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Case Report

Delayed anaphylaxis due to gadolinium- A rare clinical scenario

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ABSTRACT

Acute respiratory distress syndrome is a sudden in onset, diffuse inflammatory form of lung injury which may be associated with a variety of etiologies such as pneumonia, sepsis, aspiration, and severe trauma. Prompt recognition and treatment of acute respiratory distress syndrome is critical to reduce the associated high mortality. Severe lung injury presenting as acute respiratory distress syndrome secondary to gadolinium contrast media (gadobutrol) is rarely reported. We describe an interesting case of a 47-year-old woman who presented to the emergency department with acute respiratory failure after gadolinium administration. She was diagnosed with acute respiratory distress syndrome, was admitted to the intensive care unit due to requiring mechanical ventilation. Her condition improved with epinephrine and steroids and she was successfully extubated and discharged from the hospital in one week.

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Introduction

The contrast agent gadolinium has been in use for imaging studies especially magnetic resonance imaging for more than 30 years due to its high reliability and low rates of adverse effects. Gadobutrol is a second-generation non-ionic macrocyclic gadolinium-based contrast agent with high thermostability. Adverse reaction due to gadobutrol such as noncardiogenic pulmonary edema is extremely rare [1]. We present an interesting case of acute respiratory distress syndrome associated with the use of gadobutrol.

Case Description

A 47-year-old female (weighted 75.5 kilogram) with previous medical history of hypothyroidism on levothyroxine only, presented to the emergency department (ED) for acute shortness of breath and cyanosis of the lips. The patient had an MRI of the breast with gadolinium (gadovist 7 milliliters intravenously) done in outpatient clinic two hours before she presented to the ED. She had no relevant history of drug or seasonal allergies. She was never exposed to dye or contrast agents before this event.

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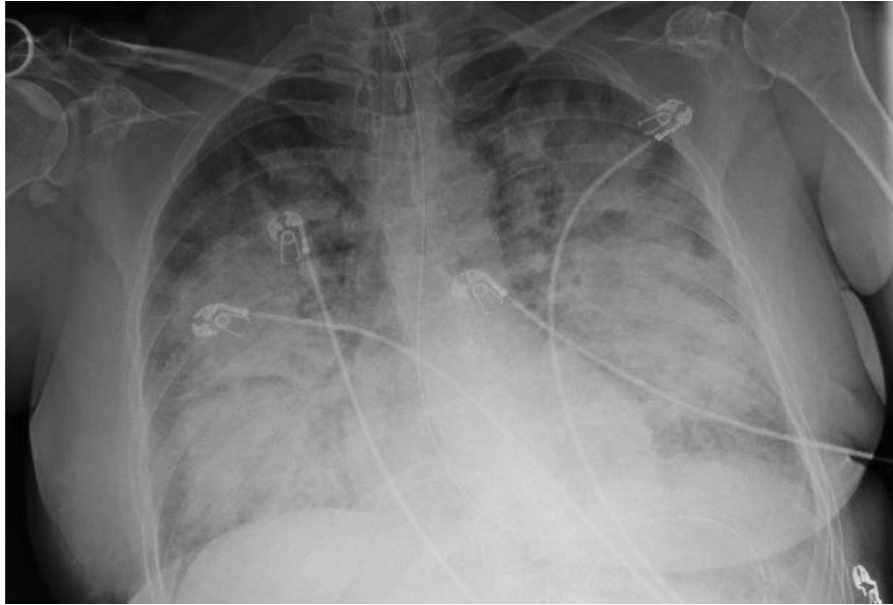


Fig. 1 – Bilateral ground glass opacities noted on Chest X-ray at the time of admission.



Fig. 2 – Resolution of ground glass opacities on Chest X-ray at the time of discharge.

When she was brought to the ED, she was short of breath at rest and on exertion. She was in mild distress, felt nauseous, dizzy and was noted to have bilateral rales on exam. Her first vital signs included blood pressure (118/70 mmHg), heart rate 128 beats/minute, temperature (94.9-degree Fahrenheit), respiratory rate 26 and oxygen saturation of 96% on 15-liter/minute face mask. She received intravenous diphenhydramine and methyl prednisone with partial relief. Her repeat saturating pulse oxygen in the ED was 80% on 3-liter/minute

oxygen supplementation. The chest X-ray (Figs. 1-2) showed bilateral diffuse ground glass opacities. She was placed on bilevel positive airway pressure (BiPap) machine for 1 hour in the ED for symptomatic relief. However, she continued to be tachypneic, hypoxic and became hypotensive to systolic blood pressure 90 mmHg.

The patient had to be intubated and placed on mechanical ventilation due to worsening respiratory status and was started on epinephrine drip. She was managed for presumed

diagnosis of acute respiratory distress syndrome secondary to anaphylaxis from gadolinium. A full workup was undertaken to rule out other possible causes attributing to her condition. Her transthoracic echocardiogram and b-natriuretic peptide were in normal range. She had been afebrile throughout her hospital stay and pan-cultures were negative for any growth. Her Covid-19 PCR was negative twice and covid-19 antibodies were also negative. No other organ failure was observed; there were no findings suggesting anaphylaxis such as rash, wheezing, or abdominal symptoms. She was kept on epinephrine drip for about 12 hours and subsequently weaned off. The patient eventually got extubated on day four of the hospital stay and was discharged on day seven with epinephrine pen.

Discussion

Gadobutrol is a commonly used second-generation non-ionic macrocyclic gadolinium-based contrast agent (GBCA) for imaging studies. It has a higher ionic concentration than other MRI contrast agents, which allows testing with smaller doses [2]. 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 [3]. Although, GBCA is associated with lower rates of hypersensitivity reactions as compared to other iodine-based contrast agents, there has been some increase in number of reported events noted in medical literature likely due to widespread use of gadolinium [4,5].

Adverse reactions because of gadobutrol administration are characterized by their immediate onset; commonly occurring within the first 5 minutes of administration in 82.4% cases and in the first 10 minutes of administration in 95.7% cases [6]. Commonly reported adverse reactions include nausea, vomiting, urticaria, flushing, tachycardia, wheals, dizziness, and dyspnea. However, acute respiratory distress syndrome (ARDS) and anaphylactic reactions secondary to gadobutrol administration is a rarely described phenomenon in medical literature which may result in pulmonary edema. Pulmonary edema can be cardiogenic or non-cardiogenic; the latter occurs as a result of increased microvascular permeability and alveolar fluid infiltration. This drug-induced ARDS is hypothesized to occur through chemical injury to the vascular endothelium which results in hypoxia and pulmonary vascular resistance from accumulation of protein-rich substances in the alveoli [7]. The exact component of gadobutrol responsible for such severe hypersensitivity reaction and ARDS is unknown. However, the endothelial injury triggers the activation of complement system as well which play a role in promoting pulmonary edema [8,9].

In our case, the patient started having onset symptoms approximately 1-2 hour after administration of gadolinium. She was diagnosed with ARDS and treated with epinephrine, steroids, and artificial mechanical ventilation. The hospital course was uneventful, and she was successfully extubated and discharged in a week on epinephrine-pen. There are only a few reported cases of gadolinium induced severe reactions [1,7,10-12]. Some of these reactions are delayed in onset, suggesting that gadobutrol-induced ARDS may occur by a mech-

anism other than an immediate sensitivity reaction, such as anaphylaxis. Although our patient also showed delayed reactivity response to gadobutrol, given the symptoms of cyanosis, profound dyspnea and significant respiratory failure, we would include this clinical case in spectrum of anaphylactic reaction.

Conclusion

In this case report, we describe an interesting case of anaphylactic reaction to gadobutrol dye used in magnetic resonance imaging. Although gadolinium is very safe to use, caution should be practiced for allergic reactions and the patients should be advised about the possibility of delayed allergic symptoms which may occur 1-2 hours after its use.

Consent

I, Shamsuddin Anwar, as a corresponding author of this manuscript solemnly declare that no identifying information has been revealed or presented in the manuscript. The patient was informed and consented for the submission of the case report in the journal.

Declaration

I, Shamsuddin Anwar, as a corresponding author of this manuscript would like to declare that none of the authors have any conflict of interests in writing and submission of the manuscript. We have not received any funding or compensation of any form in writing of the article.

REFERENCES

- [1] Kerget B, Aksakal A, Afşin DE, et al. Acute respiratory distress syndrome after the use of gadolinium contrast agent. *Respir Med Case Rep* 2018;25:336–8. Published 2018 Oct 24. doi:10.1016/j.rmcr.2018.10.018.
- [2] Scott LJ. Gadobutrol: A Review in Contrast-Enhanced MRI and MRA [published correction appears in *Clin Drug Investig*. 2018 Aug 23;] [published correction appears in *Clin Drug Investig*. 2018 Sep 10;]. *Clin Drug Investig*. 2018;38(8):773–84. doi:10.1007/s40261-018-0674-9.
- [3] Nicholas BA, Vricella GJ, Smith M, Passalacqua M, Gulani V, Ponsky LE. Contrast-induced nephropathy and nephrogenic systemic fibrosis: minimizing the risk. *Can J Urol* 2012;19(1):6074–80.
- [4] Brockow K, Sánchez-Borges M. Hypersensitivity to contrast media and dyes. *Immunol Allergy Clin North Am* 2014;34(3):547–viii. doi:10.1016/j.iac.2014.04.002.
- [5] Kato K, Fujimoto S, Inukai S, Takatsu H, Kono Y, Kasai K. Late-onset acute respiratory distress syndrome induced by a gadolinium-based contrast agent. *Respir Med Case Rep* 2019;29:100990. Published 2019 Dec 26. doi:10.1016/j.rmcr.2019.100990.
- [6] Forsting M, Palkowitsch P. Prevalence of acute adverse reactions to gadobutrol—a highly concentrated macrocyclic

- gadolinium chelate: review of 14,299 patients from observational trials. *Eur J Radiol* 2010;74(3):e186–92. doi:10.1016/j.ejrad.2009.06.005.
- [7] Guru PK, Bohman JK, Fleming CJ, et al. Severe Acute Cardiopulmonary Failure Related to Gadobutrol Magnetic Resonance Imaging Contrast Reaction: Successful Resuscitation With Extracorporeal Membrane Oxygenation. *Mayo Clinic Proceedings* 2016;91(3):362–6 Mar. doi:10.1016/j.mayocp.2015.12.010.
- [8] Vandenplas O, Hantson P, Dive A, Mahieu P. Fulminant pulmonary edema following intravenous administration of radiocontrast media. *Acta Clin Belg* 1990;45(5):334–9. doi:10.1080/17843286.1990.11718107.
- [9] Hussain M, Xu C, Ahmad M, et al. Acute Respiratory Distress Syndrome: Bench-to-Bedside Approaches to Improve Drug Development. *Clin Pharmacol Ther* 2018;104(3):484–94. doi:10.1002/cpt.1034.
- [10] Demirhan A, Yasar Tekelioglu U, Akkaya A, et al. Magnetic resonance imaging contrast agent related pulmonary edema: a case report. *Eur Rev Med Pharmacol Sci* 2012;16(Suppl 4):110–12.
- [11] Park J, Byun IH, Park KH, Lee JH, Nam EJ, Park JW. Acute Respiratory Distress Syndrome after the Use of Gadolinium Contrast Media. *Yonsei Med J* 2015;56(4):1155–7. doi:10.3349/ymj.2015.56.4.1155.
- [12] Kato K, Fujimoto S, Inukai S, Takatsu H, Kono Y, Kasai K. Late-onset acute respiratory distress syndrome induced by a gadolinium-based contrast agent. *Respir Med Case Rep* 2019;29:100990 Published 2019 Dec 26. doi:10.1016/j.rmcr.2019.100990.