CASE IN POINT

Gadolinium Intermediate Elimination and Persistent Symptoms After Magnetic Resonance Imaging Contrast Agent Exposure

Brent Wagner, MD[a,b,c]; Olivia X. Jastrzemski[a]; Sasha R. Vigil[a]; Lien Tang[a]; Shreeti Patel[a]; Amy Cunningham[a]; Joshua DeAguero, PhD[a,b,c]; Karol Dokladny, PhD[a,b,c]; G. Patricia Escobar, DVM[a,b,c]; Jing Yang, PhD[a]; Frederick Gentry[a]; Ian Henderson, PhD[a,b,c]; Rachel Coyte, PhD[d]; Martin L. Kirk, PhD[a]; James H. Degnan, PhD[a]; Bevan T. Choate, MD[b]

Background: Gadolinium is the most widely used diagnostic heavy metal contrast agent in the Military Health System and Veterans Health Administration (VHA). Used for enhancing magnetic resonance imaging (MRI), gadolinium can also have toxic effects. From 1999 to 2025 use of contrast-enhanced MRI in VHA facilities has risen to a mean (SD) 2.6 (2.8) MRIs with gadolinium each for 939,928 patients.

Case Presentation: A 65-year-old Air Force veteran and retired mechanical technician sought nephrology consultation. His medical history included posttraumatic stress disorder, cervical spondylosis, ulnar nerve injury, bilateral sensorineural hearing loss, dyslipidemia, and hypertension. Twenty-five days before consultation, the patient started a contrast-enhanced MRI for elevated prostate-specific antigens. During the MRI, he experienced claustrophobia, sweating, shortness of breath, a metallic taste, and hot sensations in the groin, chest, "kidneys," and lower back, and the MRI was halted. Some symptoms reappeared days later, resulting in a 4-day hospitalization. Serum gadolinium measured 0.1 ng/mL, and 24-hour urine gadolinium was 0.3 mcg. Back-extrapolation of gadolinium elimination rates suggested exposure to 0.5% to 8.0% of a standard contrast dose. At 107 days post-MRI, serum and urine gadolinium were undetectable, but the metallic taste persisted.

Conclusions: Our findings suggest that detectable gadolinium in serum and urine may reflect subclinical exposure, even at doses below standard prescriptions. Clinicians must consider gadolinium as a potential cause of pleiotropic symptoms even when, as in this case, symptoms persist despite undetectable levels of gadolinium.

Author affiliations can be found at the end of this article.
Correspondence: Brent Wagner (brent.wagner@va.gov)

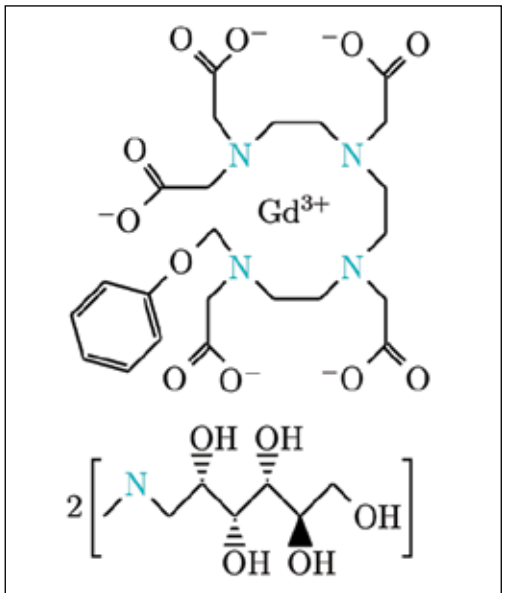
Fed Pract. 2025;42(11):e0631. Published online November 25. doi:10.12788/fp.0631

Magnetic resonance image (MRI) contrast agents can induce profound complications, including gadolinium encephalopathy, kidney injury, gadolinium-associated plaques, and progressive systemic fibrosis, which can be fatal.[1-10] About 50% of MRIs use gadolinium-based contrast (Gd^{3+}), a toxic rare earth metal ion that enhances imaging but requires binding with pharmaceutical ligands to reduce toxicity and promote renal elimination (Figure 1). Despite these measures, Gd^{3+} can persist in the body, including the brain.[11,12] Wastewater treatment fails to remove these agents, making Gd^{3+} a growing pollutant in water and the food chain.[13-15] Because Gd^{3+} is a rare earth metal ion in the milieu intérieur, there is an urgent need to study its biological and long-term effects (Appendix 1).

CASE PRESENTATION

A 65-year-old Vietnam-era veteran presented to nephrology at the Raymond G. Murphy Veterans Affairs Medical Center (RGMVAMC) in Albuquerque, New Mexico, for evaluation of gadolinium-induced symptoms. His medical history included metabolic syndrome, hypertension, hyperlipidemia, hypogonadism, cervical spondylosis, and an elevated prostate-specific antigen, previously assessed with a contrast-enhanced MRI in 2019 (Gadobenic acid, 19 mL). Surgical history included cervical fusion and ankle hardware.

The patient had a scheduled MRI 25 days earlier, following an elevated prostate specific antigen test result, prompting urologic surveillance and concern for malignancy. In preparation for the contrast-enhanced MRI, his right arm was cannulated with a line primed with gadobenic acid contrast. Though the technician stated the infusion had not started, the patient's symptoms began shortly after entry into the scanner, before any programmed pulse sequences. The patient experienced claustrophobia, diaphoresis, palpitations, xerostomia, dysgeusia, shortness of breath, and a sensation of heat in his groin, chest, "kidneys," and lower back. The MRI was terminated prematurely in response to the patient's acute symptomatology. The patient continued experiencing new symptoms intermittently during the following week, including lightheadedness, headaches, right clavicular pain, raspy voice, edema, and a sense of doom.



Gadobenate dimeglumine/gadobenic acid
(MultuHance)
Gd-BOPTA
$C_{36}H_{62}GdN_5O_{21}$
1058.1 g/mol
U.S. Approval 2004
log (K_{therm}) = 22.6
log (K_{cond}) = 18.4

FIGURE 1. Magnetic resonance imaging contrast agents are polyaminocarboxylic acid ligands engineered to tightly chelate gadolinium, a toxic rare earth metal, and facilitate its elimination.
Source: Brent Wagner, reprinted with permission.

TABLE 1. Laboratory Results

Characteristics	Reference range, adults[a]	Preconsultation	At consultation
Sodium, mmol/L	137–145	143	141
Potassium, mmol/L	3.4–4.8	4.1	3.8
Chloride, mmol/L	98–107	106	112
Carbon dioxide, mmol/L	20–31	27	22
Urea nitrogen, mg/dL[b]	9–20	20	14
Creatinine, mg/dL[b]	0.66–1.25	1.22	1.14
Glucose, mg/dL[b]	74–99	93	88
Calcium, mg/dL	8.4–10.2	9.5	9.6
Magnesium, mg/dL	2.5–4.5	2.1	–
Bilirubin, direct, mg/dL	0.0–0.4	0.1	0.4

[a]Reference range used at the Raymond G. Murphy Veterans Affairs Medical Center.
[b]Conversion: urea nitrogen units to mM × 0.357; creatinine units to μM × 88.4; glucose units to mM × 0.056.

The patient presented to the RGMVAMC emergency department (ED) 8 days after the MRI with worsening symptoms and was hospitalized for 10 days. During this time, he was referred to nephrology for outpatient evaluation. While awaiting his nephrology appointment, the patient presented to the RGMVAMC ED 20 days after the initial episode with ongoing symptoms. "I thought I was dying," he said. Laboratory results and a 12-lead electrocardiogram showed a finely static background, wide P waves (> 80 ms) with notching in lead II, sinusoidal P waves in V1, R transition in V2, RR' in V2, ST flat in lead III, and sinus bradycardia (Table 1 and Appendix 2).

The patient's medical and surgical histories were reviewed at the nephrology evaluation 25 days following the MRI. He reported that household water was sourced from a well and that he filtered his drinking water with a reverse osmosis system. He served in the US Army for 10 years as an engineer specializing in mechanical systems, power generation, and vehicles. Following Army retirement, the patient served in the US Air Force Reserves for 15 years, working as a crew chief in pneudraulics. The patient reported stopping tobacco use 1 year before and also reported regular use of a broad array of prescription medications and dietary supplements, including dexamethasone (4 mg twice daily), fluticasone nasal spray (50 mcg per nostril, twice daily), ibuprofen (400 mg twice daily, as needed), loratadine (10 mg daily), aspirin (81 mg daily), and metoprolol succinate (50 mg nightly). In addition, he reported consistent use of cholecalciferol (3000 IU daily), another supplemental vitamin D preparation, chelated magnesium glycinate (3 tablets daily for bone issues), turmeric (1 tablet daily), a multivitamin (Living Green Liquid Gel, daily), and a mega-B complex.

Physical examination revealed a well-nourished, tall man with hypertension (145/87 mmHg) and bilateral lower extremity edema. Oral examination showed poor dentition, including missing molars (#1-3, #14-16, #17-19, #30-31), with the anterior teeth replaced by bridges supported by dental implants. The review of systems was otherwise unremarkable, with nocturia noted before the consultation.

TABLE 2. Cursory Urinary Laboratory Results 4 Months After Gadolinium Exposure

Characteristic	Reference range, adults[a]	Results
Osmolality, mOsm/kg		591
Volume, mL		1575
Creatinine, mg/24 h	800–2800	1939
Creatinine, mg/dL		123.1
Sodium, mmol/L		114
Potassium, mmol/L		52
Albumin, mg/dL	0–1.9	1.6
Albumin, µg/min	0–20	18
Citric acid, mg/24 h	60–660	694

[a]Reference range used at the Raymond G. Murphy Veterans Affairs Medical Center; determined by the patient population and the laboratory methods used.

Serum and urine gadolinium testing, (Mayo Clinic Laboratories) revealed gadolinium levels of 0.3 mcg/24 h in the urine and 0.1 ng/mL in the serum. Nonzero values indicated detectable gadolinium, suggesting retention. The patient had a prior gadolinium exposure during a 2019 MRI (about 1340 days before) and suspected a repeat exposure on day 0, although the MRI technician stated that no contrast was administered.

Given his elevated vitamin D levels, the patient was advised to minimize dietary supplements, particularly vitamin D, to avoid confounding symptoms. The plan included monitoring symptoms and a follow-up evaluation with repeat laboratory tests on day 116.

At the nephrology follow-up 4 months postexposure, the patient's symptoms had primarily abated, with a marked reduction in the previously noted metallic dysgeusia. Physical examination remained consistent with prior findings. He was afebrile (97.7 °F) with a blood pressure of 111/72 mmHg, a pulse of 63 beats per minute, and an oxygen saturation of 98% on ambient air. Laboratory analysis revealed serum and urine gadolinium levels below detectable thresholds (< 0.1 ng/mL and < 0.1 mcg/24 h). A 24-hour creatinine clearance, calculated from a urine volume of 1300 mL, measured at an optimal 106 mL/min, indicating preserved renal function (Tables 2 and 3). Of note, his 24-hour oxalate was above the reference range, with a urine pH below the reference range and a high supersaturation index for calcium oxalate.

DISCUSSION

Use of enhanced MRI has increased in the Veterans Health Administration (Figure 2). A growing range of indications for enhanced procedures (eg, cardiac MRI) has contributed to this rise. The market has grown with new gadolinium-based contrast agents, such as gadopiclenol. However, reliance on untested assumptions about the safety of newer agents and need for robust clinical trials pose potential risks to patient safety.

Without prospective evidence, the American College of Radiology (ACR) classifies gadolinium-based contrast agents into 3 groups: Group 1, associated with the highest number of nephrogenic systemic fibrosis cases; Group 2, linked to few, if any, unconfounded cases; and Group 3, where data on nephrogenic systemic fibrosis risk have been limited. As of April 2024, the ACR reclassified Group 3 agents (Ablavar/Vasovist/Angiomark and Primovist/Eovist) into Group 2. Curiously, Vueway and Elucirem were approved in late 2022 and should clearly be categorized as Group 3 (Table 4).

There were 19 cases of nephrogenic systemic fibrosis or similar manifestations, 8 of which were unconfounded by other factors. These patients had been exposed to gadobutrol, often combined with other agents. Gadobutrol—like other Group 2 agents—has been associated with nephrogenic systemic fibrosis.[16,17] Despite US Food and Drug Administration (FDA) documentation of rising reports, many clinicians remain unaware that nephrogenic systemic fibrosis is increasingly linked to Group 2 agents classified by the ACR.[18] While declines in reported cases of nephrogenic systemic fibrosis may suggest reduced incidence, this trend may reflect diminished clinical vigilance and underreporting, particularly given emerging evidence implicating even Group 2 gadolinium-based contrast agents in delayed and underrecognized presentations. This information has yet to permeate the medical community, particularly among nephrologists. Considering these cases, revisiting the ACR guidelines may be prudent.

TABLE 3. Patient UroRisk Profile

Characteristic	Reference range, adults[a]	Results
Calcium, mg/d	0–250	110
Oxalate, mg/d	10–45	51
Citrate, mg/d	≥ 320	786
pH	5.5–7	5.2
Volume, L	2–4	1.07
Sodium, mEq/d	0–200	99
Potassium, mEq/d	19–135	48
Magnesium, mg/d	≥ 60	160
Calcium oxalate	0–2	2.59
Brushite	0–2	0.21
Sodium urate	0–2	1.45
Uric acid	0–2	5.80
Phosphate, mg/d	≤ 1100	537
Creatinine, mg/d	800–2000	1504
Sulfate, mmol/d	0–30	10

[a]Reference range used at the Raymond G. Murphy Veterans Affairs Medical Center; determined by the patient population and the laboratory methods used.

To address this growing concern, clinicians must adopt stricter vigilance and actively pursue updated information to mitigate patient risks tied to these contrast agents.

There exists an illusion of knowledge in disregarding the confounded exposures of MRI contrast agents. Ten distinct brands of contrast agents have been approved for clinical use. With repeated imaging, patients are often exposed to varying formulations of gadolinium-based agents. Yet investigators commonly discard these data points when assessing risk. By doing so, they assume—without evidence—that some formulations are inherently less likely to provoke adverse effects (AEs) than others. This untested presumption becomes perilous, especially given the limited understanding of the mechanisms underlying gadolinium-induced pathologies. As Aldous Huxley warned, "Facts do not cease to exist because they are ignored."[19]

Gadolinium Persistence

Contrary to expectations, gadolinium persists in the body far longer than initially presumed. Symptoms associated with gadolinium exposure (SAGE) encapsulate the chronic, often enigmatic maladies tied to MRI contrast agents.[20] The prolonged retention of this rare earth metal offers a compelling hypothesis for the etiology of SAGE. It has been hypothesized that Lewis base-rich metabolites increase susceptibility to gadolinium-based contrast agent complications.[21]

The blood and urine concentration elimination curves of gadolinium are exponential and categorized as fast, intermediate, and long-term.[1] For urinary elimination, the function of the curves is exponential. The quantity of gadolinium in the urine at a time (t) after exposure ($D_{[Gd]}(t)$) is equal to the product of the amount of gadolinium in the sample (urine or blood) at the end of the fast elimination period ($D_{[Gd]}(t_0)$) and the exponential decay with k being a rate constant.

To the authors' knowledge, we are the only research team currently investigating the rate constant for the intermediate- and long-term phase gadolinium elimination. The Retention and Toxicity of Gadolinium-based Contrast Agents study was approved by the University of New Mexico Health Sciences Center Institutional Review Board on May 27, 2020 (IRB ID 19-660). The data for the patient in this case were compared with preliminary results for patients with exposure-to-measurement intervals < 100 days.

The patient in this case presented with detectable gadolinium levels in urine and serum shortly after an attempted contrast-enhanced MRI procedure (Figure 3). The presence of detectable gadolinium levels in the patient's urine and serum suggests a likely exposure to a contrast agent about 27 days before his consultation. While the technician reported that no contrast was administered during the attempted MRI, it remains possible that a small amount was introduced during cannulation, potentially triggering the patient's symptoms. Linear modeling of semilogarithmic plots for participants exposed to contrast agents within 100 days (urine: $P = 1.8 \times 10^{-8}$, adjusted $r^2 = 0.62$; blood: $P = .005$, adjusted $r^2 = 0.21$) provided clearance rates (k values) for urine and blood. Extrapolating from these models to the presumed exposure date, the intercepts estimate that the patient received between 0.5% and 8% of a standard contrast dose.

TABLE 4. ACR Reported MRI Adverse Events by Group

Group	Generic	Adverse events[a]
I	Gadodiamide	6982
	Gadopentetate dimeglumine	7163
	Gadoversetamide	4258
II	Gadobenate dimeglumine	3932
	Gadobutrol	611
	Gadoteric acid	497
	Gadoteridol	3330
	Gadoxetate disodium	424

Abbreviations: ACR, American College of Radiology; MRI, magnetic resonance imaging.
[a]Unique cases of nephrogenic systemic fibrosis, skin fibrosis, skin tightness, skin plaque, and decreased joint range of motion listed on the US Food and Drug Administration Adverse Event Reporting System as of June 30, 2024; gadopiclenol was not yet in wide use at the time of the review and had no listed adverse events.

MRI contrast agents can cause skin disease. Systemic fibrosis is considered one of the most severe AEs. Skin pathophysiology involving myeloid cells is driven by elevated levels of monocyte chemoattractant protein-1, which recruits circulating fibroblasts via the C-C chemokine receptor 2.[22,23] This occurs alongside activation of NADPH oxidase Nox4.[4,24,25] Intracellular gadolinium-rich nanoparticles likely serve as catalysts for this reactive cascade.[2,18,22,26,27] These particles assemble around intracellular lipid droplets and ferrule them in spiculated rare earth-rich shells that compromise cellular architecture.[2,18,21,22,26,27] Frequently sequestered within endosomal compartments, they disrupt vesicular integrity and threaten cellular homeostasis. Interference with degradative systems such as the endolysosomal axis perturbs energy-recycling pathways—an insidious disturbance, particularly in cells with high metabolic demand. Skin-related symptoms are among the most frequently reported AEs, according to the FDA AE reporting system.[18]

Studies indicate repeated exposure to MRI contrast agents can lead to permanent gadolinium retention in the brain and other vital organs. Intravenous (IV) contrast agents cross the blood-brain barrier rapidly, while intrathecal administration has been linked to significant and lasting neurologic effects.[18]

Gadolinium is chemically bound to pharmaceutical ligands to enhance renal clearance and reduce toxicity. However, available data from human samples suggest potential ligand exchanges with undefined physiologic substances. This exchange may facilitate gadolinium precipitation and accumulation within cells into spiculated nanoparticles. Transmission electron microscopy reveals the formation of unilamellar bodies associated with mitochondriopathy and cellular damage, particularly in renal proximal tubules.[2,18,22,26,27] It is proposed that intracellular nanoparticle formation represents a key mechanism driving the systemic symptoms observed in patients.[1,2,18, 22,26,27]

Any hypothesis based on free soluble gadolinium—or concept derived from it—should be discarded. The high affinity of pharmaceutical ligands for gadolinium suggests that the cationic rare earth metal remains predominantly in a ligand-bound, soluble form. It is hypothesized that gadolinium undergoes ligand exchange with physiologic substances, directly leading to nanoparticle formation. Current data demonstrate gadolinium precipitation according to the Le Chatelier's principle. Since precipitated gadolinium does not readily re-equilibrate with pharmaceutical ligands, repeated administration of different contrast agent brands may contribute to nanoparticle growth.[26]

Meanwhile, a growing number of patients are turning to chelation therapy, a largely untested treatment. The premise of chelation therapy is rooted in several unproven assumptions.[18,21] First, it assumes that clinically significant amounts of gadolinium persist in compartments such as the extracellular space, where they can be effectively chelated and cleared. Second, it presumes that free gadolinium is the primary driver of chronic symptoms, an assertion that remains scientifically unsubstantiated. Finally, chelation proponents overlook the potential harm caused by depleting essential physiological metals during the process, assuming without evidence that the scant removal of gadolinium outweighs the risk of physiological mineral depletion.

These assumptions underpin an unproven remedy that demands critical scrutiny. Recent findings reveal that gadolinium deposits in the skin and kidney often take the form of intracellular

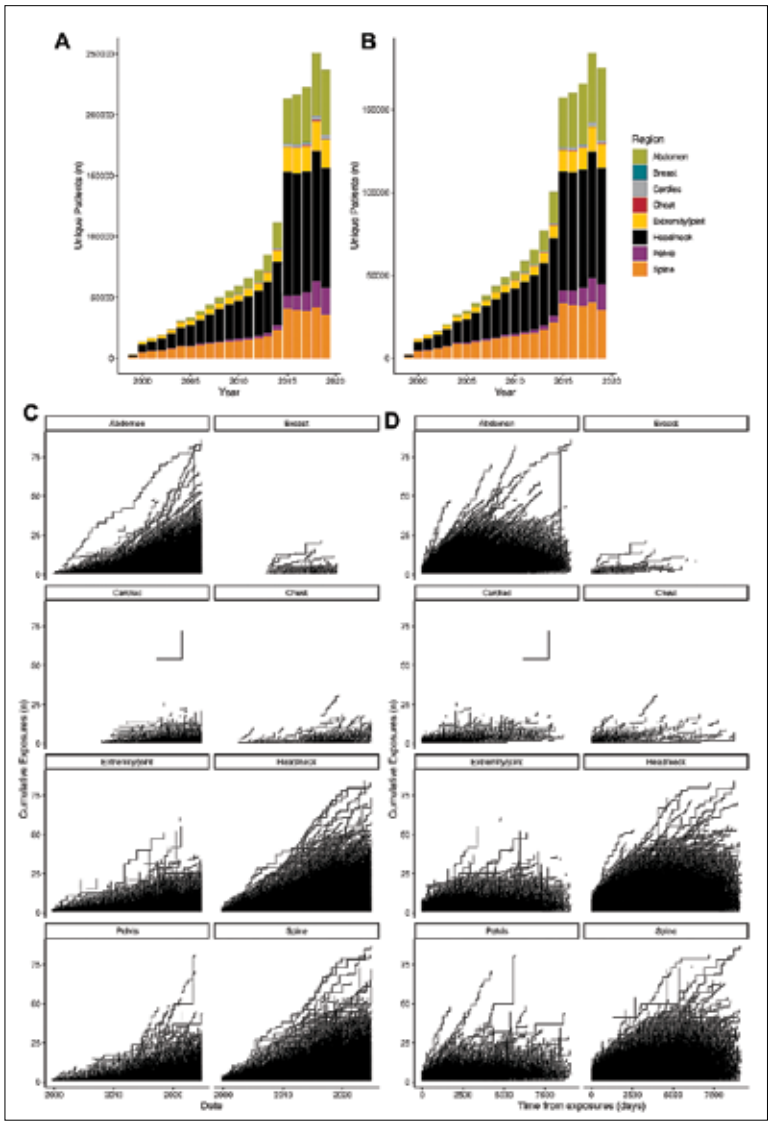


FIGURE 2. Rising use of gadolinium-enhanced MRI in VA facilities. A, a cohort of 939,928 unique VA patients, each undergoing ≥ 1 contrast-enhanced MRI procedure. The mean (SD) number of procedures per patient was 2.6 (2.8). Exposure to gadolinium after a single procedure correlates with an increased likelihood of future exposures. B, for 494,926 patients with ≥ 2 contrast-enhanced procedures, the mean (SD) number of exposures rises to 4.0 (3.3). This pattern suggests that an initial exposure is a risk factor for subsequent exposures, highlighting a form of conditional probability that merits further analysis. C, cumulative count of individuals with contrast-enhanced MRIs over time. The cohort (October 1, 1999, to October 20, 2024) included 2,403,709 unique individuals. Cumulative contrast agent exposures ranged from 0 to 87 (median, 2; mean, 3.34). D, cumulative count of individuals with contrast-enhanced MRI procedures relative to days from first exposure. Time from first to last exposure ranged from 0 days (for single exposures) to 9143 days (median, 309; mean, 1212). Repeated gadolinium exposures are common.

Abbreviations: MRI, magnetic resonance imaging; VA, US Department of Veterans Affairs.

nanoparticles, directly challenging the foundation of chelation therapy. Chelation advocates must demonstrate that these intracellular gadolinium deposits neither trigger cellular toxicity nor initiate a cytokine cascade. Chelation supporters must prove that the systemic response to these foreign particles is unrelated to the symptoms reported by patients. Until then, the validity of chelation therapy remains highly questionable.

The causality of the symptoms, mainly whether IV gadolinium was administered, was examined. The null hypothesis stated that the patient was not exposed to gadolinium. However, this hypothesis was contradicted by the detection of gadolinium in the serum and urine 27 days after the potential exposure.

Two plausible explanations exist for the nonzero gadolinium levels detected in the serum and urine. The first possibility is that minute quantities of gadolinium were introduced during cannulation, with the amount being sufficient to persist in measurable concentrations 27 days postexposure. The second possibility is that the gadolinium originated from an MRI contrast agent administered 4 years earlier. In this scenario, gadolinium stored in organ reservoirs such as bone, liver, or kidneys may have been mobilized into the extracellular fluid compartment due to the administration of high-dose steroids 20 days after the recent contrast-enhanced MRI procedure attempt. Coyte et al reported elevated gadolinium levels in the serum, cord blood, breast milk, and placenta of pregnant women with prior exposure to MRI contrast agents.[28] These findings suggest that gadolinium, stored in organs such as bone may be remobilized by variables affecting bone remodeling (eg, high-dose steroids).

Significantly, the patient exhibited elevated urinary oxalate levels. Previous research has found that oxalic acid reacts rapidly with MRI contrast agents, forming digadolinium trioxalate. While the gadolinium-rich nanoparticles identified in tissues such as the skin and kidney (including the human kidney) are amorphous, these in vitro findings establish a proof-of-concept: the intracellular environment facilitates gadolinium dissociation from pharmaceutical chelates.

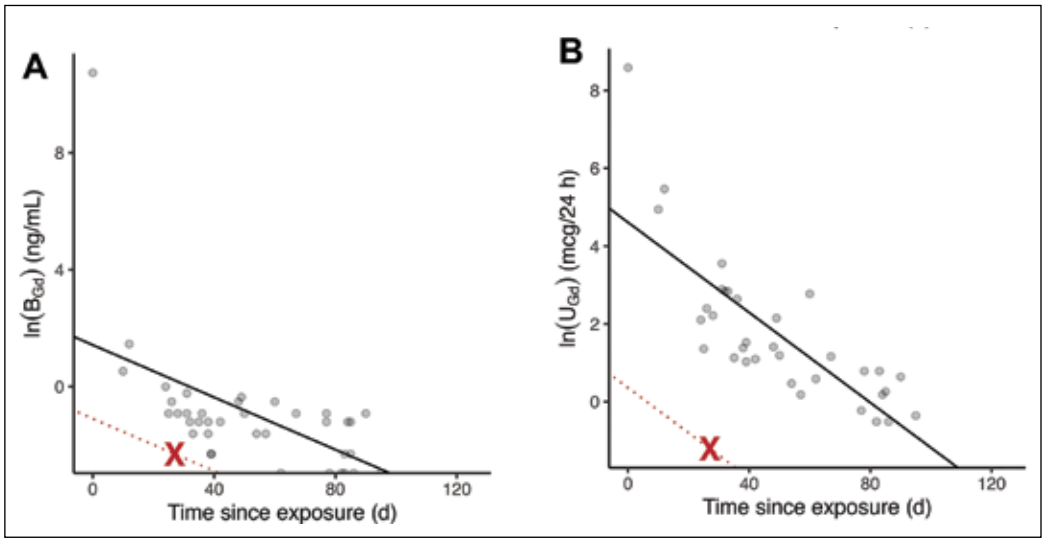


FIGURE 3. Estimate gadolinium exposure using back-extrapolation based on serum (A) and urine (B) gadolinium levels. This analysis derives from data collected under an institutional review board-approved protocol (#19-660). By measuring gadolinium concentrations in blood and urine 27 days postexposure, we calculated rate constants (*k*) for first-order elimination using Equation (1). Assuming standard, prescription label-recommended doses of gadolinium-based contrast agents, the extrapolated x-intercept suggests the patient experienced exposure to 0.5% to 8.0% of the standard magnetic resonance imaging contrast agent dose.

Furthermore, in vitro experiments show that proteins and lysosomal pH promote this dissociation, underscoring how human metabolic conditions—particularly oxalic acid concentration—may drive intracellular gadolinium deposition.

Patient Perspective

"They put something into my body that they cannot get out." This stark realization underpins the patient's profound concern about gadolinium-based contrast agents and their potential long-term effects. Reflecting on his experience, the patient expressed deep fears about the unknown future impacts: "I'm concerned about my kidneys, I'm concerned about my heart, and I'm concerned about my brain. I don't know how this stuff is going to affect me in the future."

He drew an unsettling parallel between gadolinium and heavy metals: "Heavy metal is poison. The body does not produce this kind of stuff on its own." His reaction to the procedure left a lasting impression, prompting him to question the logic of using a substance that cannot be purged: "Why would you put something into someone's body that you cannot extract? Nobody—nobody—should experience what I went through."

The patient emphasized the lack of clear research on long-term outcomes, which compounds his anxiety: "If there was research that said, 'Well, this is only going to affect these organs for this long,' OK, I might be able to accept that. But there is no research like that. Nobody can tell me what's going to happen in 5 years."

STRENGTHS AND LIMITATIONS

A significant strength of this approach is the ability to track gadolinium elimination and symptom resolution over time, supported by unique access to intermediate and long-term clearance data from our ongoing research protocol. The investigators were equipped to back-extrapolate the exposure, which provided a rare opportunity to correlate gadolinium levels with clinical outcomes. The primary limitation is the lack of a defined clinical case definition for gadolinium toxicity and limited mechanistic understanding of SAGE, which hinders diagnosis and management.

Metabolites, proteins, and lipids rich in Lewis bases could initiate this process as substrates for intracellular gadolinium sedimentation. Future studies should investigate whether metabolic conditions such as oxalate

burden or altered parathyroid hormone levels modulate gadolinium compartmentalization and tissue retention. If gadolinium-rich nanoparticle formation and accumulation disrupt cellular equilibrium, it underscores an urgent need to understand the implications of long-term gadolinium retention. The research team continues to gather evidence that the gadolinium cation remains chelated from the moment MRI contrast agents are administered through to the formation of intracellular nanoparticles. Retained gadolinium nanoparticles may act as a nidus, triggering cellular signaling cascades that lead to multisymptomatic illnesses. Intracellular and insoluble retained gadolinium challenges proponents of untested chelation therapies.

CONCLUSIONS

This case highlights emerging clinical and ethical concerns surrounding gadolinium-based contrast agent use. Clinicians may benefit from considering gadolinium retention as a contributor to persistent, unexplained symptoms—particularly in patients with recent imaging exposure. As contrast use continues to rise within federal health systems, regulatory and administrative stakeholders would do well to re-examine current safety frameworks. Informed consent should reflect what is known: gadolinium can remain in the body long after administration, potentially indefinitely. The long-term consequences of cumulative exposure remain poorly defined, but the presence of a lanthanide element in human tissue warrants greater attention from researchers and regulators alike. Interest in alternative imaging modalities and long-term safety monitoring would mark progress toward more transparent, accountable care.

Acknowledgments

The authors thank the research participants of Study 19-660, *Retention & Toxicity of Gadolinium-based Contrast Agents,* whose invaluable contributions propel scientific discovery, and the generosity of donors to the Kidney Institute of New Mexico, whose support fuels research and amplifies scholarly voice.

Author affiliations

[a]University of New Mexico, Albuquerque
[b]New Mexico Veterans Affairs Health Care System, Albuquerque
[c]Kidney Institute of New Mexico, Albuquerque
[d]New Mexico Institute of Mining and Technology, Socorro

Author disclosures

The authors report no actual or potential conflicts of interest with regard to this article.

Disclaimer

The opinions expressed herein are those of the authors and do not necessarily reflect those of *Federal Practitioner,* Frontline Medical Communications Inc., the US Government, or any of its agencies.

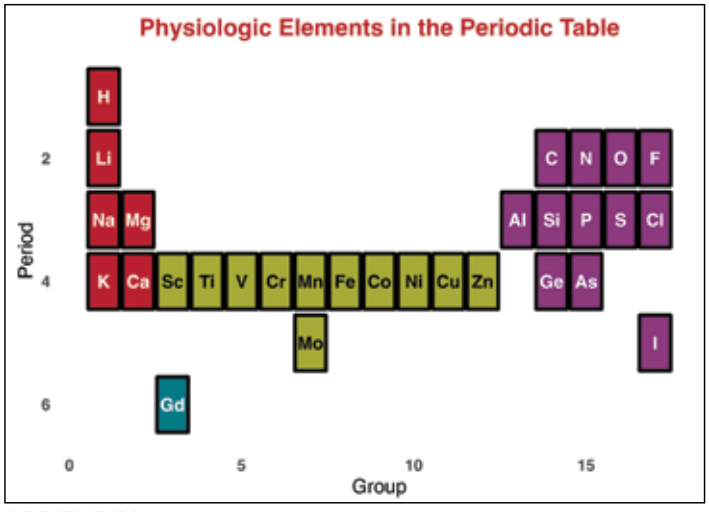
Ethics and consent

This case report complies with the ethical principles outlined in the World Medical Association Declaration of Helsinki. The patient provided verbal consent for the publication of the clinical details and any accompanying images. Specific dates were obscured and identifiers removed to protect patient identity. The University of New Mexico Health Sciences Center Institutional Review Board (IRB) approved a related project (Retention & Toxicity of Gadolinium-based Contrast Agents, IRB# 19-660). Data from this study were referenced for Figure 5. The authors obtained data under a second IRB-approved protocol (Incidence and Prevalence of Gadolinium-Based Contrast Agent Use in VA Facilities; IRB# 1576476). This protocol operated as a subsidiary of the data repository protocol, Gadolinium-Based Contrast Agent Use in VA Facilities (IRB# 1576574) at the New Mexico VA Health Care System. These data are in Figure 4.

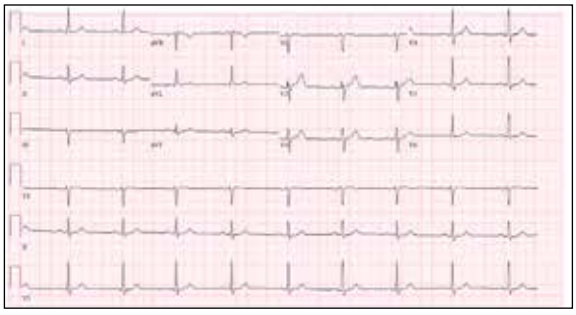
References

1. Jackson DB, MacIntyre T, Duarte-Miramontes V, et al. Gadolinium deposition disease: a case report and the prevalence of enhanced MRI procedures within the Veterans Health Administration. *Fed Pract*. 2022;39:218-225. doi:10.12788/fp.0258
2. Do C, DeAguero J, Brearley A, et al. Gadolinium-based contrast agent use, their safety, and practice evolution. *Kidney360*. 2020;1:561-568. doi:10.34067/kid.0000272019
3. Leyba K, Wagner B. Gadolinium-based contrast agents: why nephrologists need to be concerned. *Curr Opin Nephrol Hypertens*. 2019;28:154-162. doi:10.1097/MNH.0000000000000475
4. Wagner B, Drel V, Gorin Y. Pathophysiology of gadolinium-associated systemic fibrosis. *Am J Physiol Renal Physiol*. 2016;311:F1-F11. doi:10.1152/ajprenal.00166.2016
5. Maramattom BV, Manno EM, Wijdicks EF, et al. Gadolinium encephalopathy in a patient with renal failure. *Neurology*. 2005;64:1276-1278. doi:10.1212/01.WNL.0000156805.45547.6E
6. Sam AD II, Morasch MD, Collins J, et al. Safety of gadolinium contrast angiography in patients with chronic renal insufficiency. *J Vasc Surg*. 2003;38:313-318. doi:10.1016/s0741-5214(03)00315-x
7. Schenker MP, Solomon JA, Roberts DA. Gadolinium arteriography complicated by acute pancreatitis and acute renal failure. *J Vasc Interv Radiol*. 2001;12:393. doi:10.1016/s1051-0443(07)61925-3
8. Gemery J, Idelson B, Reid S, et al. Acute renal failure after arteriography with a gadolinium-based contrast agent. *AJR Am J Roentgenol*. 1998;171:1277-1278. doi:10.2214/ajr.171.5.9798860
9. Akgun H, Gonlusen G, Cartwright J Jr, et al. Are gadolinium-based contrast media nephrotoxic? A renal biopsy study. *Arch Pathol Lab Med*. 2006;130:1354-1357. doi:10.5858/2006-130-1354-AGCMNA
10. Gathings RM, Reddy R, Santa Cruz D, et al. Gadolinium-associated plaques: a new, distinctive clinical entity. *JAMA Dermatol*. 2015;151:316-319. doi:10.1001/jamadermatol.2014.2660
11. McDonald RJ, McDonald JS, Kallmes DF, et al. Gadolinium deposition in human brain tissues after contrast-enhanced MR imaging in adult patients without intracranial abnormalities. *Radiology*. 2017;285(2):546-554. doi:10.1148/radiol.2017161595
12. Kanda T, Ishii K, Kawaguchi H, et al. High signal intensity in the dentate nucleus and globus pallidus on unenhanced T1-weighted MR images: relationship with increasing cumulative dose of a gadolinium-based

contrast material. *Radiology*. 2014;270(3):834-841. doi:10.1148/radiol.13131669
13. Schmidt K, Bau M, Merschel G, et al. Anthropogenic gadolinium in tap water and in tap water-based beverages from fast-food franchises in six major cities in Germany. *Sci Total Environ*. 2019;687:1401-1408. doi:10.1016/j.scitotenv.2019.07.075
14. Kulaksız S, Bau M. Anthropogenic gadolinium as a microcontaminant in tap water used as drinking water in urban areas and megacities. *Appl Geochem*. 2011;26:1877-1885.
15. Brunjes R, Hofmann T. Anthropogenic gadolinium in freshwater and drinking water systems. *Water Res*. 2020;182:115966. doi:10.1016/j.watres.2020.115966
16. Endrikat J, Gutberlet M, Hoffmann KT, et al. Clinical safety of gadobutrol: review of over 25 years of use exceeding 100 million administrations. *Invest Radiol*. 2024;59(9):605-613. doi:10.1097/RLI.0000000000001072
17. Elmholdt TR, Jørgensen B, Ramsing M, et al. Two cases of nephrogenic systemic fibrosis after exposure to the macrocyclic compound gadobutrol. *NDT Plus*. 2010;3(3):285-287. doi:10.1093/ndtplus/sfq028
18. Cunningham A, Kirk M, Hong E, et al. The safety of magnetic resonance imaging contrast agents. *Front Toxicol*. 2024;6:1376587. doi:10.3389/ftox.2024.1376587
19. Huxley A. *Complete Essays. Volume II, 1926-1929*. Chicago; 2000:227.
20. McDonald RJ, Weinreb JC, Davenport MS. Symptoms associated with gadolinium exposure (SAGE): a suggested term. *Radiology*. 2022;302(2):270-273. doi:10.1148/radiol.2021211349
21. Henderson IM, Benevidez AD, Mowry CD, et al. Precipitation of gadolinium from magnetic resonance imaging contrast agents may be the Brass tacks of toxicity. *Magn Reson Imaging*. 2025;119:110383. doi:10.1016/j.mri.2025.110383
22. Do C, Drel V, Tan C, et al. Nephrogenic systemic fibrosis is mediated by myeloid C-C chemokine receptor 2. *J Invest Dermatol*. 2019;139(10):2134-2143. doi:10.1016/j.jid.2019.03.1145
23. Drel VR, Tan C, Barnes JL, et al. Centrality of bone marrow in the severity of gadolinium-based contrast-induced systemic fibrosis. *FASEB J*. 2016;30(9):3026-3038. doi:10.1096/fj.201500188R
24. Bruno F, DeAguero J, Do C, et al. Overlapping roles of NADPH oxidase 4 for diabetic and gadolinium-based contrast agent-induced systemic fibrosis. *Am J Physiol Renal Physiol*. 2021;320(4):F617-F627. doi:10.1152/ajprenal.00456.2020
25. Wagner B, Tan C, Barnes JL, et al. Nephrogenic systemic fibrosis: evidence for oxidative stress and bone marrow-derived fibrocytes in skin, liver, and heart lesions using a 5/6 nephrectomy rodent model. *Am J Pathol*. 2012;181(6):1941-1952. doi:10.1016/j.ajpath.2012.08.026
26. DeAguero J, Howard T, Kusewitt D, et al. The onset of rare earth metallosis begins with renal gadolinium-rich nanoparticles from magnetic resonance imaging contrast agent exposure. *Sci Rep*. 2023;13(1):2025. doi:10.1038/s41598-023-28666-1
27. Do C, Ford B, Lee DY, et al. Gadolinium-based contrast agents: Stimulators of myeloid-induced renal fibrosis and major metabolic disruptors. *Toxicol Appl Pharmacol*. 2019;375:32-45. doi:10.1016/j.taap.2019.05.009
28. Coyte RM, Darrah T, Olesik J, et al. Gadolinium during human pregnancy following administration of gadolinium chelate before pregnancy. *Birth Defects Res*. 2023;115(14):1264-1273. doi:10.1002/bdr2.2209



APPENDIX 1. The periodic table of physiologic elements excludes rare earth metals, such as gadolinium. The f-block elements, including gadolinium, are named for their partially filled f-electron orbitals. The electronic configuration of cationic gadolinium (Gd^{3+}) is $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 4s^2\ 3d^{10}\ 4p6\ 5s^2\ 4d^{10}\ 5p6\ 4f^7$, while the configuration of anionic iodine (I^+), the physiologic element with the highest atomic number, is $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 3d^{10}\ 4s^2\ 4p^6\ 4d^{10}\ 5s^2\ 5p^5$. The unpaired electrons in the f-orbitals of gadolinium confer its distinct chemical, electromagnetic, and optical properties. These properties arise from the electron orbital configuration, which governs the behavior of all elements. Mammals do not naturally incorporate rare earth metals, including gadolinium, into the usual physiologic milieu.



APPENDIX 2. Electrocardiogram showing a finely static background consistent with the electric hospital stretcher artifact. Key findings include sinus bradycardia, wide P waves (> 80 ms) with notching in lead II, sinusoidal P waves in lead V1, an R transition in lead V2, an RR' pattern in lead V2, and flat ST segments in lead III.