaphylaxis is extremely rare and occurs in 0.004%–0.01% of cases with intravenous contrast injections [5]. The incidence of anaphylactic reactions to GBCA is so rare; therefore, not sufficient data are available in regard to the rate of anaphylaxis and shock, as shown in this case report. Data on GBCA-induced anaphylaxis related mortalities are variable. Prince et al [6] reported a mortality rate of 0.0019% (3 of 158,796 cases). Jung et al [5] reported a mortality incidence rate of 0.0007%, and according to the US Food and Drug Administration, the overall mortality rate was reported as 0.00008% from 2004 to 2009 (40 deaths per 51 million administered MRI contrast material doses) [6]. The age at the time of death ranged from 9 months to 89 years with the mean age of 60 years old. The male to female ratio was 2.7 (but sex was only reported for 37 of the deaths) [6].

Most reported cases of hypersensitivity and anaphylaxis were resolved without any lasting effects. GBCA-induced anaphylaxis progressing to death is dependent on many factors, including the vigilance of the medical team, their skill level in identifying anaphylaxis, and the proximity of treatment [6,12]. For example, the death of 1 patient occurred when a power injection was administered instead of a manual injection. The medical team was not present in the room at the time of the anaphylaxis onset, there were no early recognition and treatment, and the patient passed away [6].

There has been some research in the area of assessing a patient's risk of adverse reactions due to GBCA injections, such as skin allergy testing, but there remains a need for diagnostic measures with a higher degree of sensitivity. The best preventive measure at this time includes a careful history and allergy assessment of all patients. There is no level I evidence that corticosteroid pretreatment reduces or prevents severe reactions to GBCA [14]. In the reported cases of anaphylaxis, patients received a variety of treatments, including epinephrine, dopamine, nor-epinephrine, hydration, and β_2 agonist inhalation treatments [5]. Physicians, nurses, and technicians administering these compounds should be made aware of the potential harm of GBCA. To be prepared for the possibility of developing anaphylaxis, centers should provide training and resources to their medical staff so that they can respond in a rapid and efficient manner.

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