Endovascular neurointervention is typically performed with iodinated contrast medium (ICM) under fluoroscopy. However, some patients may be contraindicated to such procedures based on their sensitivity to ICM. In this report, we describe a case of successful coil embolization of a direct carotid cavernous fistula using angiography with gadolinium-based contrast agents in a patient with severe allergic reaction to ICM. The clinical decision-making for this patient was further complicated by comorbidities of renal impairment, drug allergies, and previously severe gastrointestinal bleeding.

**Key Words:** Gadolinium; Carotid cavernous fistula; Aneurysm

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**CASE REPORT**

An elderly patient presented with acute reduced right visual acuity, right 3rd nerve palsy, headache, and vomiting. She had a history of a 5 mm right cavernous internal carotid artery (ICA) aneurysm discovered during investigation for headache 6 years prior, managed with serial imaging (Fig. 1A).

Her medical history was also remarkable for previous severe gastrointestinal bleeding and multiple drug allergies, including to proton pump inhibitors and iodinated contrast mediums (ICMs). Her previous allergic reactions to ICM included urticaria responsive to steroids and an episode of cardiac arrest after administration of 75 mL iopamidol (Niopam-370; Bracco Ltd.) for computed tomography (CT) angiography. The patient also had mild renal impairment (stage 2 chronic kidney disease) with an estimated glomerular filtration rate (EGFR) of 78 mL/min/1.73 m².

Magnetic resonance (MR) time-resolved angiography of the brain showed a carotid cavernous fistula (CCF) secondary to rupture of the known medial pointing cavernous ICA sidewall (likely superior hypophyseal artery) aneurysm decompressing into the cavernous sinus, petrosal sinuses, and pterygoid venous plexus. There was no reflux to the superior ophthalmic veins nor cortical venous reflux. There was no intracranial hemorrhage (Fig. 1B).

Multidisciplinary discussion involving neurointerventional radiology, neurosurgery, immunology, and pharmacy was conducted, with consensus to offer endovascular intervention in the first in-
Fig. 1. Magnetic resonance angiography (MRA) axial images showing previously unruptured right cavernous internal carotid artery aneurysm 6 years prior in time-of-flight sequence (A), evidence of rupture into the cavernous sinus in the present admission in time-resolved imaging of contrast kinetics sequence (B), and complete occlusion on control MRA in 6 months post embolization (C). Image quality of gadolinium enhanced digital subtraction angiography images in lateral projection on pre-procedural (D) and post-coiling injections (E). Image quality of gadolinium enhanced three-dimensional rotational (F) and axial reformatted (G) images in cone-beam computed tomography acquisition used for working projection curation and procedure planning.
stance using gadolinium-based contrast agent (GBCA) as the intraprocedural contrast agent. This use received exceptional approval by the institutional medicines and therapeutics committee.

**Procedure**

The procedure was performed under general anesthesia. No premedication with steroid or other anti-allergic medications was given as the patient previously tolerated GBCA administration. A 6 Fr guide-catheter was introduced transfemorally and parked in the right distal ICA. A conventional biplane and three-dimensional (3D) rotational angiogram was obtained for procedure planning using a neuroangiography protocol of an Artis Q biplane angiography machine (Siemens Healthineers). A microcatheter (SL-10; Stryker) was navigated into the aneurysm. A dual-lumen balloon (Eclipse 2L, 6×20 mm; Balt Extrusion) was then deployed across the neck of the aneurysm (jailing technique). Seven detachable coils were deployed resulting in complete occlusion of the fistula (Fig. 1D–G).

The patient tolerated the procedure well with no evidence of anaphylactoid reaction, nephrogenic systemic fibrosis, or contrast induced nephropathy. No significant change in her renal function was observed. Her serum creatinine on the day before and after the procedure were 68 umol/L and 66 umol/L, respectively (normal range: 49–90 umol/L). Her EGFR before and after the procedure were 78 mL/min/1.73 m² and 81 mL/min/1.73 m², respectively (normal range: >90 mL/min/1.73 m²). Her neurological deficits improved following the embolization procedure. MR angiography 6 months post embolization demonstrated enduring occlusion of the fistula (Fig. 1C).

**DISCUSSION**

### Management of Patients with Allergic Reaction to Iodinated Contrast Medium

Allergic reactions to ICM are common and affect up to 3% of the population depending on definition. Intravenous corticosteroids (typically methylprednisolone 40 mg or hydrocortisone 200 mg IV) given 4–5 hours prior to injection have been proven to reduce the incidence and severity of these allergic reactions.¹

In patients with an undifferentiated type of contrast reaction, changing from a high-osmolar, ionic ICM to a low-osmolar, non-ionic ICM or changing from one to another low-osmolar ICM, have been recommended to reduce the likelihood of a subsequent contrast reaction.²

There is a paucity of high-level evidence on patients with severe allergic reactions given its the low incidence (0.06%). It may be sensible to consider alternative contrast agents with a different chemical structure such as carbon dioxide and GBCAs. In neurointervention, carbon dioxide is contraindicated due to risk of cerebral ischemia. Therefore, GBCAs are the only alternative for these patients at present, as they have no cross reactivity with ICM.

### Gadolinium-Based Contrast Agent in Catheter-Directed Angiography

GBCAs are widely adopted as a contrast agent in MR imaging for their paramagnetic properties. Gadolinium is also a heavy metal element that attenuates photons. Gadolinium has a higher K-edge (50.2 keV) than iodine (33 keV), which favors imaging at higher kilovoltages (77–96 kVp) than ICM-enhanced imaging (63–73 kVp).

Currently, there are no GBCAs designed or recommended for catheter-directed arteriography. However, it has been adopted on an exceptional basis for interventions in various body organs, such as coronary,³ visceral, extremity, and biliary.⁴ Interventions that require high-volume contrast use (e.g., aortic interventions) may not be suitable. GBCAs are also increasingly used in dual energy and spectral CT.⁵

In neurointervention, there are a small number of reports on using GBCA in diagnostic angiograms,⁶ carotid stenting⁷ and stroke thrombectomy.⁸ To our knowledge, this is the first report in the literature on using GBCA to embolize an arteriovenous fistula, which are typically high-flow and relatively complex lesions requiring larger volumes of contrast administration.

### Contrast Safety

GBCAs have a plasma half-life of about 2 hours and are nearly 100% cleared from the blood stream within 24 hours. The shift from linear group 1 to macrocyclic group 2 agents also
have greatly reduced the risk of nephrogenic systemic fibrosis, even in patients with advanced renal failure. ProHance is a group 2 agent with an excellent safety profile, and therefore was chosen for our intervention. Each mL of ProHance contains 279.3 mg gadoteridol, 0.23 mg calteridol calcium, 1.21 mg tromethamine, and water for injection. In adults with normal renal function undergoing contrast enhanced MR imaging, a typical dose of 0.1 mmol/kg (0.2 mL/kg) is recommended. In suboptimal studies, a supplementary dose of 0.2 mmol/kg (0.4 mL/kg) 30 minutes after initial injection is recommended. Therefore, the dose limit is 0.3 mmol/kg (0.6 mL/kg).

The clinical consequences of overdose have not been reported. Naturally, the clinical concerns would be increased risk for nephrogenic systemic fibrosis or central nervous system deposition, of which long term effects remain unknown.

In an “average” patient weighting 50–75 kg, this translates into 30–45 mL volume of undiluted contrast for use. Prior to our intervention, we tested the visibility of contrast ex vivo in our angiosuite and determined that around 70% concentration would permit satisfactory image quality for the complexity of our intervention. This is likely to vary depending on machine, patient, and disease factors.

Careful individual consideration should be made prior to undertaking neurointervention using GBCA. Given the paucity of clinical data, the patient must be fully informed of the potential risks, benefits, and alternatives. Discussion should also be made regarding potential use of ICM in case of need. Once the decision to treat is made, strategies can be implemented to minimize the contrast dose to maximize safety.

Presently, for patients with grade 2 and grade 3 chronic kidney disease (EGFR >30 mL/min/1.73 m²), no additional consideration or precautions are necessary. For patients with grade 4 and grade 5, guidelines recommend individual consideration and usage of newer GBCA agents, and counseling patients at low risk (<1%) of developing nephrogenic systemic fibrosis.

In addition, measures should be taken to optimize renal function, such as hydration and renal replacement therapy. Preprocedural cross-sectional imaging should be obtained to understand angioanatomy and minimize the need of contrast in navigation. In complex dynamic pathology, it may be sensible to perform a diagnostic angiogram in the first instance, followed by second stage intervention. The treatment approach may have to be modified based on contrast concerns and other patient needs. In our patient, placing a flow diverting stent would require the least amount of contrast. However, as the patient had previous severe gastrointestinal bleeding and allergy to proton pump inhibitors, it would not be safe to load her with double antiplatelet therapy. A transvenous embolization approach would probably require a significantly higher contrast load and was considered less favorable.

CONCLUSION

We report the first in literature case of CCF embolization using GBCA as a contrast agent for angiography. The challenges in technique and decision-making in managing these patients were illustrated. A good understanding of contrast properties and a sensible appreciation of risks and benefits are crucial in ensuring best patient outcomes.

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None.

Ethics Statement

Informed consent is obtained from the patient for research publication. Institutional Review Board approval is waived for the use of anonymized patient data for retrospective clinical case report.

Conflicts of Interest

The authors have no conflicts to disclose.

Author Contributions

Concept and design: YLL and PJC. Analysis and interpretation: YLL. Data collection: YLL, SR, and PJC. Writing the article: YLL. Critical revision of the article: YLL, SR, and PJC. Final approval of the article: PJC. Overall responsibility: PJC.

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