



## Case Report



# Transient Global Amnesia Induced by Iodixanol During Percutaneous Coronary Intervention: A Rare Neurological Adverse Reaction

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## Abstract

**Background:** Iodixanol is a non-ionic contrast medium. The most common adverse effects of iodixanol include skin rashes and kidney injury. To date, there have been no reports of Transient Global Amnesia (TGA) for iodixanol after post-marketing surveillance. This case is to declare a heretofore unreported adverse effect of iodixanol during Percutaneous Coronary Intervention (PCI).

**Case presentation:** A 71-year-old man, with a history of coronary artery disease was admitted to outpatient department for chest pain and tightness. Before combined Coronary Arteriography (CAG) and PCI using 100ml iodixanol. Iodixanol-induced TGA, which manifested sudden amnesia after the procedure, was diagnosed by urgent Computed Tomography (CT). CT result did not reveal any recent cerebral ischemia, and physical examination showed no obvious neurological deficit. The patient recovered uneventfully within 24 hours, and without any neurological sequelae.

**Conclusion:** This case serves to describe that iodixanol may induce transient amnesia. Given the wide use of iodixanol in cardiology, clinicians should be aware of this potential adverse effect.

## Keywords

Adverse Effect; Iodixanol; Transient Global Amnesia

## Introduction

Iodixanol injection is a water-soluble, low-osmolar, non-ionic, hexa-iodinated Contrast Medium (CM) which is used for Coronary Angiography and Percutaneous Coronary Intervention (PCI) [1]. Compared to ionic CM, non-ionic CM has been confirmed to reduce the incidence of adverse reactions. Adverse reaction of CM can be divided by immediate and late. The late reactions are of low incidence within 0.5 to 2% of patients that are exposed to non-ionic CM [2]. Late-onset reactions become apparent from 1 h to 7 days after the exposure of CM [3].

Transient global amnesia is a clinical syndrome characterized by sudden onset of amnesia lasts less than 24 hours, associated with recognition impairment without accompanied by compromise of other neurologic deficits [4,5]. The most common adverse effects of iodixanol include skin rashes, erythema, angioedema and renal injury. To be our best knowledge,

there are no reports of transient global amnesia associated with the use of iodixanol. Here, we describe a rare case of transient global amnesia in a patient after administration of iodixanol undergoing Coronary Arteriography (CAG) and PCI.

## Case Report

A 71-year old male, with a history of coronary artery disease, presented to outpatient department with typical chest tightness after exercise. The patient was diagnosed with coronary atherosclerotic cardiopathy, hypertension, diabetes, hyperlipemia, lacunar infarction. The hematologic report showed mild erythropenia (red cell count,  $3.96 \times 10^{12}/L$ ), decreased hemoglobin (hemoglobin, 129 g/L). The liver function index disclosed abnormal with aspartate aminotransferase (58.4 U/L) and alanine aminotransferase (99.5 U/L). Other results of routine blood tests, including thyroid function evaluation and coagulative screening, were within the normal range. Cardiac ultrasonography after admission displayed enlarged left atrial diameter and decreased left ventricular relaxation function. The patient was pre-treated with heparin sodium injection (12500 units), double antiplatelet regimen including aspirin (100 mg qd) and ticagrelor (90 mg bid). Meanwhile, preoperative 0.9% sodium chloride injection was used to accelerate the excretion of contrast agent (CM). Coronary angiogram was administrated by non-ionic CM iodixanol. A total of 100 ml iodixanol was used during the operation. The image of coronary angiogram showed the presence of stent stenosis of Right Coronary Artery (RCA) and Left Circumflex Branch (LCX), thus physician conducted a Percutaneous Transluminal Coronary Angioplasty (PTCA) to RCA and Percutaneous Coronary Intervention (PCI) to LCX, with the placement of two drug-eluting stents ( $2.5 \times 35$  mm and  $3.0 \times 35$  mm). The whole procedure was successful, but the patient manifested sudden amnesia accompanied with forgetting own daughter's name two hours later, mainly concerning the memory loss itself. Then the patient was administrated by urgent Computed Tomography (CT) and electrocardiography. Such situation lasted about one hour, and then returned back to normal. During this period, the patient was submitted to a neurological assessment, the neurological examination was normal. A brain CT imaging showed normal structure without pathological changes. Patient was prescribed with double antiplatelets including aspirin and ticagrelor. After follow-up, neurological test was negative, the patient was clinically and neuroradiologically stable without recurrent amnesia.

## Discussion

Transient Global Amnesia (TGA) usually occurs in patients aged 50 to 70 years old, characterized by the abrupt onset of severe anterograde amnesia. Patients remain features of retrograde

amnesia without focal neurologic defects [6]. The pathogenesis of TGA still remains unclear. The diagnostic criteria for TGA is listed as follows: 1. Presence of attack was witnessed by a capable observer; 2. Presence of an anterograde amnesia; 3. No other cognitive impairment except for amnesia; 4. No clouding of consciousness or loss of personal identity; 5. No significant neurologic or epileptic features; 6. No recent history of head injury or seizures; 7. Resolution of the attack within 24h [7]. The most symptom of our patient accorded with diagnostic criteria for TGA. The presence of anterograde amnesia was witnessed in this patient by an experienced clinician without other cognitive impairment except for amnesia. The patient had clear cognition but loss of personal identify to her daughter. There was no clouding of consciousness or loss of personal identity and resolution of symptoms within 24 h. So the patient was diagnosed with TGA. The risk factors for TGA are mainly considered cardiovascular risk factors, including ischemic heart disease and carotid atheromasia [8]. TGA usually have a higher incidence with risk factors and an advanced age of about seventy ages [9]. Our patient is at high risk factors of TGA due to combination of both advanced age and cardiovascular disease.

Drugs have been known to be an important role in causing amnesia. The increasing incidence of amnesia may be related with drugs, including sibutramine, iomeprol [10,11]. Aspirin is known to exacerbate respiratory disease [12], nevertheless most common side effect is bleeding, as well as ticagrelor. There are no case reports of amnesia associated with aspirin and ticagrelor, and the patient has taken both drugs for a long period of time before admission. Clinical follow up post-discharge showed no residual or recurrent amnesia, so transient amnesia induced by two antiplatelet drugs can be excluded in this patient. The most possible causative agent for transient amnesia may be iodixanol.

Iodixanol is a water-soluble, non-ionic contrast medium for CAG. The common adverse effects of iodixanol include angina pectoris, chest pain, headache, altered sense of smell, paresthesia, pruritus, erythema, skin rash, dysgeusia, nausea, etc. The rare adverse reactions are acute renal failure, agitation, amnesia, anaphylactoid reaction, anxiety, back pain, bronchitis. Case of contrast-induced encephalopathy using iodixanol was ever reported [13]. In a double-blind randomized phase III study, one serious adverse event of amnesia was reported in a patient administrated by iodixanol [14]. However, no reported event during post-marketing surveillance of iodixanol showed the occurrence of amnesia. The mechanism of iodixanol-associated amnesia is still unknown. The neurological adverse reactions with non-ionic CM in animal experiments has been described, however neurotoxicity has never been demonstrated in humans [15]. We found out a possible original hypothesis about that neurological adverse reaction with non-ionic CM

in humans. To our knowledge, no cases of transient amnesia associated with iodixanol have been reported to date. Our report is the first case of iodixanol-induced amnesia after post-marketing surveillance. The patient in our case suffered from amnesia after taking iodixanol about 2 hours without other neurological symptoms, and the pattern of amnesia is temporary rather than progressive. An urgent Computed Tomography (CT) was performed, CT scan did not show any recent cerebral hemorrhage. Due to the short duration of symptoms, the patient was not medicated. Approximately one hour later, amnesia was disappeared and there was no further amnesic episode.

In a conclusion, we consider that the occurrence of amnesia is associated with iodixanol. This case is the first report of iodixanol related with amnesia after post-marketing surveillance. This case reminds clinicians and pharmacists to focus on the potential adverse reactions to iodixanol.

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