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Late-onset acute respiratory distress syndrome induced by a gadolinium-based contrast agent

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ABSTRACT

Rapid decline of pulmonary function in acute respiratory distress syndrome (ARDS) can make ARDS a dangerous and potentially life-threatening condition. Gadolinium-based contrast agents are considered safe alternatives to iodine-based contrast agents, with comparatively fewer adverse effects and a lower incidence of serious adverse events, such as dyspnea or hypotension. There are five reported cases of gadolinium-induced ARDS.

A 59-year-old woman with respiratory failure 30 min after gadolinium administration was diagnosed with ARDS; she was admitted to the intensive care unit. Her condition improved by artificial respiration management and adrenaline and steroids administration. She was discharged on day 13.

Considering ARDS occurred 30 min after gadolinium administration and findings suggesting anaphylaxis, such as wheezing and failure in organs other than the lungs, were absent, the involvement of any immediate-onset reaction was excluded; thus, a diagnosis of gadolinium-induced ARDS was made.

1. Introduction

Acute respiratory distress syndrome (ARDS) is a dangerous condition that can result in death owing to rapid decline of the pulmonary function. Gadolinium is a safe alternative to iodine-based contrast agents, with a lower incidence of serious adverse events such as dyspnea and hypotension [1] and comparatively fewer adverse effects [2], as noted in the study patient. There have been five previously reported cases of gadolinium-induced ARDS [3–7]; however, the mechanism of onset remains unknown.

2. Case report

The patient was a 59-year-old woman with a history of rheumatoid arthritis. She was administered oral methotrexate 8 mg/day weekly and bucillamine 150 mg/day. She was not allergic to drugs; she had no relevant family history. She experienced circumferential abnormal sensation in her chest that had been gradually worsening since one month. She sought medical attention on the day of admission. Symptoms associated with myelitis were suspected; contrast-enhanced MRI using gadobutrol was obtained on the same day. There were no clear abnormal findings on the chest radiograph obtained just before contrast-enhanced MRI (Fig. 1). There were no problems immediately after receiving the contrast agent, and the test was completed. However, acute-onset dyspnea was observed 30 min after administering the contrast agent. The SpO2 level decreased to 80%, and arterial blood gas level decreased (PaO2 = 40 mmHg) (room air). Chest auscultation revealed bilateral rhonchi, and chest radiography images showed infiltrative shadows (Fig. 1). Chest computed tomography scan also revealed bilateral infiltrative shadows; these findings suggested pulmonary edema (Fig. 1). Anaphylaxis and pulmonary edema associated with contrast-enhanced MRI were suspected, and 0.3 mg adrenaline was intramuscularly injected; artificial respiration management was initiated. After intubation, breathing was characterized by oxygenation failure at an arterial partial pressure of oxygen (paO2) of 82 mmHg at 6 cm H_2O positive end-expiratory pressure, with a fraction of inspired oxygen (FiO2) at 0.8. Heart function was normal according to the echocardiographs obtained subsequently. The brain natriuretic peptide (BNP) level decreased from 31.7 pg/mL before onset to 23.3 pg/mL after onset, negating the likelihood of cardiogenic pulmonary edema. No other organ failure was observed; there were no findings suggesting anaphylaxis such as rash, wheezing, or abdominal symptoms. Considering the delayed onset 30 min after gadobutrol administration, ARDS associated with anaphylactic reactions was also excluded. The possibility of other diseases such as infection causing ARDS was also excluded, leading to a diagnosis of gadobutrol-induced ARDS.

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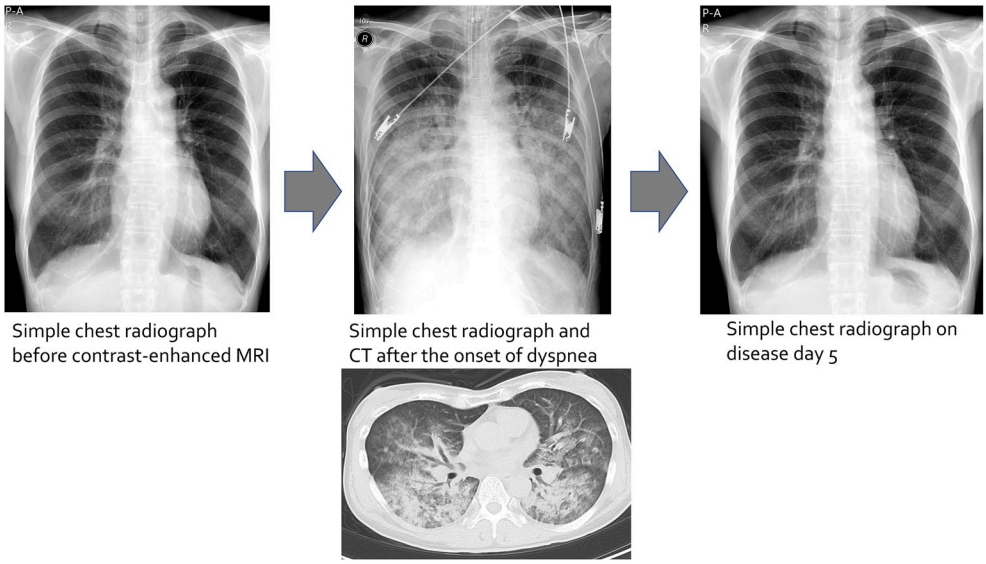

Fig. 1. Simple chest radiograph obtained just before contrast-enhanced MRI. No abnormal abnormal findings in the lungs. Bilateral infiltrative shadows on a simple chest radiograph and CT after the onset of dyspnea. Simple chest radiograph on disease day 5. Improvement in infiltrative shadows was observed.

The patient was treated through positive-pressure ventilation with an artificial respirator and methylprednisolone 1000 mg/day for 3 days. Chest radiography images revealed improved pulmonary edema after 5 days. Chest radiography performed on disease day 5 also revealed improved pulmonary edema (Fig. 1); thus, she was extubated on the same day. Symptoms did not worsen thereafter; she was discharged on day 13.

3. Discussion

Gadobutrol is a second-generation non-ionic macrocyclic gadolinium-based contrast agent (GBCA). It has a higher ionic concentration than other MRI contrast agents, which allows testing with smaller doses [8]; it is commonly used in contrast-enhanced MRI tests. However, GBCA administered to patients with decreased renal function can trigger nephrogenic systemic fibrosis; thus, use in patients with chronic renal failure is not usually recommended [9].

Nevertheless, GBCA is associated with lower rates of adverse events than iodine-based contrast agents [2]. With the recent advances in imaging technologies, the numbers of MRI machines and images taken are increasing. The number of reports on adverse effects is also proportionately increasing [10]. Headache, dizziness, nausea and vomiting, cough, and laryngeal discomfort are the commonly reported side effects. Itchiness, rash, redness, and sneezing have also been observed [11,12].

The incidence of serious adverse events, such as dyspnea and anaphylactic hypotension, in this patient was low [1]; the incidences of adverse events after gadobutrol administration and anaphylaxis are 0.55% and 0.01%, respectively [13].

Anaphylactic reactions because of gadobutrol administration are characterized by their immediate onset; they occur in the first 5 min of administration in 82.7% cases and in the first 10 min of administration in 95.7% cases [14].

Table 1
Previously reported cases of gadolinium-based contrast agent-induced acute respiratory distress syndrome.

	Reference 3)	Reference 4)	Reference 5)	Reference 6)	Reference 7)
Sex	Male	Female	Female	Female	Female
Age	37 years old	46 years old	26 years old	42 years old	49 years old
Underlying diseases	–	–	–	Hypertension	–
Tested site	Spine	Submandibular mass	Abdomen	Cervical tumor	Abdomen
Gadolinium-based contrast agent	Gadobutrol	Gadobutrol	Gadobutrol	Gadobutrol	Gadobutrol
Time between administration and onset	Unknown	30 min	50 min	30 min	90 min
PaO2/FiO2	122 mmHg/1.0	138.5	63.5	n/a	48.6 mmHg/0.4
Routine chest radiography	Increased pulmonary vascular markings	Bilateral pulmonary infiltrative shadows	Bilateral pulmonary infiltrative shadows	Bilateral pulmonary infiltrative shadows	Bilateral pulmonary infiltrative shadows
Cardiac function	Good	Good	Good	Good	Good
Dyspnea	+	+	+	+	+
Lip edema	+	+	+	(-)	(-)
Wheezing	(-)	+	+	(-)	+
Loss of consciousness	+	(-)	(-)	(-)	(-)
Nausea and vomiting	(-)	(-)	+	+	(-)
Abdominal pain	(-)	(-)	(-)	(-)	(-)
Rash	(-)	(-)	(-)	(-)	(-)
Treatment	Noradrenaline, dopamine	Intramuscular adrenaline injection, steroid, steroid pulse therapy	Intramuscular adrenaline injection, steroid, norepinephrine	Steroid, steroid pulse therapy	Steroid
Outcome	Discharge without complications	Discharge without complications	Discharge without complications	Discharge without complications	Discharge without complications

ARDS is a dangerous condition characterized by a sudden drop in pulmonary function; thus, it is potentially life-threatening.

Pulmonary edema can be cardiogenic or non-cardiogenic [15]; the latter occurs as a result of increased microvascular permeability and alveolar fluid infiltration [16]. General drug-induced ARDS is caused by chemical injury of the vascular endothelium and epithelium, which triggers hypoxia and pulmonary vascular resistance by the accumulation of protein-rich substances in the alveoli [17,18]. The etiology of MRI contrast agent-induced pulmonary edema is largely unknown; however, some hypothesized mechanisms include endothelial injury triggered by the activation of the complement system and direct chemical stimulation of the alveoli [16,17].

Two reported cases of ARDS induced by CT contrast agents [19,20] are similar to this case in terms of delayed onset after the administration of the contrast agent.

To our knowledge, there are five reported cases of gadolinium-induced ARDS [3–7] (Table 1). The patient was diagnosed with ARDS following symptoms such as dyspnea that occurred 30–90 min after gadobutrol administration. The patient was treated by administration of adrenaline and steroids as well as artificial ventilation; ARDS followed good courses. However, the symptoms were delayed, occurring 30–90 min after gadobutrol administration, suggesting that gadobutrol-induced ARDS occurs by a mechanism other than an immediate reaction, exemplified by symptoms such as anaphylaxis. Delayed reactions are noted in reports on the above-mentioned iodine-based contrast agents, suggesting the involvement of similar mechanisms of onset with GBCA administration. Similar to that in previously reports, our patient developed delayed-onset ARDS after gadobutrol administration and followed a good clinical course.

Previous reports have concluded that an immediate reaction was unlikely considering that ARDS development was delayed; however, the patients displayed symptoms such as cyanose, wheezing, and nausea, indicative of failure of organs other than the lungs; this suggests the involvement of anaphylaxis. However, failure of organs other than the lungs was not observed in the present case, and ARDS had a delayed onset, strongly suggesting that gadobutrol-induced ARDS onset did not involve mechanisms of an immediate reaction.

The effectiveness of subcutaneously injected gadobutrol diluted to 1:10 to test for IgE-mediated GBCA allergies has been reported [21], but its actual effectiveness is questionable because the study did not define any criteria for ARDS and as mentioned previously, the onset of gadobutrol-induced ARDS appears to take form of some mechanism other than an immediate reaction. This test was not performed in this patient considering the risk of fatal outcomes if it triggered ARDS recurrence.

Our results suggest that gadobutrol-induced ARDS occurs through a mechanism other than that of an immediate reaction.

Declaration of competing interest

I declare on behalf of my co-authors and myself that we do not have any conflict of interest to declare.

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