Rare Cases of Contrast-Induced Encephalopathies

Abstract
Cortical blindness (CB) due to contrast-induced encephalopathy is a rare complication in endovascular procedure. Although exact mechanism is not known, disruption of blood–brain barrier (BBB) by contrast agent is supposed to be caused. We report two cases of contrast-induced encephalopathies after coil embolization of unruptured aneurysm. A 68-year-old woman with unruptured basilar artery aneurysm was treated with endovascular stent-assisted coil embolization. The procedure was successfully accomplished within 172 min using about 160 ml of contrast medium (iopamidol). However, she manifested with CB 3 h after the procedure and seizure on the next day. Immediate computed tomography revealed the cortical enhancement in both occipital lobes. Diffusion-weighted imaging–magnetic resonance imaging and fluid-attenuated inversion recovery sequence 1 day after the procedure revealed edema in both occipital lobes with no findings of ischemia or hyperperfusion. Electroencephalography showed sharp and slow waves in both occipital lobes. She required endotracheal intubation on day 2 to maintain airways and breathing. Her sensorium improved 4 days after the procedure with administration of steroid and anticonvulsant. She was extubated on day 4 after the procedure. She was discharged with persisting CB as a sequel.

Keywords: Cerebral angiogram, computed tomography angiogram, contrast-induced encephalopathy, cortical blindness

Introduction
Contrast-induced encephalopathy (CIE) is a rare complication of endovascular interventions. The presentations may include cortical blindness (CB), hemiparesis, seizure, and coma. In most reported cases, the symptoms are self-limiting but may become fatal.[1] Here, we document a case of permanent CB in CIE after digital subtraction angiography for aneurysmal coiling using iopamidol, which is a type of nonionic monomer low-osmolar contrast agent. Another case of CIE became fatal.

Case Reports
Case report 1
A 68-year-old woman presented to us with unruptured basilar artery aneurysm. She had undergone clipping of internal carotid artery (ICA) aneurysm 8 years back. The size of basilar artery to aneurysm was 5 mm 8 years back. The patient was on regular clinical and radiological follow-up with us. Recent imaging showed an increase in size of aneurysm from 5 to 8 mm. Therefore, coiling of basilar top aneurysm was planned. On admission, her neurological history included hypertension on medical management.

Cerebral angiogram revealed an 8-mm size unruptured basilar top aneurysm [Figure 1a]. She underwent endovascular procedure with contrast iodinated agent for basilar tip aneurysm. She received 260 ml of iopamidol for angiography and stent-assisted coiling. The procedural time was 172 min. (We used 6-Fr guiding catheter, 4.2-Fr microcatheter, and target 360 coil.) The procedure was uneventful. The neurological examination was normal at the end of the procedure.

The cerebral angiogram showed complete obliteration of basilar tip aneurysmal sac with no coil migration [Figure 1b]. The patient complained of decreased vision in both eyes 3 h after the procedure. Computed tomography (CT) brain [Figure 2] was performed which showed subarachnoid contrast enhancement in bilateral occipital lobe sulci with loss of gray-white differentiation and sulcal effacement.

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There was no intracerebral hemorrhage. She was treated with aspirin 100 mg/day, clopidogrel 75 mg/day, and argatroban.

On postprocedure day 1, she developed generalized convulsions. She was treated with levetiracetam 1 g/day, phenobarbital 750 mg/day, and methylprednisolone 500 mg/day to control seizure. Magnetic resonance imaging (MRI) brain and electroencephalogram (EEG) were performed.

EEG showed slow and sharp waves in bilateral occipital lobes [Figure 3].

MRI showed hyperintensities in fluid-attenuated inversion recovery sequence. There was no restriction in diffusion-weighted imaging (DWI) sequence of MRI brain [Figure 4].

CT brain done after 48 h showed resolution of contrast enhancement [Figure 5].

The patient became drowsy on postprocedure day 2 and hence intubated. Her sensorium gradually improved on day 4, and subsequently, she was extubated. Her sensorium completely improved on day 6 after the procedure. There were no further seizure episodes. CT brain done on day 5 [Figure 6] showed no bleed or infarct with persistence of hypodensities in both occipital lobes.

She was discharged from hospital with persisting CB on the 7th postprocedural day.

**Case report 2**

Here, we discuss a 62-year-old woman with no comorbidities presented to our hospital with unruptured right cavernous ICA aneurysm. Coiling of the right cavernous aneurysm was planned after cerebral angiogram findings [Figure 7].

Stent-assisted coiling was performed for cavernous ICA aneurysm. Coil migration was noted into the distal ICA during the procedure. Migrated coil was extracted with stent retrieval device [Figure 8].

Stent-assisted coiling was performed. The figure shows obliteration of aneurysmal sac by coils, and luminal patency of ICA is maintained by the stent at the end of the procedure.

Her neurological examination was normal at the end of the procedure (Glasgow Coma Scale [GCS]-15).

A CT scan [Figure 9] was performed at the end of coiling, which showed blood and contrast extravasation in the right frontoparietal area. Her GCS was 15 without any neurological deficits.

She developed left hemiparesis and became drowsy 3 h after the procedure. Her right pupil was dilated. A CT scan brain [Figure 10] showed a redistribution of sulcal hyperdensities in both hemispheres (right > left).

Her sensorium deteriorated rapidly 14 h after the procedure. GCS was 4. CT brain [Figure 11] showed hydrocephalus. She was intubated to maintain airway and electively ventilated. An external ventricular drainage was inserted for hydrocephalus [Figure 12].

CT scan brain on day 2 [Figure 13] and day 3 [Figure 14] showed persistent hyperdensities with severe edema and mass effect. The patient was treated with anticonvulsants, steroids, and anti-edema measures. The patient died 3 days after the procedure.
Discussion

We reviewed literature on CIE by 16 authors comprising 27 cases (including 2 from our series) [Table 1]. CIE affected all age groups. The youngest reported in the study was 17 years old and the eldest was 82 years old. Both sexes were affected (male: 10, female: 1). Females were more involved than male population.

Most of the symptoms were noticed within few 12 h after the procedure. Three patients had symptoms during intervention, 9 occurred immediately after completion of intervention, 5 happened within 1 h of intervention, 3 occurred within 3 h of intervention, and 6 occurred within 6–12 h after intervention.

CB, altered sensorium, and hemiparesis were the most common neurological findings noticed after CIE [Table 2].
Cortical blindness

The incidence of CB was 1% with contrast cerebral angiography.\(^\text{[10]}\) CB is characterized by partial or complete loss of perceived vision, normal fundi, normal pupillary reflexes, and unaltered extraocular movements. The onset of CB occurs from minutes up to 12 h after angiography. In most of the cases, blindness resolved, but in our case, CB persisted.

We reviewed these patients for the region of the brain involved. The literature showed an affinity of the occipital lobe in CIE [Table 3].
## Table 1: Review of literature

| Study detail           | Age | Sex | Diagnosis                                           | Symptoms after DAS | Time for onset of symptoms | Region involved in brain | Time for radiological resolution | Time for clinical resolution | Contrast agent | Dose of contrast | Recovery complete |
|------------------------|-----|-----|-----------------------------------------------------|--------------------|-----------------------------|--------------------------|----------------------------------|-------------------------------|----------------|-----------------|------------------|
| Zhao et al.[1]         | 71  | Female | ICA and MCA stenosis                                 | Coma               | At completion               | Bilateral occipital       | No                              | No              | Iopamidol      | 110 ml           | Died after 56 days |
| Current report         | 68  | Female | Aneurysm coiling                                     | Blindness          | 3 h                         | Right hemispheric (right more than left) | 1                              | 4               | Iopamidol      | 110 ml           | Persisting blindness |
| Potsi et al., 2012[1]  | 71  | Female | Coiling of cavernous ICA                             | Left hemiparesis, altered sensorium | 3 h                         | Right cerebral hemispheric sulci | 1                              | 4               | Iopromide      | 25 ml            | Died after 2 days   |
| Haussen et al., 2013[1]| 89  | Female | Diagnostic angiogram to rule out aneurysm             | Left hemianopia, left hemisensory loss | During intervention | Right occipital and parietal | 1                              | 1.5             | Ionic contrast | 18 cc           | Yes              |
| Guimaraens et al., 2010[4] | 51  | Male | Stent for aneurysm                                   | Disorientation, left hemiparesis, visual disturbances | 30 m                       | Right cerebral sulci | 2                              | 5               | Iopromide nonionic | 30 ml           |                  |
| Roccaglisi et al., 2009[1] | 65  | Male | Tinnitus                                             | Blindness, altered sensorium | During intervention | Bilateral occipital | 48                             | 1 year | Iohexol | Not available | Yes             |
| Till et al., 2009[1]   | 17  | Male | Feeders in hemangioblastoma                          | Blindness          | During intervention | Bilateral occipital, right thalamus, cerebellum | 5                              | 2 m             | Iopromide      | 44 ml            |                  |
| Niimi et al., 2008[1]  | 41  | Male | Aneurysm coiling                                     | Blindness          | 3 h                         | Right parietal           | 1 m                            | Not available Iopromide       | 297 ml          | Left homonymous hemianopia |                  |
| 46 Male                |     |     | Aneurysm coiling                                     | Right homonymous hemianopia | 1 h                         | No abnormality           | 1 m                            | Not available Iopromide       | 225             |                  |
| 54 Female              |     |     | Aneurysm coiling                                     | Blindness          | 3 h                         | Bilateral occipital      | 1 m                            | Iopromide      | 62 ml           |                  |
| 47 Female              |     |     | Aneurysm coiling                                     | Right homonymous hemianopia, altered sensorium | 1 h                         | Bilateral occipital      | 7                              | Not available Iopromide       | 384 ml          |                  |
| Shinoda et al., 2004[1] | 62  | Female | Aneurysm coiling                                     | Blindness altered sensorium | During intervention | Bilateral occipital, left frontal, temporal | 21                             | 17              | Ioversol       | 150 ml           | Persistent left lower quadrantanopia |
| Saigal et al., 2004[1] | 45  | Female | Investigating aneurysm basilar and carotid stenosis | Blindness          | 12 h                        | Bilateral occipital      | 16                             | Not available Iohexol nonionic | Not available |                  |
| 74 Female              |     |     | Investigating aneurysm                                | Blindness altered sensorium | 1 h                         | Left parietal occipital | 2                              | Not available Iohexol nonionic | Not available |                  |
| 73 Female              |     |     | Investigating aneurysm                                | Blindness altered sensorium | 20 m                        | Bilateral occipital      | 5                              | Not available Iohexol nonionic | Not available |                  |

Contd...
### Table 1: Contd...

| Study detail          | Age  | Sex   | Diagnosis                                      | Symptoms after DAS                              | Time for onset of symptoms | Region involved in brain            | Time for radiological resolution | Time for clinical resolution | Contrast agent                  | Dose of contrast | Recovery complete |
|-----------------------|------|-------|-----------------------------------------------|------------------------------------------------|----------------------------|------------------------------------|---------------------------------|------------------------------|----------------------|------------------|------------------|
| Lantos 1989[10]       | 49   | Female| Blindness, nystagmus                           | During intervention                             |                           | Right occipital, pons, both thalami, midbrain | 16 h                            | 18 h                         | Diatrizoate meglumine (ionic) | 30                |                  |
|                       | 64   | Male  | Dizziness                                      | During intervention                             |                           | Left parietal occipital              | 3                               | 18 h                         | Iothalamate meglumine (ionic) | 12                |                  |
|                       | 71   | Male  | Carotid artery atherosclerosis                 | Blindness altered sensorium                    | 20 min                    | Bilateral occipital                 | 10                              | Not available                | Iohexol               | 38               |                  |
|                       | 68   | Female| Blindness altered sensorium                   | Immediately after completion                   |                           | Bilateral occipital                 | 6                               | Few hours                    | Iohexol               | 24               |                  |
| Leong and Fanning 2012[11] | 51| Female| Aneurysm coiling                              | Right hemiparesis, hemisensory loss, hemineglect | Immediately after completion | Left frontoparietal                | 12 months                       | Gliosis                      | Iopromide            | 220 ml          | Persistent right limb spasticity, modified Rankin 2 |
| Dangas et al., 2001[12] | 82 | Male  | Carotid artery stent                          | Left hemiparesis                               | Immediately               | Right frontoparietal                | 2                               | 2                           | Ioxaglate             | 50 ml            |                  |
| Hsiu-Yu et al.[13]    | 80   | Male  | Carotid artery stent                          | Right hemiparesis                              | Immediately               | Left frontoparietal                 | 2                               | 4                           | Iohexol               | 250 ml           |                  |
| Numaguchi et al., 1984[14] | 53 | Female| Investigating meningioma feeders              | Left partial motor seizure                     | Immediately               | Right temporofrontal                | 1                               | 14                          | Diatrizoate meglumine | 60 ml            |                  |
| Kubota et al.[15]     | 66   | Female| Left paracarotid aneurysm coiling             | Right hemiparesis, aphasia, altered sensorium, seizures | Immediately               | Left temporoparietal                | 4                               | 12 m                        | Iomeprol              | 80 ml            | Yes              |
| T. Kawasaki et al.    | 75   | Male  | Right ICA aneurysm coiling                    | Left hemiparesis                               | Immediately               | Right frontoparietal                | 1                               | ?                           |                      |                  |                  |
|                       | 65   | Female| Left ICA aneurysm coiling                     | Right hemiparesis                              | Immediately               | Left frontoparietal                 | 1                               | ?                           |                      |                  |                  |

ICA – Internal carotid artery; MCA – middle cerebral artery; VA-PICA – Vertebral artery- Posterior inferior cerebellar artery; SCA – Superior cerebellar artery
Why occipital lobe and visual cortex?

BBB (blood brain barrier) is incomplete in the posterior cerebral circulation, hence, occipital lobes and visual cortex are more susceptible locations for contrast induced encephalopathies.\cite{16,17}

Niimi et al.\cite{7} reported four cases of CB due to endovascular procedure. They performed 137 intra-arterial treatment procedures for posterior circulation aneurysms & identified cortical blindness as complication in 4 patients. During the same time period, they treated 500 anterior cerebral circulation aneurysms without this complication.\cite{7}

They identified four patients with cerebral vision loss complications. During the same time period, 500 aneurysms of the anterior cerebral circulation were treated without this complication. In his series, the visual field loss was unilateral in two and bilateral in two patients. Recovery was complete in three patients and almost normal in the fourth patient. The amount of contrast used and the duration of the procedure were similar among all patients. The four patients had no identified specific risk factors for developing procedure-associated occipital dysfunction.

In most of the cases, symptoms were self-resolving and less fatal. The time for radiological recovery ranged from 1 day to 12 months

Review of radiology findings in contrast-induced encephalopathy

The clinical features of CIE resemble neurological deficit due to embolism and hemorrhagic complications following angiography or endovascular interventions. Typical radiological findings include abnormal cortical contrast enhancement and edema, subarachnoid contrast enhancement, and striatal contrast enhancement – if the CT is performed soon after presentation. The enhancement resolves by 25 h in most of the cases. The diagnosis of contrast encephalopathy is, therefore, made by finding typical CT findings.\cite{11}

The possible risk factors for contrast encephalopathy include hypertension and renal failure.\cite{9} Roccatagliata et al.\cite{3} in their patients, obtained DWI sequence of MRI brain 3.5 h after symptom onset. It did not demonstrate any signal abnormality, thereby ruling out the presence of ischemic brain tissue within a time window useful for acute stroke management with thrombolysis. The complete absence of signal abnormality on initial DWI and a normal follow-up CT makes an embolic mechanism highly unlikely in our patient even if cases of falsely negative DWI studies have been reported.

Review of pathophysiology of contrast-induced encephalopathy

The mechanism of CIE is controversial. The disruption of the BBB after injection of the iodinated contrast agent is considered for this pathology.

Hyperosmolar contrast solutions cause water to diffuse out of the endothelial cells causing them to dehydrate and shrink in size. This decrease in size results in an opening of the tight junctions between the endothelial cells of the BBB allowing the iodinated materials to move into the neuronal tissues.\cite{18} Thus, under the conditions of intravenous injection, contrast media with lower osmolality should possess fewer neurotoxic effects.

The neurotoxicity of contrast medium appears inversely related to the hydrophilicity of the agent. Wible et al.\cite{19} performed animal experiments on a rat with ionic and nonionic contrast agents. They injected the contrast agent into cerebral cisterns of rat. Rats were monitored for seizures, dyspnea, blindness, and death. They reported that IOPROMIDE is lethal at small doses compared to other nonionic contrast material.

Iopromide is the most common contrast agent associated with this condition. 10 out of 26 were associated with this contrast (38%). All types of iodinated contrast agents can induce the development of neurotoxicity. Iopromide is a nonionic monomer low-osmolar contrast agent, which has been reported in cases of reversible CIE.\cite{20,21}

The volume of contrast ranged from 12 cc of ionic contrast to 384 cc of nonionic contrast.

The time for clinical recovery was 12 h to 12 months. One patient died after 56 days. The patient in our study died after 48 h. One patient had recovered from hemiparesis but had spasticity in limbs even after a year.

Zhao et al.\cite{1} reported death of a 71-year-old woman after cerebral angiogram during evaluation of tinnitus. The patient went into coma during the procedure and died 56 days after the procedure.\cite{1}
Literature analysis showed CB as a manifestation of CIE in 12 patients. All have bilateral occipital lobe involvements on CT brain scan. All patients had clinical and radiological resolution within in weeks after the procedure with conservative treatment. In our case, CB persisted even after radiological resolution. Therefore, CB due to contrast cerebral angiogram may not resolve in all cases (even after radiological resolution). In our second case report, the patient died on the 3rd day after the procedure. Only one case fatality due to CIE was reported in the literature.[1]

This observation and a review of the literature highlight that CIE may not always have a benign outcome and can cause permanent deficits. This potential harmful effect should be recognized by the angiographer and the interventionist.[11]

Conclusion
Although contrast-induced CB is self-resolving and associated with benign outcomes in previous studies, we present a case of permanent CB after DSA using iopamidol for aneurysmal coiling in the posterior circulation. Another case of CIE was fatal. Unfortunately, there is no effective treatment currently available for such a severe CIE. Further studies are needed to prevent the occurrence of severe complications and effective treatment.

Declaration of patient consent
The authors certify that they have obtained all appropriate patients consent forms. In the form the patients have given their consent for images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

References
1. Zhao W, Zhang J, Song Y, Sun L, Zheng M, Yin H, et al. Irreversible fatal contrast-induced encephalopathy: A case report. BMC Neurol 2019;19:46.
2. Potsi S, Chourouzi D, Moumtzouoglou A, Nikiforaki A, Gkouvas K, Drevelegas A. Transient contrast encephalopathy after carotid angiography mimicking diffuse subarachnoid haemorrhage. Neurrol Sci 2012;33:445-8.
3. Haussen DC, Modir R, Yavagal DR. Unilateral contrast neurotoxicity as a stroke mimic after cerebral angiogram. J Neuroimaging 2013;23:231-3.
4. Guimaraens L, Vivas E, Fonsegra A. Transient encephalopathy from angiographic contrast: a rare complication in neurointerventional procedures. Cardiovasc Interv Radiol. 2010; 33: 383-388.
5. Roccatagliata L, Taveira-Lopes R, Rossignol MD, Biondi A. Cortical blindness and retrograde amnesia following cerebral angiography studied by early diffusion weighted MR imaging. A case report. Neuroradiol J 2009;22:600-4.
6. Till V, Koprivsek K, Stojanovic S, Avramov P, Vulekovic P. Transient cortical blindness following vertebral angiography in a young adult with cerebellar haemangioblastoma. Pediatr Radiol 2009;39:1223-6.
7. Niimi Y, Kupershmit MJ, Ahmad S, Song J, Berenstein A. Cortical blindness, transient and otherwise, associated with detachable coil embolization of intracranial aneurysms. AJNR Am J Neuroradiol 2008;29:603-7.
8. Shinoda J, Ajimi Y, Yamada M, Onozuka S. Cortical blindness during coil embolization of an unruptured intracranial aneurysm-case report. Neurol Med Chir (Tokyo) 2004;44:416-9.
9. Saigal G, Bhatia R, Bhatia S, Wakhloo AK. MR findings of cortical blindness following cerebral angiography: Is this entity related to posterior reversible leukencephalopathy? AJNR Am J Neuroradiol 2004;25:252-6.
10. Lantos G. Cortical blindness due to osmotic disruption of the blood-brain barrier by angiographic contrast material: CT and MRI studies. Neurology 1989;39:567-7.
11. 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.
12. Dangas G, Monsein LH, Laureno R, Peterson MA, Laird JR Jr., Saijer LF, et al. Transient contrast encephalopathy after carotid artery stenting. J Endovasc Ther 2001;8:111-3.
13. Hsu-Yu F, Yeh-Lin K, Chiung-Jen W. Transient contrast encephalopathy after carotid artery stenting mimicking diffuse subarachnoid hemorrhage: A case report. Catheter Cardiovasc Interv 2009;73:123-6.
14. Numaguchi Y, Fleming MS, Hasuo K, Puyau FA, Nice CM Jr. Blood-brain barrier disruption due to cerebral arteriography: CT findings. J Comput Assist Tomogr 1984;8:936-9.
15. Kubota T, Yamazaki T, Maeda M, Koujo T, Nakanishi T, Senoo M, et al. A case of contrast-induced encephalopathy after coil embolization of unruptured internal carotid artery aneurysm. Surg Cereb Stroke 2013;41:116-122.
16. Studdard WE, Davis DO, Young SW. Cortical blindness after cerebral angiography. Case report. J Neurosurg 1981;54:240-4.
17. Horwitz NH, Wener L. Temporary cortical blindness following angiography. J Neurosurg 1974:40:583-6.
18. Waldron RL 2nd, Bridenaugh R, Purkenson M, Dempsey EW. The effect of angiographic contrast media at the cellular level in the brain. Radiology 1973;108:187-9.
19. Wible JH Jr., Barco SJ, Scherrer DE, Wojdyla JK, Adams MD. Neurotoxicity of non-ionic X-ray contrast media after intracranial administration in rats. Eur J Radiol 1995;19:206-11.
20. Parry R, Rees JR, Wilde P. Transient cortical blindness after coronary angiography. Br Heart J 1993;70:563-4.
21. Kamata J, Fukami K, Yoshida H, Mizunuma Y, Moriai N, Takino T, et al. Transient cortical blindness following bypass graft angiography. A case report. Angiology 1995;46:937-46.