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A five-year-old boy with anaphylaxis reaction to gadolinium-based MR contrast medium: a case report

Seung Hun Woo[1], Jung Bum Han[1], Tae Young Ahn[2] and Jung Yun Bae[1*]

Abstract

Magnetic resonance imaging (MRI) is one of the most widely used tests in orthopedic areas. Gadolinium-based magnetic resonance (MR) contrast media are commonly used for MRI tests. They are known to be safe with little side effects and low incidence of acute adverse reactions. Although not common, immediate hypersensitivity reaction can occur in some patients after administration of gadolinium-based MR contrast media, causing skin rash, vascular edema, dyspnea, abdominal pain, hypotension, altered mental status, cardiopulmonary arrest, and even death. During a knee joint MRI test in a 5-year-old boy, anaphylaxis, a serious symptom, occured after injecting gadolinium-based MR contrast medium. Here we report this case along with a literature review.

Keywords Pediatrics, Anaphylaxis, Gadolinium-based Magnetic Resonance (MR) contrast media, Severe acute adverse reaction

Background

Magnetic resonance imaging (MRI) is one of the most widely used tests in the orthopedic field due to its excellent resolution. It can be utilized in various imaging techniques to effectively visualize not only bone tissues, but also soft tissues such as nerves, ligaments, and vascular muscles effectively. Gadolinium-based magnetic resonance (MR) contrast media are commonly used for MRI tests. They are known to be safe with a low incidence of acute adverse reactions. This is primarily because concentrations of gadolinium-based contrast media are significantly lower than those of osmotic nonionic iodine contrast media used in computed tomography (CT) scans [1].

Adverse reactions to contrast media, including iodinated contrast media and gadolinium-based contrast media, can have a wide range of clinical manifestations depending on underlying mechanisms. These reactions can be categorized into physiological reactions and hypersensitivity reactions. Their severity can be mild, moderate, or severe [2]. Physiological reactions are primarily caused by direct chemical toxicity of iodinated contrast agents and differences in osmotic pressure. Caution is necessary as these reactions frequently occur at high doses [3].

A vasovagal response is commonly seen as hypotension and bradycardia caused by vagal hyperactivity. It can also be induced by stimuli such as anxiety and peripheral vascular catheterization [3]. On the other hand, hypersensitivity reactions can occur regardless of dose, making it challenging to predict. They can be further classified into allergic reactions involving immunological mechanisms

*Correspondence:
Jung Yun Bae
nari1006@gmail.com
[1]Department of Orthopedic Surgery, Pusan National University Yangsan Hospital, Pusan National University School of Medicine, 20, Geumo-ro, Mulgeum-eup, Yangsan-si 50612, Gyeongsangnam-do, Korea
[2]Department of Orthopedic Surgery, Pusan National University Hospital, 179 Gudeok-ro, Seo-gu, Busan, Korea

and non-allergic hypersensitivity reactions with unidentified mechanisms. Most adverse reactions to gadolinium are mild and physiological, including coldness, warmth, or pain at the injection site, nausea, vomiting, headache, paresthesia, and dizziness [2].

Although adverse reactions to gadolinium are rare, cases showing immediate hypersensitivity reactions following its administration have been reported. These reactions can manifest as skin rash, vascular edema, dyspnea, abdominal pain, hypotension, altered mental status, cardiopulmonary arrest, and even death in some severe cases [4]. Anaphylaxis, a severe symptom, has been mainly reported in adults, with little mention of such cases in pediatric patients. In this article, the authors report a case of anaphylaxis after injecting gadolinium-based contrast media during knee joint magnetic resonance imaging procedure in a 5-year-old child along with a literature review.

Case presentation

A 5-year-old male patient visited the hospital with a lump in his left knee joint. His body weight was 21.3 kg (82.8 percentile). Physical examination detected a mild oppressive pain when touching the inner lump of the left distal femur. Simple radiography showed a slight elevation of the cortical bone inside the distal femur (Fig. 1). The size was smaller than that observed on physical examination. Therefore, a decision was made to perform a knee MRI at the hospital to confirm the lump. The child had a history of left lower lobe compartment resection due to

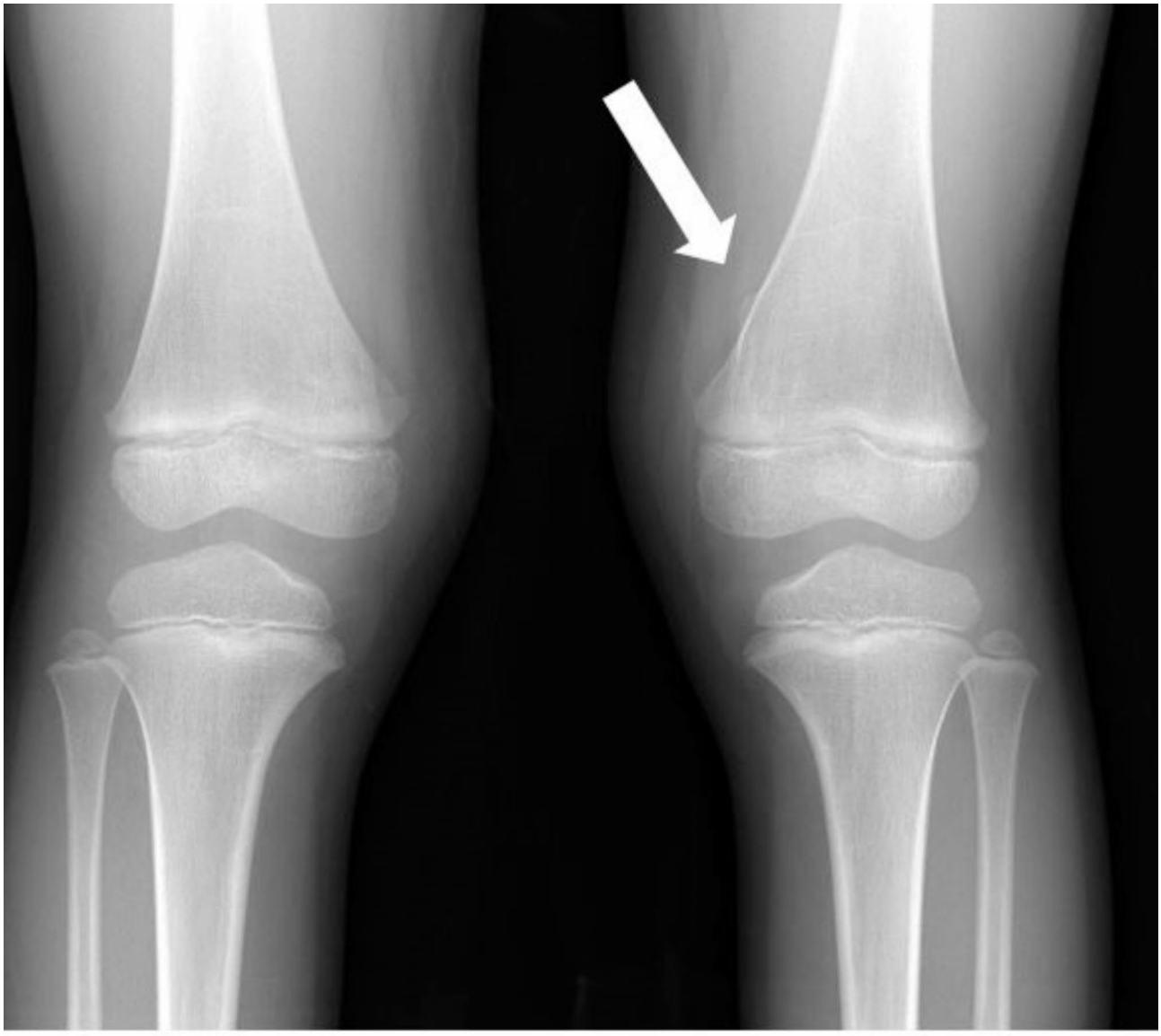

Fig. 1 Knee radiograph showing a slight elevation of cortical bone inside the distal femur indicated by an arrow

congenital cystic adenomatoid malformation (CCAM) at the age of two. At that time, chest CT scans were performed twice using contrast medium, showing no abnormalities. In addition, the patient had allergic rhinitis. He received medication intermittently.

Knee MRI was performed at this hospital using a contrast medium (solution Gadovist, Bayer Schering Pharma AG, Germany 3 mg). The patient underwent knee MRI while being conscious and accompanied by his mother. He did not receive any sedatives. At 10 min after injecting the contrast medium, the child complained symptoms of dizziness and lethargy. Thirty minutes later, he complained of severe dizziness, abdominal pain, and headache. He vomited three times. He was transferred to the emergency room with suspected anaphylaxis. Upon arrival to the emergency room, he had a blood pressure of 80/40 mmHg, a pulse rate of 100 beats/minute, a respiratory rate of 32, a body temperature of 36.4 °C, an oxygen saturation (SpO_2) of 95%, and a blood sugar level of 125 mg/l. Physiological saline was rapidly administered. However, there was no increase in blood pressure after 5 min. Therefore, epinephrine at a dose of 0.2 mg was injected intramuscularly. A continuous infusion of 5 mcg/kg/min of dopamine was initiated at 40 min after symptom occurrence. At 65 min, a second dose of 0.2 mg of epinephrine was administrated and a transnasal humidified oxygen delivery system (Optiflow™, Fisher and Paykel Healthcare Limited, Auckland, New Zealand) was applied with FiO_2 70% at a flow rate of 20 L/min. At 75 min, a continuous infusion of norepinephrine at 0.05 mcg/kg/min was started. Chest X-ray was performed at 120 min. Three hours later, administration of methylprednisolone was started, with findings on both lungs suggesting diffuse ground glass opacity or pulmonary edema, especially on the right side (Fig. 2). Norepinephrine continuous infusion was stopped after 4 h and 40 min and Optiflow™ setting was reduced to 40% FiO_2 at a flow rate of 10 L/min. Subsequently, the child was transferred to the intensive care unit. The Optiflow™ was removed the next morning. It was replaced with nasal cannula 2 L. Dopamine infusion was discontinued. On the third day, pulmonary edema showed improvement. The child maintained SpO_2 at more than 95% without oxygen supplementation. He was in good physical condition with a normal food intake. On the fourth day, he was discharged without any notable symptoms.

Discussion and conclusions

Gadolinium-based magnetic resonance (MR) contrast media are generally considered to be safer than iodinated contrast agents [1]. However, with increasing use of gadolinium-based contrast media in clinical settings, the number of reports on acute adverse reactions associated with their use is increasing [5]. Severe anaphylactic reactions following the administration of gadolinium-based magnetic resonance (MR) contrast media are extremely rare. According to Jung and others, the incidence of anaphylaxis after injecting gadolinium contrast medium was approximately 0.008% and the mortality rate due to gadolinium contrast-induced anaphylaxis ranged from 0.0007–0.0019%.[4] In addition, it has been reported that these immediate hypersensitivity reactions occur more frequently in women than in men. However, the severity is higher in men [4]. Patients who have asthma or other allergic diseases face an increased risk of immediate hypersensitivity when they are exposed to contrast media multiple times [4]. According to Ahn and Kang et al., the recurrence rate was 15 ~ 30% in patients with a history of hypersensitivity. The frequency of recurrence can be reduced by administering a different type of gadolinium-based contrast agent or by implementing premedication [6]. Various methods are employed to predict and prevent recurrence or occurrence, including corticosteroid or antihistamine premedication, skin-prick tests, drug provocation tests, and switching medications [6, 7]. Although studies focusing exclusively on anaphylactic reactions in pediatric patients are scarce, a few studies have examined adverse reactions to gadolinium-based contrast agents. Some of these studies have included pediatric patients as part of the overall patient population, while others have focused exclusively on pediatric patients. McDonald et al. Have conducted a retrospective study on acute reactions to gadolinium-based contrast agents (GBCAs) and observed an incidence of 0.10% (17/16,237) for allergic-like reactions and an incidence of 0.14% (23/16,237) for physiologic reactions. They reported no severe reactions [8], similar to the present case. Similarly, Hojreh et al. Have reported 19 acute adverse events (19/8156; 0.23%) in 17 patients (17/2109; 0.81%) who showed no severe reactions [9]. In the study by Ahn and Kang et al., the incidence of hypersensitivity reactions to Gadolinium-based contrast agents was 0.2% in patients under 19 years old, which was lower than the incidence of 0.5% observed in patients aged 20 to 69 years [6].

When hypotension occurs as an acute adverse reaction to contrast agents, it is necessary to differentiate between anaphylaxis and vasovagal reactions. Most vasovagal reactions are mild and self-limiting. Thus, close patient observation is recommended until symptoms subside. Vasovagal reactions are characterized by a slow heart rate with generally normal or slightly decreased respiration. They often occur immediately after or during contrast agent injection. They might be associated with patient anxiety. They present with overall pallor, coolness of the skin, and occasionally diaphoresis [2, 3]. On the other hand, anaphylaxis is a severe allergic reaction that occurs systemically, affecting multiple organs within a short

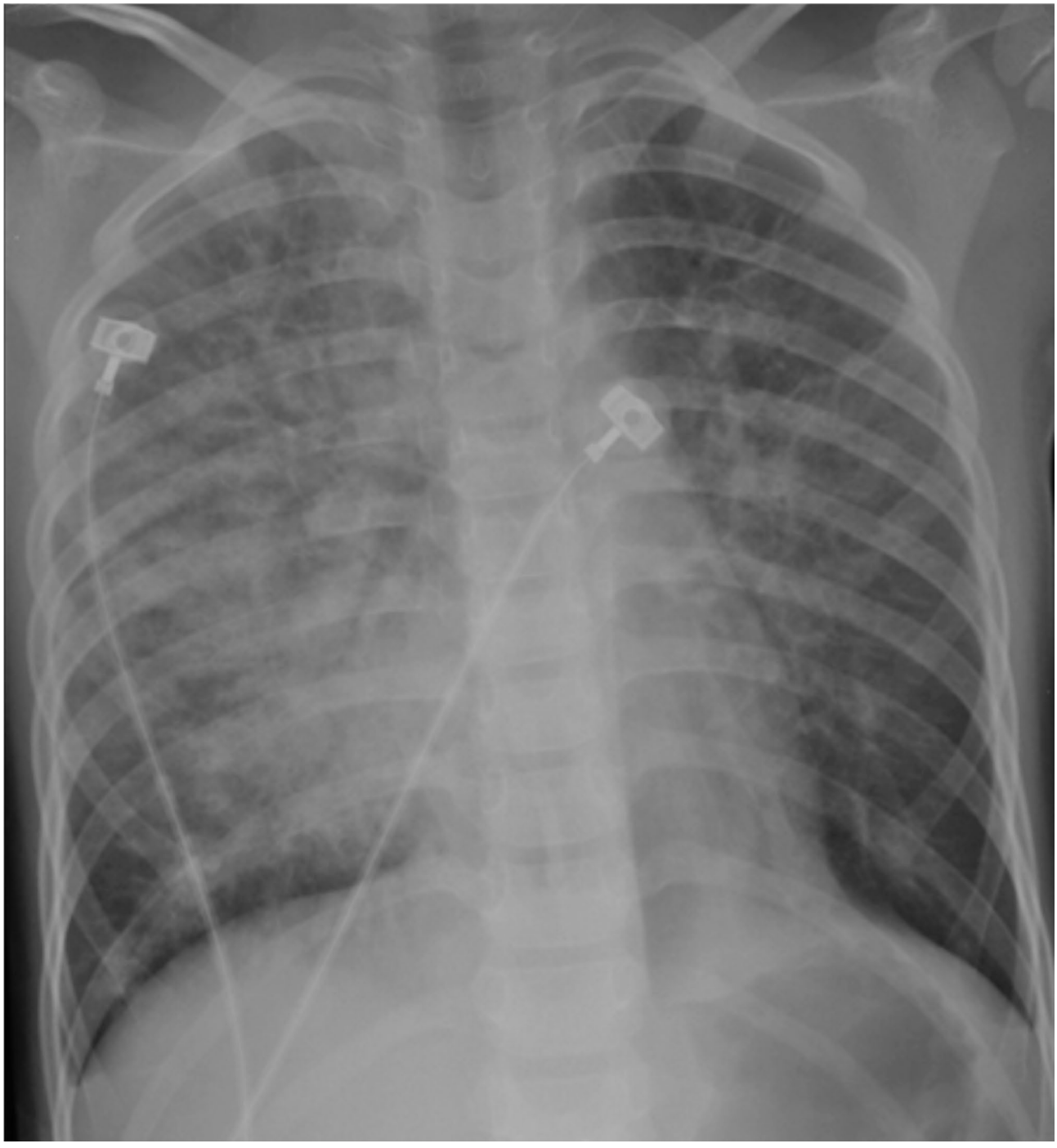

Fig. 2 Chest radiography conducted at 2 h after injecting the contrast medium

period of time. Without appropriate treatment, it can be life-threatening. Anaphylaxis is characterized by an increased heart rate and a weak pulse felt in both peripheral and carotid arteries [10]. It may be accompanied by dyspnea and increased respiratory rate. It can occur immediately after injection, during injection, or within minutes after injection. In rare cases, delayed anaphylaxis shock may occur hours after injecting the contrast medium [11].

Anaphylaxis is diagnosed based on diagnostic criteria outlined by the World Allergy Organization in 2019, which define it as a severe form of immediate hypersensitivity. In the present case, the patient experienced symptoms at 10 min after administration of the contrast agent. He had all respiratory compositions, hypotension,

and severe gastrointestinal symptom suggesting a diagnosis of anaphylaxis [10]. Despite rapid infusion of physiological saline and assuming a shock position, his hypotension did not improve. Additionally, he exhibited symptoms such as tachycardia, increased respiratory rate, decreased oxygen saturation, recurrent vomiting, and decreased level of consciousness. These findings indicate a higher probability of anaphylaxis rather than a vasovagal reaction. Most anaphylaxis cases show clinical manifestations within minutes after the causative agent is administrated. It might be fatal if rapid and accurate diagnosis and treatment are not performed. Anaphylaxis requires early diagnosis and treatment. Thus, treatment with adrenaline should be started when in doubt, even if symptoms do not fully meet the diagnostic criteria for anaphylaxis. According to ESUR Guidelines on Contrast Agents 10.0, in cases of anaphylaxis, the resuscitation team is called, airway suction is performed if necessary, and leg elevation is performed when hypotension occurs. Oxygen is administrated at 6–10 L/min using a mask and intramuscular adrenaline is administrated at 0.3 ml or 0.3 mg for patients aged 6–12 years or at 0.15 ml or 0.15 mg for patients under 6 years old. Injections can be repeated if necessary. In addition, 1 to 2 L of 0.9% physiological saline is rapidly administrated through the intravenous route. An H1-blocker (e.g., diphenhydramine at 25–50 mg) is also administrated [12]. In the present case, abnormality was detected relatively quickly. After abnormality was detected, proper treatment was performed, resulting in a successful recovery without any residual effects.

Anaphylactic reactions due to gadolinium-based magnetic resonance (MR) contrast media are rare. Their incidence is even lower in pediatric patients. However, when they do occur, they can be life-threatening. Thus, caution must be exercised. MRI tests typically have a longer test duration than CT scans. It is difficult to determine a patient's condition with an MRI because the patient and the operator are separated due to the magnetic field. Moreover, in the case of children, examinations are often conducted after a sedation, making diagnosis more difficult. A monitoring device is required to immediately identify the patient's condition. The operator should always closely monitor the patient with possible side effects in mind. Sufficient training for medical staff in the examination room is needed to take prompt action in the event of any adverse reactions. Thus, close attention is needed and care should be taken. For this reason, it may be useful to educate not only medical staff, but also patients and guardians to recognize that this disease is a fatal emergency. It is important to provide patients with documents recording anaphylaxis symptoms and medical help request methods as there is a possibility of recurrence.

Abbreviations

CCAM	Congenital cystic adenomatoid malformation
CT	Computed Tomography
MR	Magnetic Resonance
MRI	Magnetic Resonance Imaging
SpO2	Oxygen Saturation

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Not applicable.

Author contributions
All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by T.A., J.H. and S.W. The first draft of the manuscript was written by S.W. and J.B. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Conflict of interest
The authors have no conflicts of interest to disclose.

Data availability
The data presented in this study are available from the corresponding author upon reasonable request.

Declarations

Competing interests
The authors declare no competing interests.

Ethical approval and consent to Participate
This study was approved by the Institutional Review Board of Pusan National University Yangsan Hospital (Approval No. 05-2023-009).

Consent for publication
Informed consent for publishing data of this study was obtained from the patient's legal guardian. In addition, radiographic images used in this study were completely anonymized. There is no information that can identify the patient.

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