Immediate Adverse Reactions and Anaphylaxis associated with gadolinium-based contrast agents in a patient with meningioma: case report and literature review

ABSTRACT

Object. Gadolinium chelates are relatively safe contrast media used in MRI. Immediate severe adverse effects are exceptionally rare.The incidence of immediate hypersensitivity reactions to MR contrast media was 0.079%, and the recurrence rate of hypersensitivity reactions was 30% in patients with previous reactions(5). The risk factors for immediate hypersensitivity reactions to MR contrast media were the female sex, allergies and asthma.

Case. We report a case of anaphylactic shock due to Gadobenatedimeglumine. While undergoing a magnetic resonance imaging examination, 36 year-old female patient became severely hypotensive, lost consciousness, and had generalized erythema immediately after the intravenous injection of this product. She recovered rapidly after injection of epinephrine and her blood volume was restored with intravenous fluids.

Conclusions. Although gadolinium is a safe contrast medium, anaphylactoid reactions do occur. Some are severe. Reactions to MR imaging contrast media are uncommon enough that radiologists may not be as familiar with their management as they are with the treatment of complications associated with iodinated radiographic contrast media. Gadobenatedimeglumine is comparable to gadodiamide in terms of safety and efficacy for imaging of CNS lesions.

Keywords: gadolinium; magnetic resonance, contrast agents, contrast enhancement, adverse reaction, Anaphylaxis

INTRODUCTION

Magnetic resonance imaging (MRI) has proved to be a valuable diagnostic modality for central nervous system(CNS) disease. Although intrinsic tissue contrast is high, administration of intravenous contrast media has been shown to improve both lesion detection and differential diagnosis. The largest class of contrast media in use today inMRI, both in terms of number of doses and number of agents, is the gadolinium chelates (12).
Allergic-like reactions to IV gadolinium containing contrast agents, although relatively rare, do occur (4).
Gadolinium chelates are relatively safe contrastmedia used in MRI. Immediate severe adverse effectsare exceptionally rare and mostly concern mild anaphylactic reactions(6).
Acute adverse reactions related to gadopentetatedimeglumine and gadobenatedimeglumine were rare. When they occurred, most of the reactions were mild, although moderate and severe reactions did occur (1).
Gadobenatedimeglumineis currently approved for clinical use throughout Europe but not in the United States.
Gadobenatedimeglumine has two characteristics that distinguish it from other gadolinium chelates with extracellulardistribution and renal excretion currently available in the United States and worldwide. A small percentage of the agent is excreted via the hepatobiliary system in addition to renal excretion, as with the other gadolinium chelates (9, 8, and 14).
Safety assessments have indicated similar safety profiles for gadobenatedimeglumine and other gadolinium-based contrast agents, the reported overall incidence of adverse events being less than 0.03% in postmarketing surveillance (13).

The incidence of immediate sever hypersensitivity reactions to MR contrast media was 0.079%, and the recurrence rate of hypersensitivity reactions was 30% in patients with previous reactions. The risk factors for immediate hypersensitivity reactions to MR contrast media were the female sex, allergies and asthma. The incidence of immediate hypersensitivity reactions increased depending on the number of exposures to MR contrast media. Gadodiamide had the lowest rate (0.013%) of immediate hypersensitivity reactions, while gadobenatedimeglumine had the highest rate (0.22%). The appropriate premedication with antihistamine or systemic corticosteroid should be considered according to the severity of the previous hypersensitivity reactions(5).

Allergic-like reactions were classified as mild, moderate, or severe. Mild allergic-like reactions were characterized by one or more of the following: hives, pruritus, localized facial edema, nasal congestion, sneezing, and “scratchy throat.” Moderate allergic like reactions were characterized by one or more of the following: diffuse erythema, dyspnea, wheezing, stridor, or emergency department transfer. Severe allergic-like reactions were characterized by one or more of the following: severelaryngeal edema, cardiopulmonary collapse, anaphylactoid shock, or hospital admission.Physiologic reactions (e.g., vasovagal reactions, nausea, vomiting) and contrast medium extravasations were not analyzed because they are not allergic likereactions (3).

The decision to use one gadolinium-based contrast product over another has become more complicated and increasingly important. When prescribing gadolinium-based contrast agents, radiologists need to consider not only the risk of NSF but also the risk of acute adverse reactions (1).

We have recommended in our practice that patients with a prior history of reaction to iodinated contrast media be closely observed during gadolinium administration. Premedication with steroids and histamine blocking agents may be considered in patients who had severe reactions to iodinated contrast media, although the usefulness or necessity of such premedication has not yet. Among patients with a history of prior adverse response to gadolinium-based MR Imaging contrast media, the repeated use of such agents should also be carefully considered. Among these patients, pre-treatment with corticosteroids and the administration of a different gadolinium-based contrastagent may be useful. (9).
Allergic-like reactions to gadolinium-containing contrast media can occur despite premedication with corticosteroids and antihistamines (4).
Gadolinium chelates in appropriate volumes are useful alternative contrast media in selected high-risk patients undergoing angiographic studies (15).
To the best of our knowledge, the first reported use of a gadolinium chelate for intraarterial DSA was by Kinno et al in 1993 in a patient with a severe allergy to iodinated contrast media (7).

To our knowledge and according to literatures, there was not any correlation with underlying disease and there is no report in meningioma.
We report a case of anaphylactic shock due to Gadobenatedimeglumine. While undergoing a magnetic resonance imaging examination, 36year-old female patient became severely hypotensive, lost consciousness, and had generalized erythema immediately after the intravenous injection of this product. She recovered rapidly after injection of epinephrine and her blood volume was restored with intravenous fluids.

CASE report

A 36-year-old female patient with a personal history of headache, while undergoing MRI scans, developed bronchospasm in the first minute of Gadolinium infusion.She became severely hypotensive, lost consciousness, and had generalized erythema immediately after the intravenous injection of this product. The procedure was cancelled and acute treatment of the reaction took place. The patient reported 2 additional MRI scans with definite use of unknown contrast media in the past 2 months with the same adverse effect that was not noted before performing MRI in our center.

Within 5 minutes of MR contrast IV injection; the patient suffered severe cardiovascular collapse. MRI procedure was aborted and administration of Gadolinium discontinued. Aggressive IV fluid resuscitation and IV epinephrine administration were necessary to re-establish cardiovascular stability. Some periorbital and labial oedema were noted.

She had no prior history of allergies and asthma. She had no comorbidities and past medical history was negative.

She recovered rapidly after she was given injection of epinephrine and her blood volume was restored with intravenous fluids.
MRI revealed meningioma (Fig 1). She was admitted to our neurosurgery department. Surgical resection was performed. The postoperative period was uneventful and during the early postoperative period had resolution of symptoms.

DISCUSSION

Gadolinium chelates are being increasingly used in clinical MRI practice for a wide spectrum of disease processes and types of exams (12).
The incidence of adverse reactions is relatively low compared with that of contrast agents used for CT
Gadolinium-based contrast agents used as medical imaging agents, can cause life-threatening or fatal anaphylaxis. There were differences in disproportionality of reporting between agents. Although differences in numbers of reports of anaphylaxis reflect relative utilization rates of the various agents, disproportionality analyses disclose significant safety signals of anaphylaxis associated with most gadolinium-based contrast agents (11).

All gadolinium-based contrast agent adverse events reported to radiology quality assurance committees were graded according to American College of Radiology criteria and divided by the total number of injections to determine incidence during the past 10 years (10).

Adverse events were more likely in women, with a female to male ratio of 3.3, and in patients with history of prior allergic reactions ($p < 0.001$).Gadobenatedimeglumine had more severe patient reactions, including arrest (defined as the patient becoming unresponsive and the code team being called) and death. From 2004 to 2009, the FDA received reports on 40 gadolinium-based contrast agent U.S. deaths unrelated to nephrogenic systemic fibrosis (10).

Gadolinium-based contrast agents are very safe, with only rare reports of death, and raises the possibility that nonionic linear gadolinium-based contrast agents and gadopentetatedimeglumine may have fewer severe immediate adverse events compared with gadobenatedimeglumine (10).

Gadobenatedimeglumine is comparable to gadodiamide in terms of safety and efficacy for imaging of CNS lesions, with a possible advantage in imaging applications owing to enhanced T1 relaxivity. This effect is thought to be due to mild protein binding. The clinical availability of gadobenatedimeglumine will add another valuable tool to the armamentarium of the diagnostic radiologist. (12).

The indexes of suspicion for the occurrence of reactions to gadolinium, and both the documentation and the management of adverse reactions, must be as rigorous for reactions associated with MR imaging contrast agents as they are for reactions associated with iodinated contrast media (9).

After gadobenatedimeglumine was substituted for gadopentetatedimeglumine, a significant transient increase occurred in the frequency of reported allergic-like reactions that demonstrated a temporal pattern suggestive of the Weber effect (a transient increase in adverse event reporting that tends to peak in the 2nd year after a new agent or indication is introduced).(3)

Although gadolinium is a safe contrast medium, anaphylactoid reactions do occur. Some are severe. Reactions to MR imaging contrast mediaare uncommon enough that radiologists maynot be as familiar with their management asthey are with the treatment of complicationsassociated with iodinated radiographic contrastmedia. Personnel must be trained andequipment for the management or resuscitationof patients experiencing reactions to gadoliniumcontrast media must be available atboth hospital-based and freestanding facilities.Gadolinium has physical properties that are well suited for radiographic imaging.DSA with a gadolinium chelate as contrast medium can provide images of suitable quality for diagnosis and intervention.The overall safety profile of gadolinium-based contrast media is excellent (15).

With the introduction of the most recent MR contrast agent approved for use in the United States, our interest in its substantial potential clinical benefits that would result from its increased relaxivity was balanced by concern that the rate of adverse effects may increase. This concern has been ameliorated with the findings of rates of adverse reactions that are comparable to those published for other MR contrast agents (2).

Although gadolinium-based contrast agents are extremely safe, death from hypersensitivity reactions and debilitating fibrosis are possible. These can be minimized by the skill and vigilance of the radiologist and MRI team (10).

Conclusions. Although gadolinium is a safe contrast medium, anaphylactoid reactions do occur. Some are severe. Reactions to MR imaging contrast media are uncommon enough that radiologists may not be as familiar with their management as they are with the treatment of complications associated with iodinated radiographic contrast media. Gadobenatedimeglumine is comparable to gadodiamide in terms of safety and efficacy for imaging of CNS lesions.

References

1.Abujudeh HH, Kosaraju VK, Kaewlai R.Acute adverse reactions to gadopentetate dimeglumine and gadobenatedimeglumine: experience with 32,659 injections.AJR Am J Roentgenol.2010;194(2):430-4

2.Bleicher AG, KanalE.Assessment of adverse reaction rates to a newly approved MRI contrast agent: review of 23,553 administrations of gadobenatedimeglumine. *AJR*2008;191:1870

3.Davenport MS, Dillman JR, Cohan RH, Hussain HK, Khalatbari S, McHugh JB, Ellis JH. effect of abrupt substitution of gadobenate dimeglumine for gadopentetatedimeglumine on rate of allergic-like reactions.Radiology 2013;266(3):773-82

4.Dillman JR, Ellis JH, Cohan RH, Strouse PJ, Jan SC. Allergic-like breakthrough reactions to gadolinium contrast agents after corticosteroid and antihistamine premedication.AJR Am J Roentgenol. 2008; 190(1):187-90

5.Jung JW, Kang HR, Kim MH, Lee W, Min KU, Han MH, Cho SH. Immediate hypersensitivity reaction to gadolinium-based MR contrast media.Radiology 2012;264(2):414-22

6.Kalogeromitros DC, Makris MP, Aggelides XS, Spanoudaki N, Gregoriou SG, Avgerinou G, Rigopoulos DG. Anaphylaxis to gadobenatedimeglumine (Multihance): a case report. Int Arch Allergy Immunol.2007;144(2):150-4

7.Kinno Y, Odagiri K, Andoh K, et al.Gadopentetatedimeglumine as an alternative contrast agent for the use in angiography.AJR Am J Roentgenol1993;16:1293–1294

8.Kirchin MA, Pirovano GP, Spinazzi A. Gadobenatedimeglumine (Gd-BOPTA): Invest Radiol1998; 33:798–809

9.Murphy KJ, Brunberg JA, Cohan RH. Adverse reactions to gadolinium contrast media: a review of 36 cases.AJR Am J Roentgenol. 1996; 167(4):847-9

10. Prince MR, Zhang H, Zou Z, Staron RB, Brill PW. Incidence of immediate gadolinium contrast media reactions.AJR Am J Roentgenol2011; 196(2):W138-43

11. Raisch DW, Garg V, Arabyat R, Shen X, Edwards BJ, Miller FH, McKoy JM, Nardone B, West DP.Anaphylaxis associated with gadolinium-based contrast agents: data from the Food and Drug Administration's Adverse Event Reporting System and review of case reports in the literature.Expert Opin Drug Saf.2014; 13(1):15-23

12. Runge VM, Armstrong MR, Barr RG, Berger BL, Czervionke LF, et al.A clinical comparison of the safety and efficacy of MultiHance (gadobenatedimeglumine) and Omniscan (Gadodiamide) in magnetic resonance imaging in patients with central nervous system pathology.Invest Radiol. 2001; 36(2):65-71

13. Shellock FG, Parker JR, Pirovano G, et al. Safety characteristics of gadobenatedimeglumine: clinical experience from intra- and interindividual comparison studies with gadopentetatedimeglumine. *J MagnReson Imaging* 2006 ; 24:1378–1385

14. Swan SK, Lambrecht LJ, Townsend R, et al. Safety and pharmacokinetic profile of gadobenatedimeglumine in subjects with renal Impairment: Invest Radiol1999; 34:443– 448
15. Spinosa DJ, Kaufmann JA, Hartwell GD.Gadolinium chelates in angiography and interventional radiology: a useful alternative to iodinated contrast mediafor angiography.Radiology 2002; 223(2):319-25.

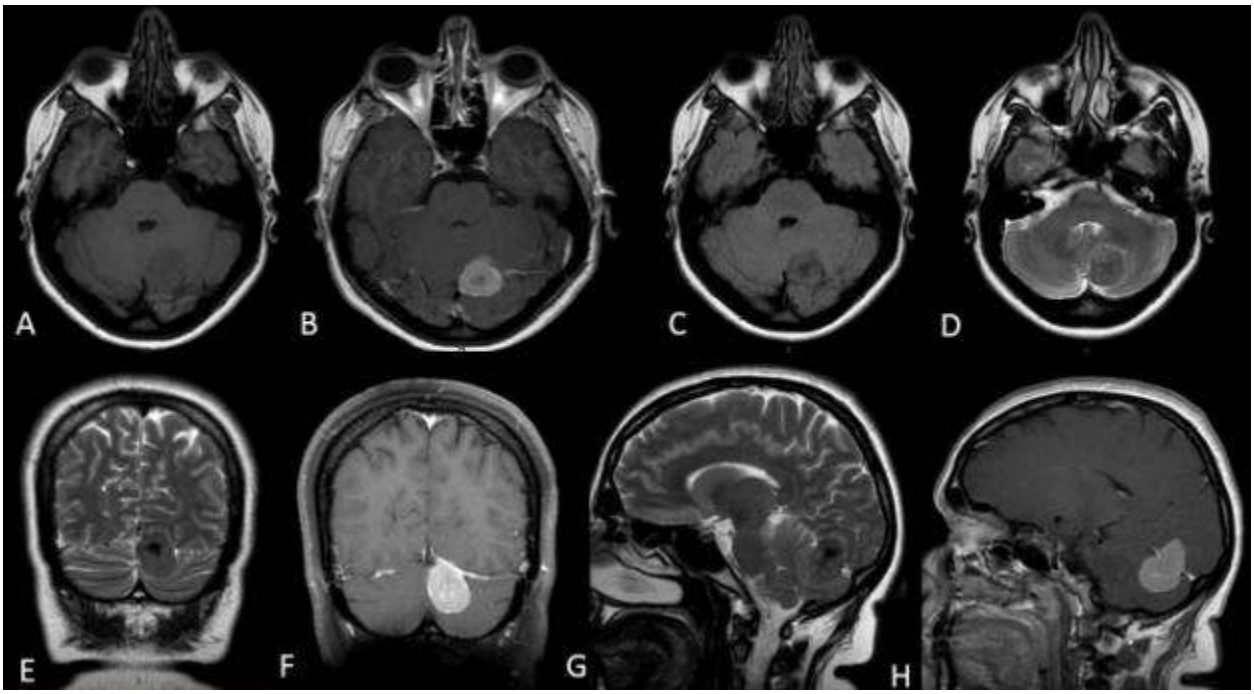

Fig 1: Preoperative MR imaging for a 36-year-old woman with tentorial meningioma. MRI demonstrated a large left medial tentorial meningioma extending along tentorium with supra and infra- tentorium components, causing significant mass effect on these structures without early signs of hydrocephalus. Axial (A) T1, (B) enhanced T1, (C)FLAIR, (D) T2; coronal (E) T2, (F) enhanced T1; sagittal (G)T2, (H) enhanced T1 MRI.