

Delayed Hypersensitivity to Iodinated Contrast: A Rare Case of Iododerma and Successful Strategy for Readministration

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Abstract

Iododerma is a rare, delayed hypersensitivity reaction to iodine with a heterogeneous spectrum of cutaneous manifestations. Abnormal renal function is a risk factor for this condition due to delayed renal clearance of iodine. Here, we discuss a young patient who developed an acneiform eruption hours after receiving intravenous iodinated contrast media during a diagnostic cerebral angiogram. The rash improved with doxycycline and topical corticosteroids. Seven days later, she required urgent cerebral endovascular intervention, necessitating iodine contrast re-exposure. She successfully tolerated an iodine contrast re-challenge with the use of premedication and intravenous hydration.

Categories: Radiology, Allergy/Immunology, Dermatology

Keywords: contrast hypersensitivity, contrast reaction, cutaneous contrast reaction, iodine contrast media, iodine contrast reaction, iododerma

Introduction

Computed tomography (CT) is an essential imaging modality. Over 90 million CT scans are performed annually in the United States [1], approximately 38% of which utilize iodinated contrast media (ICM) [2]. Adverse reactions to ICM are now relatively uncommon with the widespread use of nonionic, low-osmolality contrast agents as compared to older ionic, high-osmolality formulations [3]. They can be categorized into allergic-like reactions (urticaria, rash, wheezing) versus physiologic reactions (nausea, vomiting, headache). A large retrospective analysis in 2023 found that the frequency of allergic-like reactions to ICM was 0.32%, while that of physiologic reactions was 0.19% [4]. Despite the low overall incidence, the high volume of CT imaging performed annually results in a substantial absolute number of adverse reactions.

Iododerma is a rare cutaneous hypersensitivity reaction to iodine, most commonly from exposure to intravenous ICM, topical iodine preparations, or iodine-containing medications [5]. Renal insufficiency is a risk factor for the development of this condition due to the impaired clearance of iodine from the body [6]. However, it may also present in those with normal renal function. Although the exact pathophysiology is unknown, it is thought to be a delayed hypersensitivity reaction in which iodine acts as a hapten after binding to serum proteins [7]. Cutaneous manifestations may include pustular/acneiform, bullous, vegetative, or hemorrhagic eruptions [5,7,8]. Diagnosis relies on clinical presentation and exposure history, as histopathology can vary with the timing of biopsy [8]. No laboratory test is diagnostic of iododerma, but elevated urine iodine levels may support the diagnosis [8].

Here, we report a rare case of iododerma presenting as an acneiform eruption following exposure to intravenous ICM during a cerebral angiogram in a young patient without renal dysfunction. We also report the successful use of intravenous hydration and premedication before subsequent contrast exposure, resulting in a well-tolerated premedication drug re-challenge.

This article was previously presented as a poster at the 2018 American Academy of Allergy, Asthma and Immunology meeting on March 3, 2018.

Case Presentation

A 23-year-old female with a past medical history of chronic migraines and a right internal carotid artery (ICA) aneurysm status post coiling 12 years prior presented to the hospital for severe headaches different in character from her typical migraines. Magnetic resonance angiography (MRA) revealed an enlarging right ICA aneurysm. An endovascular angiogram was performed using 200 mL of iohexol (300 mg/mL), which revealed a thrombosed segment of the right ICA aneurysm, additional aneurysms arising from the enlarged segment, and a left dural arteriovenous (AV) fistula (Figure 1).

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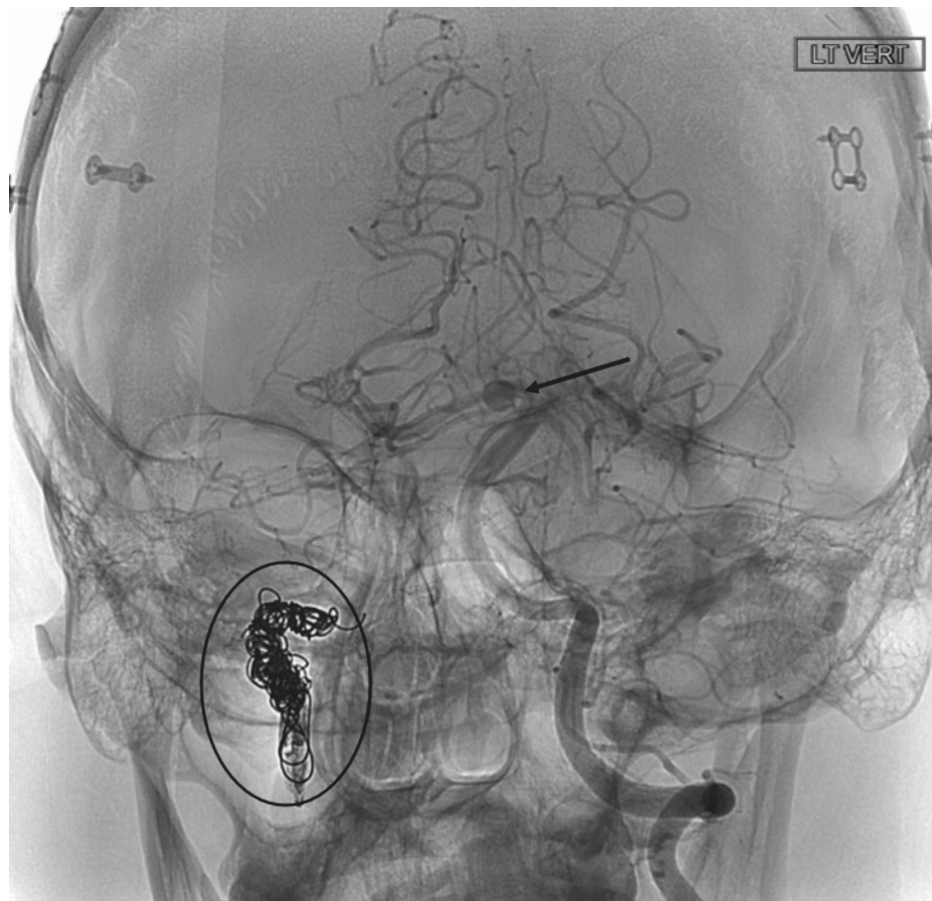


FIGURE 1: Anterior-posterior view diagnostic angiogram with selection of the left vertebral artery

Contrast opacifies the posterior and anterior circulation, revealing a 4-mm right posterior communicating artery aneurysm (arrow). Pre-existing coils are seen in the right internal carotid artery from prior treatment for a right internal carotid artery aneurysm (oval).

Five hours after the angiogram, she developed pruritic, erythematous papules on her back and was treated with intravenous diphenhydramine. The rash progressed into diffuse erythema involving the face, trunk, arms, and thighs, with hundreds of pinpoint erythematous pustules distributed across the face and chest (Figure 2). Additional erythematous papules were noted on the extremities. There was also non-pitting edema of the bilateral hands, forearms, feet, and shins.

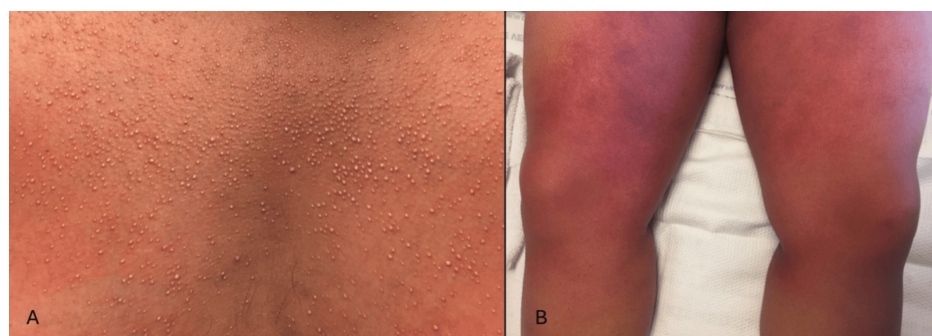


FIGURE 2: Hundreds of pinpoint pustules on the chest (A) and deep red mottling of the thighs (B)

The patient reported two prior adverse reactions to iodinated contrast. The first occurred following aneurysm coiling 12 years earlier, and the second after a contrast-enhanced CT scan several years prior. On

both occasions, she developed pruritic erythematous papules on her arms and chest within hours of contrast exposure, which persisted for approximately two weeks. These prior episodes were not associated with pustule formation. Her only medication was daily fexofenadine for seasonal allergies. She also had a documented allergy to topiramate, which previously resulted in a rash involving her arms.

Laboratory studies were notable only for mild leukocytosis, with an otherwise unremarkable basic metabolic panel (including normal renal function) and autoimmune workup. Urine and blood cultures showed no growth (Table [1](#)).

Test	Result	Reference Range
White blood cell count	10.5	4.16–9.95 x10 ³ /μL
Hemoglobin	14.8	11.6–15.2 g/dL
Hematocrit	44.4	34.9–45.2%
Platelets	183.0	143–398 x10 ³ /μL
Absolute neutrophil count	9.5	1.8–6.9 x10 ³ /μL
Absolute lymphocyte count	0.5	1.3–3.4 x10 ³ /μL
Absolute monocyte count	0.3	0.2–0.8 x10 ³ /μL
Absolute eosinophil count	0.2	0–0.5 x10 ³ /μL
Sodium	136.0	135–145 mmol/L
Potassium	4.2	3.6–5.3 mmol/L
Chloride	98	96–100 mmol/L
Total CO ₂	21	20–30 mmol/L
Creatinine	0.77	0.60–1.30 mg/dL
Urea nitrogen	11	7–22 mg/dL
Calcium	9.2	8.6–10.3 mg/dL
C-reactive protein	16.5	<0.8 mg/dL
Erythrocyte sedimentation rate	80.0	≤25 mm/hr
Antinuclear antibody	1:40	<1:40 titer
C-ANCA	<1:20	<1:20 titer
P-ANCA	<1:20	<1:20 titer
Proteinase-3 antibody	≤20	≤20 U
Myeloperoxidase antibody	≤20	≤20 U
C3	117.0	76–165 mg/dL
C4	18.0	14–46 mg/dL
dsDNA antibody	≤200	≤200 IU/mL
Antinuclear antibody	1:40	<1:40 titer
Rheumatoid factor	<10	<25 IU/mL
Urine culture	No Growth	No Growth
Blood culture	No Growth	No Growth

TABLE 1: Laboratory values

CO₂: carbon dioxide; C-ANCA: Cytoplasmic anti-neutrophil cytoplasmic antibody; P-ANCA: Perinuclear anti-neutrophil cytoplasmic antibody; C3: Complement component 3; C4: Complement component 4; dsDNA: double-stranded deoxyribonucleic acid

Two punch biopsies were obtained from her chest and forearm. Histopathologic examination demonstrated subcorneal pustules, interface dermatitis, and a superficial perivascular mixed inflammatory infiltrate composed of neutrophils and scattered eosinophils. Both specimens showed prominent folliculocentric involvement without evidence of vasculitis. Fungal staining was negative.

Based on her clinical presentation and histopathology, she was diagnosed with an acneiform eruption

secondary to iododerma. She was started on triamcinolone wet wraps and oral doxycycline 100 mg twice a day, with subsequent improvement in her rash within 48 hours. After one week of treatment, her rash had almost completely resolved.

Given her history, avoidance of ICM was strongly recommended. However, the patient later required a repeat cerebral angiogram for urgent intervention. Alternative contrast agents with lower iodine content were considered, but due to procedural requirements, the interventional team was unable to use an alternative contrast medium. A premedication protocol was therefore implemented along with intravenous hydration using normal saline.

She received one dose each of montelukast 10 mg, cetirizine 10 mg, diphenhydramine 25 mg, and famotidine 20 mg 16 hours and five hours prior to her repeat cerebral angiogram. Additionally, she was given prednisone 50 mg 13 hours, seven hours, and one hour prior to the procedure, along with oral diphenhydramine 50 mg one hour before the procedure [9].

Seven days after the initial diagnostic angiogram, she underwent repeat cerebral angiography with administration of 125 mL of iohexol (300 mg/mL) for aneurysm stenting and embolization of the AV fistula (Figure 3). Post-procedure, she received additional intravenous hydration to facilitate contrast clearance. The procedure was well tolerated without complications or recurrence of adverse reactions to ICM, including rash. She was discharged and did not require follow-up or further laboratory testing for her rash, as it had resolved.

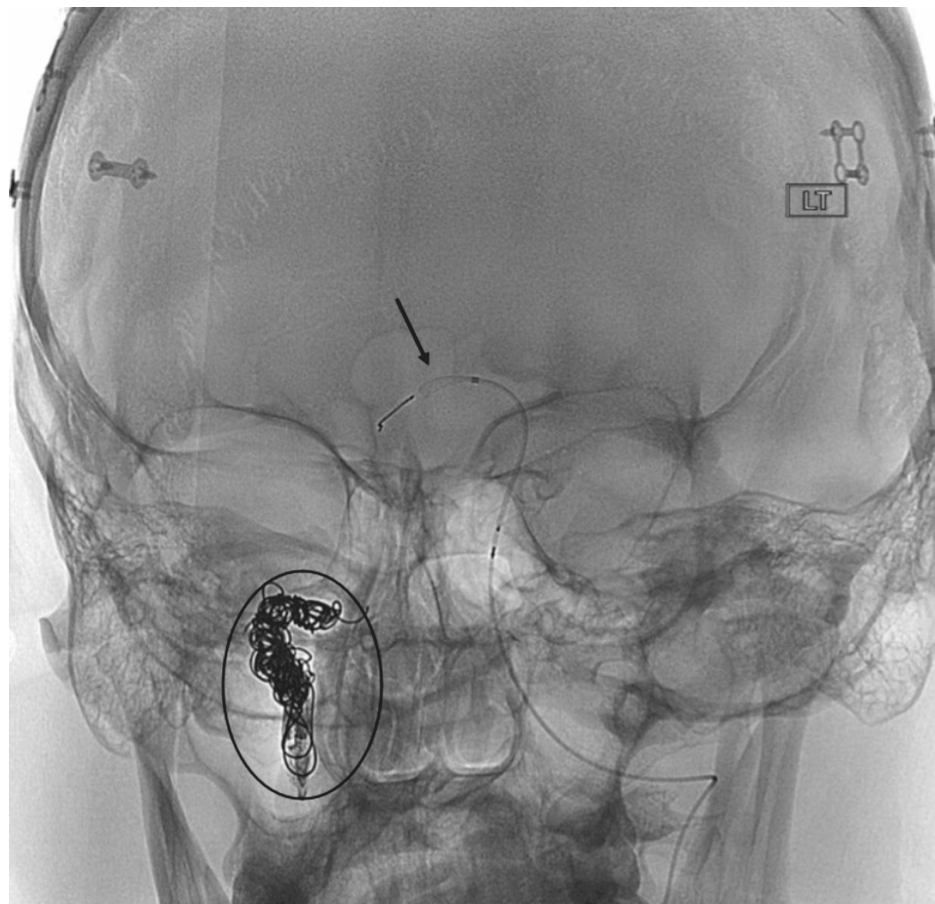


FIGURE 3: Anterior-posterior view interventional angiogram with selection of the left vertebral artery

Intra-deployment of a pipeline stent to exclude the right posterior communicating artery aneurysm (arrow). Pre-existing coils are seen in the right internal carotid artery from prior treatment for a right internal carotid artery aneurysm (oval).

Discussion

The differential diagnosis included multiple dermatoses. Sweet syndrome was considered given the abrupt onset of rash and fever but was deemed unlikely because the eruption lacked typical morphology and was

not supported by histology. Vasculitis was excluded based on negative autoimmune serologies and the absence of vasculitic changes on the skin biopsies. Pustular psoriasis was less likely, as the patient lacked a personal and family history of psoriasis. Atypical drug reaction with eosinophilia and systemic symptoms (DRESS) was considered because of the extensive rash and fever but was felt to be less likely given the absence of systemic organ involvement. Stevens-Johnson syndrome was unlikely due to the lack of mucosal involvement and was not supported by histology. Infectious pustular eruptions were excluded by negative fungal stains on biopsy. Acute generalized exanthematous pustulosis (AGEP) was strongly considered given the fever, neutrophilia, and widespread pustules on a background of erythema; however, AGEP is primarily triggered by medications rather than contrast. Iododerma was ultimately favored based on the temporal association with iodinated contrast exposure, the patient's history of two similar reactions to contrast administration, and the prominent folliculocentric pattern observed on skin biopsy.

The mainstay of treatment for iododerma involves discontinuation of iodine and prevention of re-exposure, and symptoms typically resolve. Cases of fatal iododerma have been reported, and pre-existing renal failure can impede iodine clearance, increasing morbidity [8,10-12]. Here, we present a case of iododerma in a patient with preserved renal function who demonstrated clinical improvement after treatment with topical corticosteroids and oral doxycycline.

This case presented a significant clinical challenge, as urgent repeat neurovascular intervention necessitated re-exposure to ICM. Clinicians should consider alternative contrast agents; however, this may not always be feasible due to imaging or procedural requirements. When repeat exposure is necessary, efforts should be made to minimize total iodine burden. It is important to recognize that ICM agents vary not only in osmolality but also in iodine concentration. The patient received iohexol, which is a non-ionic, low-osmolality contrast agent. We reviewed the institution's available ICM agents and considered using iodixanol (320 mg/mL iodine) rather than iohexol (350 mg/mL iodine) for its lower iodine content. However, technical requirements of the procedure necessitated iohexol, so the total volume of iohexol was reduced during the second angiogram.

Additional strategies, such as aggressive intravenous hydration with close monitoring of urine output before and after contrast re-exposure, may help facilitate iodine excretion and reduce the risk of exacerbating iododerma. While evidence specific to iododerma is limited, hydration protocols are commonly used to prevent contrast-induced nephropathy [13].

The role of a premedicated drug re-challenge in this context remains uncertain. Updated 2025 consensus guidance from the American College of Radiology and the American Academy of Allergy, Asthma, & Immunology on contrast media hypersensitivity notes insufficient evidence to support the use of premedication for delayed hypersensitivity reactions to contrast [14]. However, there are no reported cases of iododerma triggered by iodinated contrast requiring re-exposure to guide decision-making.

In this case, a premedication regimen consisting of corticosteroids, antihistamines, and leukotriene receptor antagonists was administered prior to repeat contrast exposure, and the patient tolerated the procedure without recurrence of symptoms. There are currently no established protocols for readministration of iodinated contrast in the setting of iododerma; further research may be warranted to validate these results, highlighting the novelty of this case. While causality cannot be definitively established, this outcome suggests that premedication, along with reduced contrast volume and adequate hydration, may be a reasonable strategy when re-exposure to ICM is unavoidable in those patients with prior delayed hypersensitivity reactions. Given the potential severity of iododerma, including rare fatal outcomes, a cautious and individualized approach is warranted.

Conclusions

In conclusion, this case highlights a rare presentation of iododerma following exposure to intravenous iodinated contrast, with successful tolerance to the same contrast agent during a subsequent urgent procedure using intravenous hydration and premedication. Treatment should focus on promoting iodine excretion, with particular attention to renal function, and on avoiding further exposure when possible. In cases requiring urgent re-exposure, the use of contrast agents with lower iodine content or reduction in volume of contrast administered, along with the use of hydration and premedication, may be considered for drug re-challenge.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Tiffany Truong, Monica Tsai, Lorraine Anderson

Acquisition, analysis, or interpretation of data: Tiffany Truong, Terrie S. Ahn

Drafting of the manuscript: Tiffany Truong

Critical review of the manuscript for important intellectual content: Tiffany Truong, Monica Tsai, Lorraine Anderson, Terrie S. Ahn

Supervision: Monica Tsai, Lorraine Anderson, Terrie S. Ahn

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** Lorraine Anderson declare(s) personal fees from AstraZeneca. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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