

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

3

4 **ABSTRACT**

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

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

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

17

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

19

20 **INTRODUCTION**

21 Magnetic resonance imaging (MRI) has proved to be a valuable diagnostic modality for central nervous  
22 system(CNS) disease. Although intrinsic tissue contrast is high, administration of intravenous contrast media has  
23 been shown to improve both lesion detection and differential diagnosis (12).

24 Allergic-like reactions to IV gadolinium containing contrast agents, although relatively rare, do occur (4).

25 Gadolinium chelates are relatively safe contrast media used in MRI. Immediate severe adverse effects are  
26 exceptionally rare and mostly concern mild anaphylactic reactions (6).

27 Acute adverse reactions related to gadopentetate dimeglumine and gadobenatedimeglumine were rare. When they  
28 occurred, most of the reactions were mild, although moderate and severe reactions did occur (1).

29 Safety assessments have indicated similar safety profiles for gadobenatedimeglumine and other gadolinium-based  
30 contrast agents, the reported overall incidence of adverse events being less than 0.03% in postmarketing surveillance

31 (13).

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

39 Allergic-like reactions were classified as mild, moderate, or severe. Mild allergic-like reactions were characterized  
40 by one or more of the following: hives, pruritus, localized facial edema, nasal congestion, sneezing, and "scratchy  
41 throat." Moderate allergic like reactions were characterized by one or more of the following: diffuse erythema,  
42 dyspnea, wheezing, stridor, or emergency department transfer. Severe allergic-like reactions were characterized by  
43 one or more of the following: severe laryngeal edema, cardiopulmonary collapse, anaphylactoid shock, or hospital

44 admission. Physiologic reactions (e.g., vasovagal reactions, nausea, vomiting) and contrast medium extravasations  
45 were not analyzed because they are not allergic like reactions (3).

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

49 We have recommended in our practice that patients with a prior history of reaction to iodinated contrast media be  
50 closely observed during gadolinium administration. Premedication with steroids and histamine blocking agents may  
51 be considered in patients who had severe reactions to iodinated contrast media, although the usefulness or necessity  
52 of such premedication has not yet.

53 Allergic-like reactions to gadolinium-containing contrast media can occur despite premedication with corticosteroids  
54 and antihistamines (4).

55 Gadolinium chelates in appropriate volumes are useful alternative contrast media in selected high-risk patients  
56 undergoing angiographic studies (15).

57 To our knowledge and according to literatures, there was not any correlation with underlying disease and there is no  
58 report in meningioma.

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

63

#### 64 **CASE report**

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

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

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

77 She recovered rapidly after she was given injection of epinephrine and her blood volume was restored with  
78 intravenous fluids.

79 MRI revealed meningioma (Fig 1). She was admitted to our neurosurgery department. Surgical resection was  
80 performed. The postoperative period was uneventful and during the early postoperative period had resolution of  
81 symptoms.

82

#### 83 **DISCUSSION**

84 The incidence of adverse reactions is relatively low compared with that of contrast agents used for CT  
85 Gadolinium-based contrast agents used as medical imaging agents, can cause life-threatening or fatal anaphylaxis.  
86 There were differences in disproportionality of reporting between agents (11).

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

90 Adverse events were more likely in women, with a female to male ratio of 3.3, and in patients with history of prior  
91 allergic reactions ( $p < 0.001$ ) (10).

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

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

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

102 After gadobenate dimeglumine was substituted for gadopentetate dimeglumine, a significant transient increase  
103 occurred in the frequency of reported allergic-like reactions (3)

104 Reactions to MR imaging contrast media are uncommon enough that radiologists may not be as familiar with their  
105 management as they are with the treatment of complications associated with iodinated radiographic contrast media.  
106 Personnel must be trained and equipment for the management or resuscitation of patients experiencing reactions to  
107 gadolinium contrast media must be available at both hospital-based and freestanding facilities. The overall safety  
108 profile of gadolinium-based contrast media is excellent (15). These can be minimized by the skill and vigilance of  
109 the radiologist and MRI team (10).

---

## 110 Conclusions

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

115

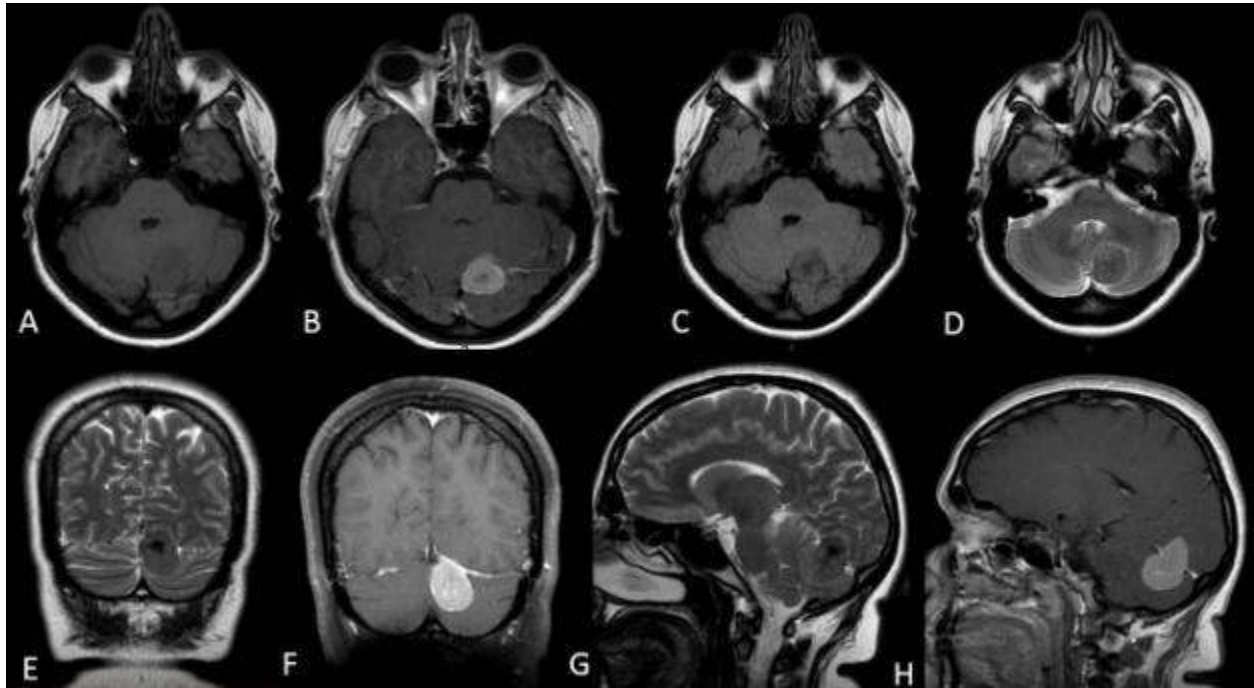
---

## 116 References

- 117 1. Abujudeh HH, Kosaraju VK, Kaewlai R. Acute adverse reactions to gadopentetate dimeglumine and  
118 gadobenate dimeglumine: experience with 32,659 injections. *AJR Am J Roentgenol*. 2010;194(2):430-4  
119 2. Bleicher AG, Kanal E. Assessment of adverse reaction rates to a newly approved MRI contrast agent: review  
120 of 23,553 administrations of gadobenate dimeglumine. *AJR* 2008;191:1870  
121 3. Davenport MS, Dillman JR, Cohan RH, Hussain HK, Khalatbari S, McHugh JB, Ellis JH.  
122 effect of abrupt substitution of gadobenate dimeglumine for gadopentetate dimeglumine on rate of  
123 allergic-like reactions. *Radiology* 2013;266(3):773-82

- 124 4.Dillman JR, Ellis JH, Cohan RH, Strouse PJ, Jan SC. Allergic-  
125 like breakthrough reactions to gadolinium contrast agents after corticosteroid and antihistamine  
126 premedication.AJR Am J Roentgenol. 2008; 190(1):187-90
- 127 5.Jung JW, Kang HR, Kim MH, Lee W, Min KU, Han MH, Cho SH. Immediate  
128 hypersensitivity reaction to gadolinium-based MR contrast media.Radiology 2012;264(2):414-22
- 129 6.Kalogeromitros DC, Makris MP, Aggelides XS, Spanoudaki N, Gregoriou SG, Avgerinou G, Rigopoulos  
130 DG. Anaphylaxis to gadobenatedimeglumine (Multihance): a case report. Int Arch Allergy  
131 Immunol.2007;144(2):150-4
- 132 7.Kinno Y, Odagiri K, Andoh K, et al.Gadopentetatedimeglumine as an alternative contrast agent for the use  
133 in angiography.AJR Am J Roentgenol1993;16:1293-1294
- 134 8.Kirchin MA, Pirovano GP, Spinazzi A. Gadobenatedimeglumine (Gd-BOPTA): Invest Radiol1998;  
135 33:798-809
- 136 9.Murphy KJ, Brunberg JA, Cohan RH. Adverse reactions to gadolinium contrast media: a review of 36  
137 cases.AJR Am J Roentgenol. 1996; 167(4):847-9
- 138 10. Prince MR, Zhang H, Zou Z, Staron RB, Brill PW. Incidence of immediate gadolinium contrast media  
139 reactions.AJR Am J Roentgenol2011; 196(2):W138-43
- 140 11. Raisch DW, Garg V, Arabyat R, Shen X, Edwards BJ, Miller FH, McKoy JM, Nardone B, West  
141 DP.Anaphylaxis associated with gadolinium-based contrast agents: data from the Food and Drug  
142 Administration's Adverse Event Reporting System and review of case reports in the literature.Expert  
143 Opin Drug Saf.2014; 13(1):15-23
- 144 12. Runge VM, Armstrong MR, Barr RG, Berger BL, Czervionke LF, et al.A clinical comparison of  
145 the safety and efficacy of MultiHance (gadobenatedimeglumine) and Omniscan (Gadodiamide) in  
146 magnetic resonance imaging in patients with central nervous system pathology.Invest Radiol. 2001;  
147 36(2):65-71
- 148 13. Shellock FG, Parker JR, Pirovano G, et al. Safety characteristics of gadobenatedimeglumine: clinical  
149 experience from intra- and interindividual comparison studies with gadopentetatedimeglumine. *J*  
150 *MagnReson Imaging* 2006 ; 24:1378-1385
- 151 14. Swan SK, Lambrecht LJ, Townsend R, et al. Safety and pharmacokinetic profile of  
152 gadobenatedimeglumine in subjects with renal Impairment: Invest Radiol1999; 34:443- 448
- 153 15. Spinosa DJ, Kaufmann JA, Hartwell  
154 GD.Gadolinium chelates in angiography and interventional radiology:  
155 a useful alternative to iodinated contrast mediafor angiography.Radiology 2002; 223(2):319-25.

156  
157  
158



159  
160  
161  
162  
163  
164  
165  
166  
  
167  
168  
169  
170

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.