Fatal anaphylactic reaction to intravenous gadobutrol, a gadolinium-based MRI contrast agent

Franckenberg, Sabine; Berger, Florian; Schäerli, Sarah; Ampanozi, Garyfalia; Thali, Michael J

Abstract: We present the rare case of a fatal anaphylactic reaction to gadobutrol, a magnetic resonance imaging contrast agent, in a 42-year-old man. The patient underwent elective magnetic resonance imaging for diagnostic clarification of a suspicious finding in the abdomen. The patient had undergone contrast-enhanced computed tomography previously without the occurrence of any adverse effects. Adverse drug reactions in gadobutrol have a very low prevalence of 0.32%-3.5%, with serious adverse drug reactions in <0.1%. There are only a few cases of fatal anaphylactoid reactions to gadolinium-based contrast agents in general. However, if an anaphylactoid reaction occurs, it can present itself with a fulminant course within minutes.

DOI: [https://doi.org/10.1016/j.radcr.2017.09.012](https://doi.org/10.1016/j.radcr.2017.09.012)

Originally published at:
Franckenberg, Sabine; Berger, Florian; Schäerli, Sarah; Ampanozi, Garyfalia; Thali, Michael J (2017). Fatal anaphylactic reaction to intravenous gadobutrol, a gadolinium-based MRI contrast agent. Radiology Case Reports:Epub ahead of print.
DOI: [https://doi.org/10.1016/j.radcr.2017.09.012](https://doi.org/10.1016/j.radcr.2017.09.012)
Quality and Safety

Fatal anaphylactic reaction to intravenous gadobutrol, a gadolinium-based MRI contrast agent

Sabine Franckenberg MDa,*, Florian Berger MDb, Sarah Schaerli MDb, Garyfalia Ampanozi MDb, Michael Thali Prof., MD, Executive MBA HSGb

a Institute of Diagnostic and Interventional Radiology, University Hospital of Zurich, Raemistrasse 100, 8091 Zurich, Switzerland
b Institute of Forensic Medicine, University of Zurich, 8057 Zurich, Switzerland

ARTICLE INFO

Article history:
Received 18 August 2017
Received in revised form 6 September 2017
Accepted 8 September 2017
Available online

Keywords:
Gadobutrol
Gadolinium
Anaphylactic reaction
MRI

ABSTRACT

We present the rare case of a fatal anaphylactic reaction to gadobutrol, a magnetic resonance imaging contrast agent, in a 42-year-old man. The patient underwent elective magnetic resonance imaging for diagnostic clarification of a suspicious finding in the abdomen. The patient had undergone contrast-enhanced computed tomography previously without the occurrence of any adverse effects. Adverse drug reactions in gadobutrol have a very low prevalence of 0.32%-3.5%, with serious adverse drug reactions in <0.1%. There are only a few cases of fatal anaphylactoid reactions to gadolinium-based contrast agents in general. However, if an anaphylactoid reaction occurs, it can present itself with a fulminant course within minutes.

© 2017 the Authors. Published by Elsevier Inc. under copyright license from the University of Washington. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Case history

A 42-year-old man underwent elective magnetic resonance imaging (MRI) for diagnostic clarification of a suspicious finding in the abdomen. The patient had undergone contrast-enhanced computed tomography previously without the occurrence of any adverse effects.

A few minutes after the application of the MRI contrast agent Gadovist (active substance: gadobutrol), the patient pressed the alarm button complaining first about nausea, then also dyspnea. With the suspected diagnosis of an allergic reaction, the patient was administered an ampoule of the antihistamine Tavegyl (2 mg/2 mL, active substance: clemastine), the H2-receptor-antagonist Zantic (50 mg/5 mL, active substance: ranitidine), and the glucocorticoid Fortecortin (40 mg/5 mL, active substance: dexamethasone) intravenously. The patient developed cold sweat, his pulse was hardly any more palpable, and he lost consciousness. Defibrillation pads were placed, the heart frequency was analyzed, and cardiac massage had to be started. With progressive swelling of the airways, the patient also had to be intubated. Resuscitation was performed for approximately 1 hour during which time the patient was transferred to the university hospital. The patient was then hemodynamically stable but sedated...
and ventilated. In the blood samples obtained upon admission to the hospital, the enzyme tryptase was considerably elevated (>200 μg/L, normal <11.4 μg/L).

Therapy with antihistamines and steroids was continued. The patient’s body was kept at a maximum of 36°C (96.8°F) to prevent further brain damage. Yet, cranial computed tomography 1 day later showed a reduced differentiation of the brain cortex and the medulla, missing contrast of the basal ganglia and general brain edema as a result of severe lack of oxygen (Fig. 1). With an overall poor prognosis and in consultation with the relatives, it was decided to stop all intensive care treatments. The patient died 2 days later.

**Autopsy**

Autopsy showed massive brain edema (1450 g, Fig. 2), venous congestion, and mild thorax trauma due to the resuscitation measurements (rib fractures and subcutaneous hemorrhage near the sternum). Besides massive brain edema, no other findings causative of death could be found. The cause of death was therefore determined to be paralysis of the respiratory system due to brain edema following lack of oxygen during long-lasting resuscitation measurements in consequence to the anaphylactic reaction to the MRI contrast agent Gadovist.

**Discussion**

There are several gadolinium-based contrast agents for contrast-enhanced MRI that are approved for clinical use. Consisting of a paramagnetic metal, they increase signal intensity and thereby tissue contrast in MRI. The contrast agent administered in the present case was gadobutrol (Gadovist; Bayer Schering Pharma AG, Berlin, Germany), a highly stable, non-ionic, macrocyclic gadolinium MRI contrast agent that was first introduced in Switzerland in 1998 [1]. Gadobutrol distributes rapidly into the extracellular space and is eliminated by glomerular filtration [2]. Gadobutrol has been placed in the lowest-risk category for the development of nephrogenic systemic fibrosis in patients with renal impairment [1,3]. Adverse drug reactions (ADRs) for gadobutrol were reported in 0.32%-3.8% [1,2,4,5], mostly in terms of nausea, vomiting, urticaria, and dizziness, with serious ADRs in <0.1% [1,2,4,5]. The onset of ADRs occurred within 5 minutes in 62% [2] to 82.4% [4] of the patients. Most of the rest of the ADRs occurred within 15 to 24 hours [2]. In the electronic database FDA Adverse Event Reporting System of the United States, there are 614 cases reported of ADRs to gadolinium-based contrast agents in general (1998-2012), of which 7.2% had a fatal outcome [6].

**Conclusion**

Anaphylactic reaction to an MRI contrast agent is a very rare complication [6,7] but can have a relentless course within minutes when it occurs. Even in a medical setting with highly trained professionals, the outcome can be fatal. Therefore, on the one hand, it is important for clinicians to know that even

---

**Fig. 1** – Computed tomography (axial view) of the edematous brain, 1 day after the incident.

**Fig. 2** – Photography of the edematous brain (1450 g) at autopsy. (A) Caudal view. (B) Cranial view.
at MRI examinations, fatal accidents can occur quite sud-

denly and to make sure resuscitation equipment as well as well-
trained staff is available all the time [8]. Forensic pathologists,

on the other hand, have to be aware of those rare causes of
fatal anaphylactic reactions while investigating sudden death
after medical treatments or examinations.

REFERENCES


