Clinical Interventions in Aging

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CASE REPORT

Case Report and Literature Review on Low-Osmolar, Non-Ionic Iodine-Based Contrast-Induced Encephalopathy

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Meng-Ru Liu[1]
Hong Jiang[2]
Xian-Lun Li[2]
Peng Yang[2]

[1]Department of Cardiology, China-Japan Friendship Hospital, Peking Union Medical College, Chinese Academy of Medial Sciences, Beijing, People's Republic of China; [2]Department of Cardiology, China-Japan Friendship Hospital, Beijing, People's Republic of China

Abstract: Contrast-induced encephalopathy (CIE) is a rare complication following percutaneous carotid and coronary interventions, and important diagnostic radiological signs include brain edema and cortical enhancement. In this report, we detail a case of probable CIE in an 84-year-old woman following a normal diagnostic coronary angiography (CAG) that involved 20 mL of the low-osmolar, non-ionic monomeric, iodine-based contrast agent iopromide (Ultravist 370). The patient was unconscious and presented with hemiparesis, hemianopia, recurrent seizures, and cardiac and respiratory arrest within minutes to hours following the procedure. Non-contrast computed tomography (CT) of the head showed increased subarachnoid density, cortical enhancement, and brain edema in the right hemisphere. Three days of rehydration, reduction in cranial pressure, and treatment with an anticonvulsant and dexamethasone resulted in a gradual recovery with no neurological deficits. This case highlights that severe neurotoxic symptoms may occur in response to low doses of low-osmolar, non-ionic, monomeric contrast agents. This finding is of importance to interventional cardiologists for diagnostic considerations and development of treatment plans.

Keywords: contrast-induced encephalopathy, coronary angiography, percutaneous carotid and coronary interventions

Introduction

Contrast-induced encephalopathy (CIE) is a rare complication of percutaneous carotid and coronary interventions.[1,2] Contrast media, which include ionic, non-ionic, low osmolarity, iso-osmolar, and high osmolarity solutions have been reported to induce CIE.[3] Clinical manifestations of CIE include encephalopathy, seizures, motor and sensory disturbances, disturbances in vision, and focal neurological deficits,[1,3,4] which fully resolve within 48–72 hours. Heterogeneity of clinical presentation necessitates evaluation of radiological signs associated with contrast encephalopathy, such as brain edema and cortical enhancement, to allow for differentiation between hemorrhagic and thromboembolic complications of angiography.[5] Contrast media-induced neurotoxic effects result from the disruption of the blood brain barrier (BBB).[6] Hypertension, diabetes mellitus, renal impairment, administration of large volumes of iodinated contrast, percutaneous coronary intervention or selective angiography of internal mammary grafts, and previous adverse reaction to iodinated contrast are common risk factors for development of CIE.[2] In this manuscript, we present a case of a patient who presented with severe symptoms of CIE following treatment with a small amount of low-osmolar, non-ionic, monomeric contrast.

Correspondence: Peng Yang
Department of Cardiology, China-Japan Friendship Hospital, Peking Union Medical College, Chinese Academy of Medial Sciences, Yinghua Dongjie 2, Chaoyang District, Beijing 100029, People's Republic of China
Tel +86-10-84205083
Fax +86-10-84205081
Email doctoryp1898@163.com

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Case Report

An 84-year-old woman with a history of hypertension, paroxysmal atrial fibrillation, and chronic bronchitis presented with intermittent chest distress, palpitation, and shortness of breath for several minutes-duration for 3 months. Coronary angiography (CAG) was performed through the right radial approach, which revealed mild plaque disease in the left anterior descending coronary artery (LAD) only. Twenty milliliters of iopromide (Ultravist 370, Bayer Healthcare, Pittsburgh, PA, USA), a low-osmolar, non-ionic, monomeric, iodine-based contrast agent, was administered during the procedure. Local anesthetic (1% lignocaine) was administered prior to CAG. The patient also received 3000 IU of heparin intra-arterially during CAG and did not complain of discomfort during the operation.

Within minutes of radial sheath removal, the patient lost consciousness, and exhibited left limb hemiplegia with muscle strength level 0 and eyes staring to the right. The patient was seen by the stroke team to determine whether she had cerebrovascular disease. Emergency computed tomography (CT) was performed, which showed no acute pathological findings (Figure 1A). Cerebral angiography showed no stenosis, thrombosis, or hemorrhage in the bilateral carotid artery, the middle cerebral artery, or the anterior cerebral artery, which indicated absence of any cerebrovascular events (Supplementary Figure S1). The patient regained consciousness spontaneously and left limb muscle strength returned to level 4, which is considered safe. The patient was then returned to the coronary care unit (CCU) for further treatment.

Ten minutes after transfer to the CCU, the patient experienced limb convulsions, jaw chomping, and lost consciousness. Physical examination revealed no response to pain stimulation, general unresponsiveness, eyes gazing to the right, and weak pupillary light reflex. The patient exhibited positive bilateral Babinski signs and neck resistance. The symptoms gradually improved after 2–3 minutes. Brain CT examination 2 hours after surgery showed multiple high-density regions in the subarachnoid space (Figure 1B), which indicated potential subarachnoid hemorrhage or contrast agent leakage. Brain computed tomography angiography (CTA) did not show evidence of macrovascular embolism (Figure 2), and emergency brain magnetic resonance imaging (MRI) showed hyperintense areas could be seen on T2-weighted image and fluid-attenuated inversion recovery (FLAIR) in frontal, parietal, temporal and occipital of right cortex, and no clear signs of subarachnoid hemorrhage were observed in diffusion-weighted imaging (DWI) (Figure 3). The patient was given fluids to accelerate excretion of contrast agent, sodium valproate 60 mg per hour to treat epilepsy, mannitol 125 mL every 6 hours to dehydrate and reduce intracranial pressure, nimodipine 10 mg once

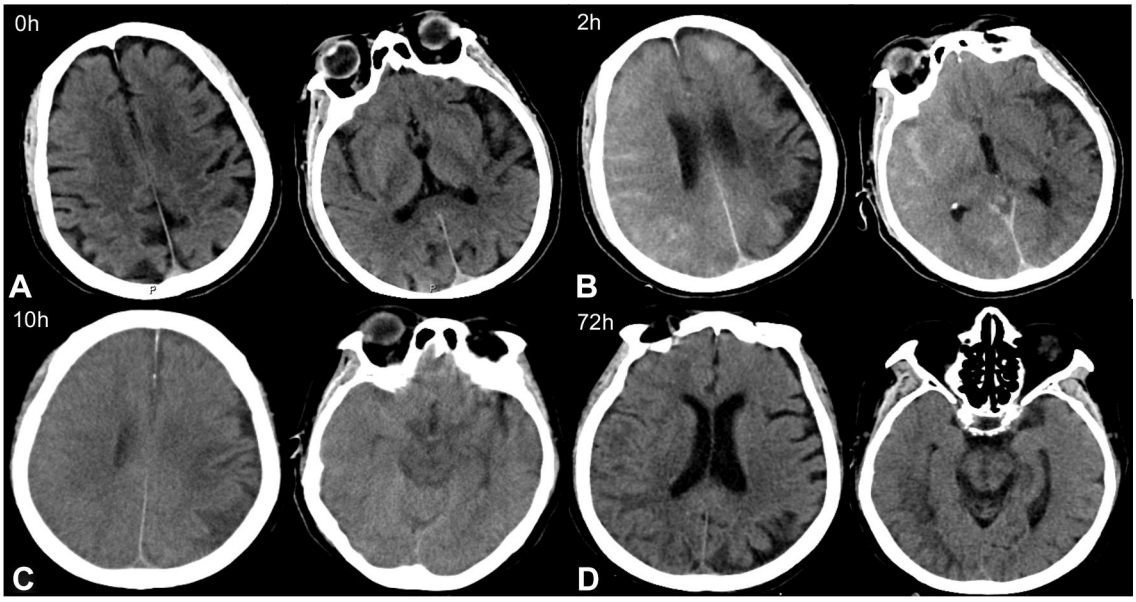

Figure 1 Contrast-induced encephalopathy in brain computed tomography (CT) scans. (**A**) Emergency brain CT showed no acute pathological findings. (**B**) Brain CT 2 hours after surgery indicated multiple high-density regions in the subarachnoid space. (**C**) Brain CT 10 hours after surgery showed significantly swollen brain tissue, particularly in the right hemisphere, the left frontal lobe, and the left occipital lobe. The high-density shading in the subarachnoid cavity was significantly denser than in previous scans. (**D**) Brain CT 72 hours after surgery showed the sulci of the right hemisphere became shallow, and low-density shadows could be seen in the frontal parietal lobe. But cerebral edema was significantly improved.

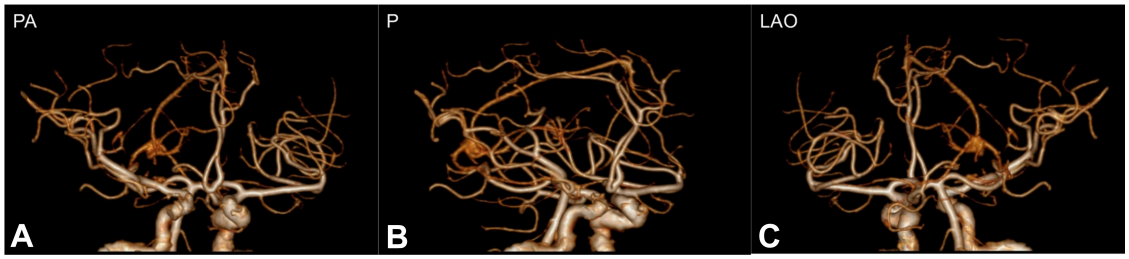

Figure 2 Computed tomography angiography (CTA) showed no evidence of macrovascular embolism in (**A**) posteroanterior (PA), (**B**) posterior (P) and (**C**) left anterior oblique (LAO) view.

a day to prevent vasospasm, and other drugs to improve clinical symptoms. Following this treatment course, the patient suffered from seizures twice and exhibited a steady decline in cardiac rhythm, blood pressure, and blood oxygen level. Brain CT examination 10 hours after surgery showed significantly swollen brain tissue, particularly in the right hemisphere, the left frontal lobe, and the left occipital lobe, with more obvious swelling in the right hemisphere (Figure 1C). The high-density shading in the subarachnoid cavity was significantly more pronounced than that in previous scans. Neurologists excluded cerebral hemorrhage, which suggested that CIE was a possibility.

The patient experienced another seizure 18 hours post CAG, then developed cardio-respiratory arrest. Physical examination showed an absence of carotid pulse and pupil dilation with weak light reflex. Cardiopulmonary resuscitation and tracheal intubation were performed immediately, and one milligram of epinephrine was administered intravenously. Following this treatment course, the patient's heart rate and blood pressure recovered. The cause of cardio-respiratory arrest was determined to be by mild cerebral hernia preceded by cerebral edema in CIE. Clinical experience and a literature search resulted in administration of 10 mg of dexamethasone once per day for 2 days in addition to treatment with anti-epilepsy drugs, reduction of cranial pressure, and fluid replacement. Following treatment, the patient's condition gradually improved. Consciousness was restored 72 hours after surgery, and the tracheal tube was removed. Brain CT reexamination showed the sulci of the right hemisphere became shallow, and low-density shadows could be seen in the frontal parietal lobe. However, cerebral edema was significantly improved compared with that observed 3 days prior (Figure 1D). These findings resulted in a decrease in drug dosage that nimodipine and dexamethasone were discontinued, sodium valproate was discontinued and changed to levetiracetam 500 mg twice a day, and mannitol was changed to 125 mL once every 12 hours. Multiple complications such as rib, shoulder blade, and lumbar vertebrae fractures, hemothorax, and loss of front teeth occurred during rescue, each of these injuries improved following active treatment. The patient was discharged after her condition improved. Follow-up 2 months after the operation showed short-term memory loss, but

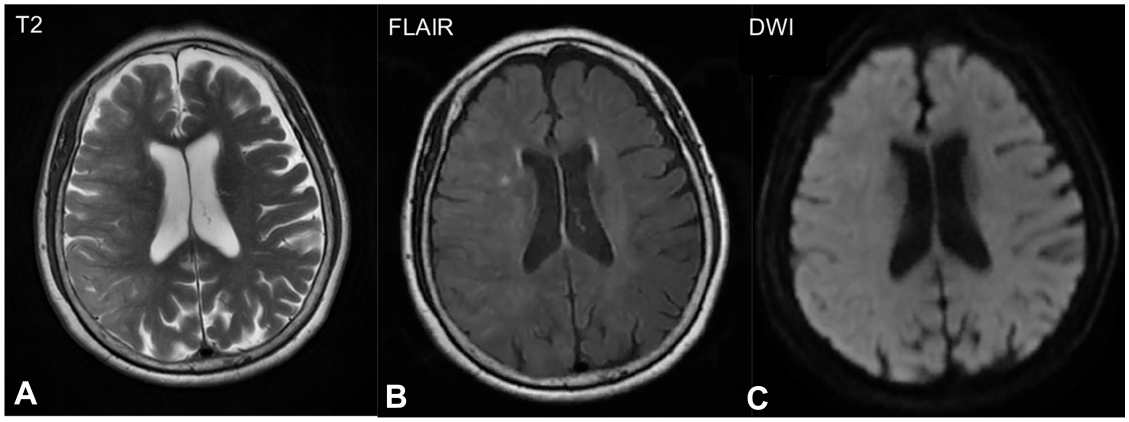

Figure 3 Brain magnetic resonance imaging (MRI) 2 hours after surgery showed hyperintense areas in the right cortex in (**A**) T2-weighted image and (**B**) fluid-attenuated inversion recovery (FLAIR) images, and no clear signs of subarachnoid hemorrhage were observed on (**C**) diffusion-weighted imaging (DWI).

neurological symptoms were absent and limb muscle strength had returned to normal. Brain MRI showed that the sulci and gyri had returned to normal in frontal, parietal, temporal and occipital, cerebral edema had disappeared, and no residual cerebral infarction or hemorrhage was observed. These findings indicated a good prognosis.

Discussion

Contrast-induced encephalopathy is a known uncommon complication associated with use of intravascular radiocontrast media during percutaneous carotid and coronary interventions.[1,7] The incidence of CIE ranges between 0.3% and 1.0%. However, use of hyperosmolar iodinated contrast agents results in an incidence of CIE of up to 4%.[8,9] Although non-ionic, low-osmolar agents are relatively less neurotoxic,[10,11] these agents are associated with pharmacological side effects such as confusion, seizure, altered cerebral function, mental aberrations, and ophthalmoplegia, all of which can induce CIE.[2,3,5] Since the first clinical description of CIE in 1970, there have been 36 cases of CIE following cardiac catheterization with non-ionic, low-osmolar contrast agents in a total of 41 patients reported in the literature (Table 1).[2,3,5,7,12–43] In this report, we presented a highly probable case of post-CAG CIE following administration of a small amount of non-ionic, low-osmolar contrast agent, with severe symptoms and spontaneous recovery.

The mechanism and causes of iodine-based contrast-induced neurotoxicity are unclear. Compared to lower osmolality or iso-osmolar solutions, hypertonic contrast agents are more likely to disrupt the BBB, resulting in increased entry into the brain, which can result in edema and direct neuronal toxicity.[44,45] However, many studies have shown that CIE can occur in response to high or low osmolality compounds.[21,25] We identified 23 of 41 (56.09%) cases that resulted from percutaneous coronary interventions (PCI), and the remaining 18 occurred during diagnostic CAG. The median volume of contrast media administered was 168.5 mL (range from 75 to 500 mL). In our case, the patient developed CIE following administration of 20 mL of iopromide, a low-osmolar, non-ionic, monomeric, iodine-based contrast agent during CAG. In addition to use of contrast agents, male gender, hypertension, diabetes mellitus, impaired renal function, impaired cerebral autoregulation, and transient ischemic attack (TIA) are risk factors for development of CIE.[46,47] In patients with renal failure, renal excretion of contrast media is delayed and brain concentrations of contrast agent can remain high, resulting in increased risk of developing CIE.[11] Furthermore, chronic hypertension impairs cerebral autoregulation and TIA may increase permeability of the BBB, which may contribute to contrast extravasation.[25,48] Review of the literature showed that the median age of patients with CIE was 63 years (range from 1.5 to 82 years), and 72.50% of patients were male. Most of the patients had diabetes, hypertension, chronic kidney disease, or other comorbidities. Our 84-year-old female patient had chronic hypertension, which is typically associated with poor control of blood pressure, which may contribute to increased blood-brain barrier permeability. Advanced age and high blood pressure may have resulted in increased risk of contrast-induced encephalopathy in response to 20 mL of contrast medium.

Clinical presentations of CIE are highly variable and include localized cortical and subcortical deficits such as hemiparesis, hemianopia, cortical blindness, speech changes, parkinsonism, and global syndromes such as confusion, seizure, and coma.[6,49] Transient cortical blindness (TCB) is the most common manifestation of CIE. Literature review indicated that symptoms of neurological dysfunction presented within minutes to hours after contrast agent administration, and most patients fully recovered within 48–72 hours.[2,3,5,7,12–43,50,51] In our case, the patient presented with hemiparesis, hemianopia, and unconsciousness within minutes of radial sheath removal, and more extreme features developed, such as recurrent seizures, and cardiac and respiratory arrest. Her symptoms resolved completely within 72 hours, which was consistent with the clinical course of CIE. We suspect that the severe symptoms of this patient were related to advanced age, hypertension, and other risk factors, which may have increased BBB permeability. This increased permeability may have allowed for contrast agent exudation and brain tissue colloid osmotic pressure changes, resulting in cerebral edema and neurotoxicity and contrast-induced encephalopathy.

Typical head CT imaging findings associated with CIE typically include local cortical enhancement, increased subarachnoid density, and brain edema,[16] which are important for differentiation of CIE from other neurological pathologies such as thromboembolism and hemorrhage following angiography. Moreover, abnormalities observed during emergency CT as measured by Hounsfield units (HU) can help to differentiate blood from contrast, with the higher attenuation (100 to 300 HU) of contrast compared with blood (40 to 60 HU).[52] On MRI, patients with

Table 1 Cases of CIE Following Cardiac Catheterization with Non-Ionic, Low-Osmolar Contrast Agents from 1970-Present

Reference	Age	Gender	Risk Factor	Procedure	Contrast Agent	Contrast Type	Contrast Volume (mL)	Presentation	Neuroimaging	Treatment Provided	Symptom Duration	Complete Symptom Resolution
Eleftheriou et al (2018)[12]	57	F	CKD, HT, DM	Diag+PCI	Iodixanol	Non-ionic, dimer, low osmolar	130	Tonic–clonic seizures	Right-sided relatively widespread edema of the parenchyma (CT)	Supportive care, acyclovir, meropenem, betamethasone.	72 h	Yes
Yen et al (2018)[13]	64	M	CKD, HT, DM	Diag+PCI	Iohexol	Non-ionic, monomer, low osmolar	100	Disorientation with raves	Normal (CT, MRI)	Hemodialysis	N/A	Yes
Dattani et al (2018)[3]	6	M	HT, DM	Diag	Iohexol	Non-ionic, monomer, low osmolar	120	Confused, aggressive, expressing verbal profanities	Normal (CT)	Supportive care	9 d	Yes
Hamra et al (2017)[14]	62	M	HT	Diag+PCI	Iohexol	Non-ionic, monomer, low osmolar	300	Right-sided homonymous hemianopia	Slight enhancement of the venous sinuses (CT)	Supportive care	48 h	Yes
Spina et al (2017)[15]	65	M	Previous CIE	Diag	Iopromide	Non-ionic, monomer, low osmolar	120	Global aphasia, bilateral limb weakness	Normal (CT, MRI)	Supportive care	24 h	Yes
Gollol Raju et al (2015)[16]	44	F	ESKD, HT, DM	Diag+PCI	Iohexol	Non-ionic, monomer, low osmolar	190	Left-sided weakness, seizure activity	Contrast enhancement of right cerebral hemisphere(CT)	Anticonvulsants, hemodialysis	72 h	Yes
Kocabay et al (2014)[2]	68	M	HT	Diag+PCI	Iopromide	Non-ionic, monomer, low osmolar	250	Monoplegia	Normal (CT and MRI)	Supportive care	12 h	Yes
	58	F	HT	Diag+PCI	Iopromide	Non-ionic, monomer, low osmolar	220	Bilateral oculomotor opthalmoplegia	Normal (CT and MRI)	Supportive care	>30 d	No

(*Continued*)

Table 1 (Continued).

Reference	Age	Gender	Risk Factor	Procedure	Contrast Agent	Contrast Type	Contrast Volume (mL)	Presentation	Neuroimaging	Treatment Provided	Symptom Duration	Complete Symptom Resolution
Kocabay et al (2014)[2]	70	M	HT	Diag+PCI	Iopromide	Non-ionic, monomer, low osmolar	130	Cerebellar dysfunction	Normal (CT and MRI)	Supportive care	14 h	Yes
	68	M	HT, DM	Diag+PCI	Iopromide	Non-ionic, monomer, low osmolar	180	Unilateral oculomotor monoplegia	Normal (CT and MRI)	Supportive care	1 h	Yes
Sridhar et al (2014)[17]	63	F	HT, DM	Diag (IMA graft)	Iopamidol	Non-ionic, monomer, low osmolar	250	Cortical blindness	Contrast enhancement of occipital lobes (CT), no ischemia or hemorrhage on MRI	Supportive care	72 h	Yes
Ting et al (2013)[18]	49	M	–	Diag	Iopromide	Non-ionic, monomer, low osmolar	205	Confusion, decrease in level of consciousness	Normal (CT and MRI/A)	Supportive care	12 h	Yes
Liao et al (2013)[19]	76	F	HT, DM	Diag	Ioversol	Non-ionic, monomer, low osmolar	125	Aphasia, cortical blindness, rightsided weakness	Hyperintensity high frontoparietal regions (MRI)	Supportive care	48 h	Yes
Terlecki et al (2013)[20]	32	M	–	Diag	Iopromide	Non-ionic, monomer, low osmolar	100	Cortical blindness	Normal (CT)	Supportive care	24 h	Yes
Law et al (2012)[21]	69	F	CKD, DM, PCR	Diag+PCI	Iodixanol	Non-ionic, dimer, low osmolar	320	Partial seizure, homonymous hemianopia, hemisensory loss, hemiparesis	Cerebral edema (CT)	Intravenous benzodiazepines, thrombolysis	24 h	Yes

Jiang et al (2012)[22]	64	M	HT, DM	Diag+PCI	Iopromide	Non-ionic, monomer, low osmolar	160	Confusion, irritability, limb paralysis, aphasia	Hyperdensity of sagittal sinus (CT). Slowing in a range occipital lobe (EEG)	Supportive care	28 h	Yes
Aykan et al (2012)[23]	68	M	HT	Diag+PCI	Iopromide	Non-ionic, monomer, low osmolar	250	Left lower extremity weakness and sensory loss	Contrast enhancement sagittal sinus and occipital lobe (CT)	Supportive care	12 h	Yes
Kocabay et al (2011)[7]	47	M	–	Diag+PCI	Iopromide	Non-ionic, monomer, low osmolar	150	Confusion, agitation, nausea, headache	Contrast enhancement of occipital lobes (CT)	Supportive care	8 h	Yes
	70	M	DM	Diag+PCI	Iopromide	Non-ionic, monomer, low osmolar	120	Confusion, agitation, nausea, headache	Contrast enhancement of occipital lobes (CT)	Supportive care	12 h	Yes
Gürer et al (2011)[24]	69	M	–	Diag+PCI	Iohexol	Non-ionic, monomer, low osmolar	100	Confusion, headache, vomiting, left hemiplegia,	Focal hyperdense lesions	Supportive care	6 h	Yes
Chisci et al (2011)[25]	76	M	CKD, DM	PCI+CAS	Iodixanol	Non-ionic, dimer, low osmolar	200	Stupor, aphasia, hemiparesis	Hyperdensity of cerebral sulci and subarachnoid spaces	Intravenous mannitol, methylprednisone,	48 h	Yes
Akhtar et al (2011)[26]	39	F	–	Diag	Iopamidol	Non-ionic, monomer, low osmolar	80	Cortical blindness	Normal (CT, vertebral angiogram)	Antiplatelet therapy, intravenous heparin	1 h	Yes
Borghi et al (2008)[27]	74	M	HT	Diag+aorto-gram	Iomeprol	Non-ionic, monomer, low osmolar	320	Cortical blindness	Normal (CT)	Supportive care	24 h	Yes

(*Continued*)

Table 1 (Continued).

Reference	Age	Gender	Risk Factor	Procedure	Contrast Agent	Contrast Type	Contrast Volume (mL)	Presentation	Neuroimaging	Treatment Provided	Symptom Duration	Complete Symptom Resolution
Sawaya et al (2007)[5]	N/A	M	–	Diag+PCI	Iohexol	Non-ionic, monomer, low osmolar	120	Agitation, confusion, convulsions, slurred speech, loss of consciousness	Normal (CT) Diffuse slowing in the theta range over both hemispheres (EEG)	Orotracheal intubation and ventilation, intravenous benzodiazepines, hydration	18 h	Yes
Tatli et al (2007)[28]	52	F	–	Diag	Iomeprol	Non-ionic, monomer, low osmolar	150	Cortical blindness	Contrast enhancement of occipital lobes (CT)	Supportive care	5 h	Yes
Yazici et al (2007)[29]	70	F	DM, HT	Diag	Iobitridol	Non-ionic, monomer, low osmolar	75	Cortical blindness	Contrast enhancement of occipital lobes (CT)	Supportive care	72 h	Yes
Frye et al (2005)[30]	18 mo	M	–	Diag	Ioversol	Non-ionic, monomer, low osmolar	7mL/kg	Myoclonus	Right holohemispheric parenchymal and subarachnoid hyperdensity cerebral edema	Intravenous benzodiazepines	24 h	Yes
Schulte A et al (2004)[31]	56	M	–	Diag	Iopromide	Non-ionic, monomer, low osmolar	135	Confusion, dysarthria, cortical blindness	Contrast enhancement right occipital lobe	Supportive care	24 h	Yes
Velden et al (2003)[32]	82	F	CKD, HT	Diag+PCI	Iomeprol	Non-ionic, monomer, low osmolar	500	Aphasia, right-sided hemiparesis	Hyperdensities filling the sulci of both cerebral hemispheres	Supportive care	40 h	Yes

Foltys et al (2003)[33]	82	M	CKD, DM, HT	Diag (IMA graft)	Iopromide	Non-ionic, monomer, low osmolar	130	Right-sided hemiparesis, aphasia	Cerebral edema and extravascularly localized contrast media left hemisphere	Supportive care	6 h	Yes
Gellen et al (2003)[34]	52	N/A	CKD	Diag (IMA graft)	Iopamidol	Non-ionic, monomer, low osmolar	400	Cortical blindness	Contrast enhancement occipital lobes	Supportive care	72 h	Yes
Yildiz et al (2003)[35]	63	M	–	Diag +Aortogram	Iomeprol	Non-ionic, monomer, low osmolar	450	Amnesia, numbness, right upper extremity numbness	Contrast enhancement right occipital lobe	Intravenous dexamethasone	12 h	Yes
Lim et al (2002)[36]	63	F	DM, HT	Diag (IMA graft)	Iopromide	Non-ionic, monomer, low osmolar	160	Cortical blindness, right homonymous hemianopia	Contrast enhancement of occipital lobes (CT, MRI)	Supportive care, intravenous heparin	48 h	Yes
Zwicker et al (2002)[37]	52	F	HT	Diag+PCI	Ioversol	Non-ionic, monomer, low osmolar	280	Cortical blindness	Contrast enhancement of occipital lobes (CT)	Supportive care, antihypertensives	36 h	Yes
Kwok et al (2000)[38]	53	M	–	Diag	Ioversol	Non-ionic, monomer, low osmolar	100	Cortical blindness, catatonia	Normal (CT, MRI)	Antiplatelet therapy, low molecular weight heparin	12 h	Yes
Vranckx et al (1999)[39]	68	M	–	Diag (IMA graft)+PCI	Iohexol	Non-ionic, monomer, low osmolar	180	Cortical blindness, aphasia, periodic alternating gaze with nystagmus	Contrast enhancement of occipital lobes, temporal lobes, thalami (CT)	CPR, temporary transvenous pacemaker	6 d	No

(*Continued*)

Table 1 (Continued).

Reference	Age	Gender	Risk Factor	Procedure	Contrast Agent	Contrast Type	Contrast Volume (mL)	Presentation	Neuroimaging	Treatment Provided	Symptom Duration	Complete Symptom Resolution
Sticherling et al (1998)[40]	55	M	–	Diag (graft)	Iomeprol	Non-ionic, monomer, low osmolar	280	Cortical blindness	Contrast enhancement of occipital lobes (CT)	Supportive care	5 d	Yes
Kamata et al (1995)[41]	62	M	CKD, HT	Diag (IMA graft)+PCI	Iopamidol	Non-ionic, monomer, low osmolar	170	Headache, confusion, cortical blindness	Contrast enhancement cerebellum, thalamus	Thrombolysis, intravenous dexamethasone, glycerine, plasma expander	12 h	Yes
Rama et al (1993)[42]	59	M	HT	Diag+PCI	Ioversol	Non-ionic, monomer, low osmolar	220	Cortical blindness	Normal (CT)	Supportive care	12 h	Yes
	45	M	HT	Diag+PCI	Ioversol	Non-ionic, monomer, low osmolar	167	Cortical blindness	Normal (CT)	Supportive care	24 h	Yes
	68	M	HT	Diag+PCI	Ioversol	Non-ionic, monomer, low osmolar	262	Homonymous hemianopia	Normal (CT)	Supportive care	15 min	Yes
Parry et al (1993)[43]	62	M	HT	Diag (IMA graft)	Iopamidol	Non-ionic, monomer, low osmolar	270	Cortical blindness, loss of coordination right arm	Contrast enhancement of occipital lobes (CT)	Supportive care	72 h	Yes

Abbreviations: HT, hypertension; DM, diabetes mellitus; CKD, chronic kidney disease; ESKD, end stage kidney disease; CT, computed tomography; MRI, magnetic resonance imaging; Diag, diagnostic; PCI, primary coronary intervention; CAS, carotid artery stenting; EEG, electroencephalogram; IMA, internal mammary artery.

CIE showed hyperintense areas on spin-spin relaxation time, FLAIR, and DWI imaging, and no change in apparent diffusion coefficient (ADC) maps, which differs from observations consistent with cerebral ischemia.[48] However, some patients with CIE have no radiological features. In addition, CSF examination is useful to rule out subarachnoid hemorrhage through absence of xanthochromia or red blood cells. Simultaneous high concentrations of iodine contrast in the CSF and serum support contrast extravasation rather than hemorrhage.[32] Brain CT of our patient immediately following the first symptom showed no acute pathological findings, but indicated multiple high-density subarachnoid regions after 2 hours. Cerebral edema occurred 10 hours after surgery. Brain MRI showed hyperintense areas in the right cortex via FLAIR imaging, which further supported a diagnosis of CIE.

Most patients with CIE have a good prognosis and recover quickly with supportive treatment including intravenous fluids and close observation. In some cases, anticonvulsive drugs can be used to treat seizures and mannitol can be used to decrease pressure in the brain. Steroid hormones such as dexamethasone can be used to reduce inflammatory reactions as necessary.[2,3,5,7,12–43] Neurological toxicity typically occurs within minutes or hours after angiography, and resolves spontaneously within 72 hours. Although the prognosis of most cases of CIE is good, some cases with persistent deficits have been reported.[4] Eight cases of autopsy-confirmed fatal cerebral edema due to contrast neurotoxicity in the early stage of angiography have been observed in response to administration of ionic high osmolar contrast agents.[53–55] Recently, a small body of literature has shown that low osmotic pressure contrast agents can induce permanent neurological dysfunction[4] and fatal cerebral edema.[56] In our case, the patient developed recurrent seizures and cardiac and respiratory arrest, but her neurological symptoms gradually improved after 3 days in response rehydration, anticonvulsant therapy, reduction of cranial pressure, and treatment with dexamethasone.

There is clinical and radiological overlap between CIE and posterior reversible encephalopathy syndrome (PRES), which is a reversible clinicoradiological subcortical vasogenic edema in patients with acute neurological symptoms (eg, seizures, encephalopathy, visual disturbances, and focal neurological deficits) that occurs more frequently in patients with uncontrolled hypertension and chronic kidney disease.[57] Magnetic resonance imaging findings in CIE with hyperintensity on DWI and FLAIR, and no change in ADC, can overlap with PRES radiological features.[58] Moreover, the pathophysiological theory underlying PRES supports endothelial dysfunction related to abrupt blood pressure changes and/or direct effects of cytokines. This results in breakdown of the blood-brain barrier and subsequent brain edema. Therefore, the pathophysiological mechanism of PRES following CAG, similar to that in CIE, may be endothelial dysfunction indirectly induced by contrast media through excessive circulating cytokines, such as endothelin-1, which have been shown to be increased by administration of moderate levels of contrast media.[59–61] In our case, CIE could also be considered a case of PRES triggered by contrast media administration.

Conclusion

Contrast-induced encephalopathy following cardiac catheterization is a rare but complex neurological disturbance. Manifestations of CIE vary, but the prognosis is typically good in conjunction with supportive treatment. Although many studies have suggested that the risk of developing CIE is higher in response to high osmolality agents, our review demonstrates that severe symptoms of CIE can also occur in response to small amounts of low-osmolar, nonionic, monomeric iodine-based contrast agents. Contrast-induced encephalopathy must be considered in differential diagnosis of stroke following cardiac catheterization. Early clinical suspicion of CIE might alter therapeutic considerations and may help to avoid potentially harmful interventions such as thrombolysis.

Ethics Approval

The Institutional Review Board of China-Japan Friendship Hospital approved the publication of the case details.

Consent for Publication

A signed informed consent was obtained from the patient for publication of the case details and any accompanying images.

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Disclosure

The authors report no conflicts of interest in this work.

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