Pearls & Oy-sters: Contrast-induced encephalopathy following coronary angiography

A rare stroke mimic

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Pearls & Oy-sters

The clinical presentation of contrast-induced encephalopathy (CIE) varies widely, including altered mental status, focal motor and sensory deficit, visual disturbance, ophthalmoplegia, global aphasia, and seizures.

Radiologically, CIE can mimic subarachnoid hemorrhage (SAH) on CT head with hyperdensity in the subarachnoid space due to iodinated contrast extravasation.

CIE is a diagnosis of exclusion that requires comprehensive workup and close monitoring of neurologic examination.

Case report

A 72-year-old woman with history of hypertension and hyperlipidemia presented with chest pain, lightheadedness, and diaphoresis. ECG revealed acute inferior myocardial injury and she was loaded with clopidogrel 600 mg and aspirin 81 mg and underwent emergent percutaneous coronary angioplasty for 100% occlusion of the right coronary artery with placement for 3 drug-eluting stents. A total of 210 mL of iodinated contrast with low osmolality (884 mOsm/kg) was used. There was no complication during the procedure. Immediately after the procedure, the patient was found to be confused. Head CT without contrast revealed hyperdensity (70 Hounsfield units [HU]) along right hemispheric gyri with mild cerebral edema, concerning for subarachnoid hemorrhage (SAH) (figure 1A). The patient was transferred to the intensive care unit at our institution for suspected hemorrhagic stroke. There was no report of seizure activity or acute or chronic renal dysfunction.

On arrival, the patient's blood pressure was 143/74 mm Hg with a heart rate of 67 bpm; other vital signs and laboratory studies were within normal limits. The neurologic examination revealed mild to moderate left hemiparesis, left sensory and visual hemineglect, and right gaze preference. Otherwise, mental status, cranial nerve, sensory, and language examination results were all normal. NIH Stroke Scale score was 10. Examination findings consistent with right middle cerebral artery (MCA) territory syndrome prompted an emergent CT angiography of head and neck 7 hours after the first CT. There was no vessel occlusion or stenosis involving the MCA, anterior cerebral artery, or internal carotid artery. There was no evidence of cerebral aneurysms, arterial-venous malformations, or vasospasm. The patient received additional iodinated contrast for CT angiography (CTA), but there was no change in the neurologic examination. Notably, the hyperdensity in the sulcal spaces had almost completely resolved on this CTA study (figure 1B). Subsequently, brain MRI without contrast was performed at 17 hours from the first CT scan and showed mild gyral fluid-attenuated

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Figure 1 CT head

inversion recovery (FLAIR) hyperintensity, which was most pronounced in the right posterior temporal, occipital, posterior frontal, and parietal lobes (figure 2A). Susceptibility-weighted imaging (SWI) did not demonstrate SAH, although the study was limited due to signal artifact in the bilateral frontal lobes (figure 2B), and there was no diffusion restriction, ruling out acute ischemic stroke (figure 2C). A 30-minute portable EEG showed mild generalized background slowing without epileptiform discharges. On hospital day 2, the patient's neurologic deficits resolved completely and spontaneously. Repeat CT scan showed resolution of the hemispheric hyperdensity and edema (figure 1, A and C). This presentation seemed most consistent with CIE.

Discussion

The most common neurologic complications associated with cardiac catheterization procedures include acute ischemic stroke secondary to atheroembolism, air embolism,

vasospasm, and intimal dissection, with an incidence ranging between 0.05% and 0.10% for diagnostic coronary angiography and between 0.12% and 0.40% for percutaneous coronary intervention (PCI).¹ CIE is rare and a recent systematic review identified only 5 case series and 38 case reports, identifying a total of 52 reported cases between 1970 and 2017.² Neurologic manifestation of CIE varies widely, including visual disturbance in 52%, focal motor and sensory deficits in 28.8%, encephalopathy in 25%, seizures in 17.3%, global aphasia in 13.5%, and ophthalmoplegia in 3.8%, which can mimic various other disorders.¹ The details of initial neurologic examination were limited in our case as it was performed at another institution. Neurologic manifestations typically occur within minutes to hours after iodinated contrast agent administration, as was seen in this case.²

The current hypothesis for the underlying mechanism of CIE is disruption of the blood–brain barrier (BBB) allowing the contrast agent to permeate into the CNS causing direct neuronal toxicity and cerebral edema. Hyperosmolality of

Figure 2 Brain MRI

contrast media is considered to cause shrinkage of endothelial cells, opening up tight junctions.³ Furthermore, contrast agents also have epileptogenic potential and can result in seizures. Underlying chronic hypertension can also lead to BBB disruption by compromising cerebral autoregulation, which could have been the possible risk factor for CIE in our patient. In addition to the direct contact of contrast with neural tissues, increased neuronal excitability by receptor activation and high lipid solubility of contrast medium are also proposed mechanisms of neuronal injury.² Cortical blindness is a prominent manifestation of CIE, which has been attributed to the relatively higher permeability of the BBB in the occipital cortex.^{2,4}

Although controversial, there is a reported correlation between the iodinated contrast dose and incidence of CIE.⁵ Literature reports that 200 mL of iodine contrast is the maximum recommended dose to prevent toxicity.⁶ The median volume of contrast medium used for cardiac catheterization in the 52 patients who developed CIE was 252 mL and ranged widely from 75 to 1,500 mL.¹ Low osmolar agents may be associated with increased risk of CIE.² Our patient received low osmolarity agents, which could have contributed to the development of CIE.

Head CT results may mimic SAH, as was seen in our case, because of hyperdensity in the subarachnoid space due to iodinated contrast extravasation. CT may also show combination of poorly localized cortical and subcortical enhancement and cerebral edema. Although it did not help differentiation in our case, the density of the lesion on the Hounsfield scale can be useful in distinguishing CIE from SAH when it is high. Blood has a density ranging between 40 and 60 HU and contrast media have higher attenuation values, usually between 50 and 1,000 HU.^{2,7} As was seen in our case, the temporal evolution of subarachnoid hyperdensity seen on serial CT scans may help differentiate CIE from SAH. CIE-related subarachnoid hyperdensity resolves within 12–24 hours, whereas 85%–93% of SAH cases continue to show hyperdensity beyond 2 days after onset.⁸ In our patient, the hyperdensity completely resolved by hospital day 2. On MRI, an increased FLAIR signal abnormality along the gyri can be seen in both SAH and CIE. In our case, the normal SWI scan argued for the latter. In order to further differentiate SAH from CIE, lumbar puncture may be helpful. Whereas SAH may show the presence of xanthochromia and red blood cells, CIE will not. Simultaneous measurement of iodinated contrast concentration in CSF and serum have been reported to be useful.⁹ These laboratory tests as well as vessel study such as conventional angiogram were not performed in our patient, given clinical and radiologic improvement by the next day.

Our case mimicked acute right MCA syndrome due to the neurologic examination showing left-sided hemiplegia, sensory and visual extinction, and right gaze preference. Similarly, Chisci et al.⁶ reported a case of CIE that presented with transient acute onset global aphasia and right hemiparesis lasting

for 24 hours, mimicking a left MCA syndrome, after PCI and left carotid artery stenting procedure. Brain MRI may help differentiate CIE from acute ischemic stroke because diffusion-weighted imaging (DWI) and apparent diffusion coefficient sequences provide a quantitative measure of water diffusion, and decreased water diffusion is seen with cytotoxic edema and most commonly with acute ischemic stroke, among other rarer conditions. Whereas FLAIR hyperintensity in the absence of DWI changes can be seen in various disorders causing vasogenic edema such as posterior reversible encephalopathy, our case was most consistent with CIE given the clinical context where symptoms occurred immediately after contrast administration. The unilateral involvement of CIE, as seen in our case, has been reported and was attributed to the position of the angiography catheter among other factors. The reason for unilaterality in our case remains unclear.

Prognosis of CIE is typically favorable with complete resolution of symptoms within 24–72 hours after contrast administration, except for some reported cases where ophthalmoplegia resolved after 10 days.⁵ Junck and Marshall¹⁰ reported that reversibility of the toxicity depends on BBB reconstitution and the rate of clearance of the offending agent.

We report a rare case of CIE following cardiac catheterization that mimicked a right MCA syndrome clinically and SAH radiologically, creating a diagnostic dilemma. Timely recognition of this rare complication associated with cardiac catheterization, close neurologic monitoring, and watchful management helped avoid unnecessary invasive procedures such as lumbar puncture and cerebral angiogram and helped reduce hospital length of stay. We emphasize the importance of awareness of this rare neurologic complication following contrast administration.

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Disclosure

The authors report no relevant disclosures. Go to Neurology.org/N for full disclosures.

Appendix Authors

Name	Location	Contribution
Yohei Harada, MD	University of Arkansas for Medical Sciences, Little Rock	Cared for the patient presented, wrote the text, assembled the figures
Supriya R. Kairamkonda, MD	University of Arkansas for Medical Sciences, Little Rock	Cared for the patient presented, wrote the text
Ushna Ilyas, MD	University of Arkansas for Medical Sciences, Little Rock	Cared for the patient presented, wrote the text
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Continued

Appendix *(continued)*

Name	Location	Contribution
Rohan S. Samant, MD	University of Arkansas for Medical Sciences, Little Rock	Cared for the patient presented, assembled figures
Vishank A. Shah, MD	University of Arkansas for Medical Sciences, Little Rock	Cared for the patient presented, supervised drafting/revision of the manuscript
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References

1. Spina R, Simon N, Markus R, Muller DW, Kathir K. Recurrent contrast-induced encephalopathy following coronary angiography. *Intern Med J* 2017;47:221–224.
2. Spina R, Simon N, Markus R, Muller DW, Kathir K. Contrast-induced encephalopathy following cardiac catheterization. *Catheter Cardiovasc Interv* 2017;90:257–268.
3. Leong S, Fanning NF. Persistent neurological deficit from iodinated contrast encephalopathy following intracranial aneurysm coiling: a case report and review of the literature. *Interv Neuroradiol* 2012;18:33–41.
4. Park JC, Ahn JH, Chang IB, Oh JK, Kim JH, Song JH. A case of unusual presentation of contrast-induced encephalopathy after cerebral angiography using iodixanol. *J Cerebrovasc Endovasc Neurosurg* 2017;19:184–188.
5. Kocabay G, Karabay CY, Kalayci A, et al. Contrast-induced neurotoxicity after coronary angiography. *Herz* 2014;39:522–527.
6. Chisci E, Setacci F, de Donato G, Setacci C. A case of contrast-induced encephalopathy using iodixanol. *J Endovasc Ther* 2011;18:540–544.
7. Schulte-Altedorneburg G, Rub K, Scheglmann K. Simultaneous ischemic and neurotoxic brain damage after coronary angiography. *Neurol Res* 2004;26:79–82.
8. Carpenter CR, Hussain AM, Ward MJ, et al. Spontaneous subarachnoid hemorrhage: a systematic review and meta-analysis describing the diagnostic accuracy of history, physical examination, imaging, and lumbar puncture with an exploration of test thresholds. *Acad Emerg Med* 2016;23:963–1003.
9. Velden J, Milz P, Winkler F, Seelos K, Hamann GF. Nonionic contrast neurotoxicity after coronary angiography mimicking subarachnoid hemorrhage. *Eur Neurol* 2003;49:249–251.
10. Junck L, Marshall WH. Neurotoxicity of radiological contrast agents. *Ann Neurol* 1983;13:469–484.

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