Irreversible fatal contrast-induced encephalopathy: a case report

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Case Report

Keywords: Digital subtraction angiography; iodinated contrast agents; complications; contrast-induced encephalopathy

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Abstract

Background: Contrast-induced encephalopathy (CIE) is a well known complication of iodinated contrast agents during angiography and vascular interventions. It can be manifested as hemiparesis, cortical blindness, speech changes, parkinsonism, confusion, seizure, and coma etc. Most of the reported CIE cases were transient and reversible. Irreversible fatal CIE cases were rarely reported. All the fatal CIE cases reported before used the ionic high osmolar contrast agents. Here we document a heretofore unreported fatal CIE after digital subtraction angiography (DSA) using iopamidol, which is a type of non-ionic monomer low osmolar contrast agent.

Case presentation: A 71-year-old woman was admitted to our neurology department for paroxysmal buzzing of the brain. The cerebral magnetic resonance angiography (MRA) indicated arteriosclerosis of cerebral arteries and stenosis of bilateral middle cerebral arteries. Then she took DSA for further diagnosis. Total amount of iopamidol used during the procedure was 110 ml. The patient manifested headache during the procedure, and then had dizziness with nausea and vomiting. Although the patient was treated with anti-edema drugs, the deterioration was continuous, she gradually became coma state, and suffered irreversible fatal cerebral edema, which had been confirmed by cerebral computed tomography (CT) scans. At last, the patient died 56 days after the procedure due to irreversible fatal cerebral edema.

Conclusions: This report indicates that iopamidol induced encephalopathy may not always have a benign outcome and can cause irreversible fatal cerebral edema.

Keywords: Digital subtraction angiography; iodinated contrast agents; complications; contrast-induced encephalopathy

Background

Contrast-induced encephalopathy (CIE) is a known but rare complication of angiography and endovascular interventions, the presentations include hemiparesis, cortical blindness, speech changes, parkinsonism, confusion, seizure, and coma etc[1, 2]. In the most reported cases, symptoms are reversible, fatal encephalopathy following iodinated contrast administration was rarely reported. Only 8 cases of autopsy proven fatal cerebral edema due to contrast neurotoxicity in the early stage of angiography were reported[1, 3, 4]. All these reported fatal cases involved the use of high osmolar contrast agents. Iopamidol is a non-ionic monomer low osmolar contrast agent, which has been reported in reversible contrast-induced encephalopathy cases[5-9]. Here we describe a patient suffered irreversible fatal encephalopathy after DSA using iopamidol.

Case Presentation

A 71-year-old woman with a history of hypertension, hyperlipemia, angina was admitted to our neurology department for paroxysmal buzzing of the brain. Physical examination showed the bilateral decreased
hearing. The cerebral magnetic resonance imaging (MRI) of the patient indicated multiple cerebral infarctions and bilateral demyelination in the centrum semiovale. The cerebral MRA indicated arteriosclerosis of cerebral arteries, and stenosis of bilateral middle cerebral arteries. For further diagnosis, the patient took DSA subsequently. Total amount of iopamidol (Bracco Imaging Italia S.r.L.) used was 110 ml during the procedure. The DSA showed that the patient had bilateral embryonal posterior cerebral arteries, the left middle cerebral artery was 40% stenosis and bilateral vertebral arteries were tortuous. There was no obvious calcification of the aortic arch, only once angiography was done in the arch using 25ml iopamidol. 10 minutes after the aortic arch angiography, the patient manifested mild headache. The pain was bearable, and the patient could cooperate the procedure. The DSA finished 20 minutes later, there was no hemorrhage or vasospasm during the procedure. Headache was continuous, and the patient suffered nausea and vomiting. The immediate physical examination showed no obvious abnormal sign. The patient was treated with 8mg ramosetron and 10mg dexamethasone. After 20 minutes observation, the symptoms were relieved. And the cerebral CT-scan at this moment was normal (Figure 1 A, B, C). 2 hours later, the patient manifested dizziness with nausea and vomiting, she was treated with 8mg ondansetron and 20mg diphenhydramine. Compound sodium chloride injection was used to facilitate the elimination of the contrast agent meanwhile. The treatment alleviated the symptoms. 4 hours after the procedure, the patient manifested dizziness again, 5mg dexamethasone was administered, but the dizziness was not relieve, and she vomited again. At 11 hours, the dizziness was alleviated, but the blood pressure rose to 183/92mmHg, the patient was drowsy, but could answer questions correctly; pupil diameters of both eyes were normal and equal, pupillary light reflex was sensitive, and the movement of the limbs was normal. Then the patient was treated with 30mg nimodipine tablets to alleviate the high blood pressure. 14 hours after the procedure the patient fell asleep, but at 17 hours, the electrocardiograph monitoring showed sudden respiratory failure, pulse oxygen saturation reduced to 88%, and gradually declined. The patient was coma state, sighing respiration, the pupil diameters of both eyes were not equal and unreactive, the left one was 4.5mm and the right one was 3mm, limbs drop test was positive, Babinski sign was negative. Cerebral hernia was considered due to the sudden deterioration. The patient was treated with oxygen inhalation, 20% mannitol, nikethamide, lobeline and diprophylline. And the patient was transferred to intensive care unit for further treatment after cardio-pulmonary resuscitation, endotracheal intubation and mechanical ventilator treatment. 2 days after the procedure, cerebral CT-scan indicated diffuse cerebral edema, loss of grey-white differentiation, effacement of the cerebral sulci and decrease in cerebrospinal fluid space (Figure 1 D, E, F). The patient was treated with dehydration, mechanical ventilator, anti-infection etc., but the diffuse cerebral edema did not improve. 9 days after the procedure, the third cerebral CT-scan showed the cerebral edema became much more serious, the ventricles were disappeared and there was hyperdense in the subarachnoid space which was considered to be pseudo-subarachnoid hemorrhage due to the serious cerebral edema [10] (Figure 1 G, H, I). 15 days after the procedure, the cerebral CT showed unrelieved diffuse edema of the brain, and the hyperdense in the subarachnoid space still existed (Figure 1 J, K, L). All these cerebral CT-scans did not show intra cerebral hemorrhage or infarct happened in this patient. The patient was continuous deep coma status, the brainstem reflexes disappeared, and died 56 days after that sudden deterioration.
Discussion And Conclusions

The prognosis of most CIE is generally reported with rapid recovery only rare reported cases with the persistent deficits[2]. Notably, there were 8 cases of autopsy proven fatal cerebral edema due to contrast neurotoxicity in the early stage of angiography[1, 3, 4]. The 8 death cases included 6 infants of these patients received cardiac angiography, and the other 3 received aortography. All the fatal cerebral edema cases reported before used the high osmolar contrast agents. and high osmolar contrast agents are no longer used in routine angiography and intervention procedures now. The case which we report here may be the first fatal cerebral edema after DSA using iopamidol. This case highlights the potential for other types of iodinated contrast agents to induce fatal encephalopathy.

Diagnosis of CIE is important, as it may have a similar presentation to embolic, and hemorrhagic complications following angiography or endovascular interventions. Typical radiological findings include abnormal cortical contrast enhancement and cerebral edema, subarachnoid contrast enhancement and striatal contrast enhancement[2, 11]. CT or MRI of the brain help us to differentiate CIE from hemorrhage or infarct. In the case which we report here, the CT-scans of the brain after DSA immediately, 2 days, 9 days and 15 days after the procedure did not indicate intra cerebral hemorrhage or infarct. Therefore, the possibility of multiple embolisms was not considered in this case. The hyperdense of subarachnoid space in the cerebral CT scans was considered to be representation due to the serious diffuse cerebral edema. The hyperdense appearance results from a combination of loss of gray-white differentiation, narrowing and effacement of the subarachnoid spaces, and corresponding engorgement of superficial pial veins[10].

The mechanism of contrast-induced encephalopathy is controversial. The disruption of the blood-brain barrier after injection of the iodinated contrast agent is widely accepted[2, 11-15]. Both of the hyperosmolality and chemotoxicity of the contrast media contribute to the neurotoxicity happening. All types of iodinated contrast agents can induce the happening of neurotoxicity, but the occurrence of fatal cerebral edema is very rare. In view of the rare happening rate of fatal cerebral edema, it tends to be an idiosyncratic reaction. Unfortunately, there is no effective treatment for this severe fatal CIE. In the Junck L and Marshall WH reported case[4], the postmortem tissue iodine concentrations test showed the highest concentration of iodine in urine, serum and kidney. The continuous renal replacement therapy and continuous blood purification maybe potential treatment for the fatal CIE.

In summary, CIE always had benign outcomes in the previous study, we presented a fatal cerebral edema case after DSA using iopamidol, this illuminates the potential to cause severe complications even fatal cerebral edema for all types of iodinated contrast agents. This severe potential harmful effect should be realized by the doctors performing angiography and interventions. Due to the rare occurrence rate, the possible mechanism of the fatal cerebral edema tends to be an idiosyncratic reaction for the iodinated contrast agents, which makes the prevention of the severe complication to be very difficult. Much more studies are needed to define the risk factors and the mechanism of the iodinated contrast agent neurotoxicity, which may help us to avoid the happening of the severe complication.
Abbreviations

CIE: Contrast-induced encephalopathy;
CT: Computed tomography;
DSA: Digital subtraction angiography;
MRA: Magnetic resonance angiography;
MRI: Magnetic resonance imaging.

Declarations

Ethics approval and consent to participate

Institutional review board of Qianfoshan hospital affiliated to Shandong University approved the study.

Consent for publication

Signed informed consent was obtained from the patient guardian for publication of this case report and accompanying neuroimages.

Availability of data and material

All data generated or analyzed during this study are included in this article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions
WZ designed and wrote the manuscript. JPZ, YS, and LLS examined the patient. MMZ, HY, JZ and WW analyzed neuroimages. JH examined the patient, designed the case report and helped to draft the manuscript. All authors read and approved the final manuscript.

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Cerebral CT after DSA immediately did not indicate obvious abnormal sign (A, B, C); 2 days after the procedure, the cerebral CT indicated diffuse cerebral edema, loss of grey-white differentiation, effacement of the cerebral sulci and decrease in cerebrospinal fluid space (D, E, F); 9 days after the procedure, the
cerebral CT showed more serious diffuse edema of the brain, loss of grey-white differentiation, effacement of the cerebral sulci and subarachnoid space, disappearance of the cerebral ventricles and enhancement in the subarachnoid space, and darkened brain in Hounsfield units (G, H, I); 15 days after the procedure, the cerebral CT showed unrelieved diffuse edema of the brain with effacement of cerebral ventricles and sulci, darkened brain in Hounsfield units, and enhancement in the subarachnoid space(J, K, L).

**Supplementary Files**

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- supplement1.jpg