

Contrast Medium-Induced Encephalopathy after Coronary Angiography– Case Report

Sebastian Andone¹, Rodica Balasa², Laura Barcutean¹, Zoltan Bajko^{2*}, Valentin Ion³, Anca Motaitianu², Adina Stoian⁴, Smaranda Maier²

¹ Doctoral School, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Romania

² Department of Neurology, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Romania

³ Department of Analytical Chemistry and Drug Analysis, Faculty of Pharmacy, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Romania

⁴ Department of Pathophysiology, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Romania

ABSTRACT

Introduction: Contrast-induced encephalopathy represents a rare, reversible complication that appears after intravenous or intra-arterial exposure to contrast agents. There is no consensus in the literature regarding the mechanism of action. However, the theoretical mechanism is set around the disruption of the blood-brain barrier and the contrast agents' chemical properties. **Case report:** The case of a 70-year-old patient, known to have hypertension and type 2 diabetes mellitus is reported. The patient had undergone a diagnostic coronary angiography during which he received 100ml of Ioversol (Optiray 350™). Soon after the procedure, the patient began experiencing a throbbing headache, followed by intense behavioural changes and aggressive tendencies. He was transferred to the Neurology Clinic. The neurological examination was without focal neurological signs; however, the patient was very aggressive and uncooperative. The CT scan revealed a mild hyper-density in the frontal lobes. MRI scan revealed no pathological changes. Conservative treatment with diuretics and hydration was administered, and the patient experienced a complete resolution of symptoms in 72 hours. **Conclusion:** Contrast-induced encephalopathy is a possible secondary complication to contrast agents and a diagnostic challenge, and it should not be overlooked, especially following procedures that use contrast agents.

Keywords: contrast-induced encephalopathy

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INTRODUCTION

Contrast-induced encephalopathy (CIE) represents a rare but reversible complication that appears secondary to intravenous or intra-arterial exposure to iodinated contrast media. Data in the literature is scarce regarding the underlying mechanisms of CIE. However, the proposed mechanism relies on the blood-brain barrier (BBB) disruption, subsequently permitting extravasation of the contrast agent into the central nervous system (CNS) [1]. CIE incidence is reported as 0.05–0.4% after diagnostic and percutaneous coronary angiography [2, 3].

The clinical features of CIE encompass a wide array of symptoms that indicate diffuse CNS involvement. These range from altered mental status, focal deficits,

visual and speech impairment and seizures. Typically they occur in patients with various risk factors, such as hypertension, chronic kidney disease, diabetes or hypersensitivity to iodine agents [4].

Early identification and diagnosis attract a favourable outcome, often with a complete resolution of the symptoms. However, due to the inconsistency of the clinical symptoms and lack of standardised protocol care, the possibility of mismanagement carries a severe prognosis including incomplete neurological recovery or even death.

CASE REPORT

The case of a 70-year-old male patient, previously diagnosed with hypertension, type 2 diabetes mellitus

* Correspondence to: Zoltan Bajko, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Romania. E-mail: zoltan.bajko@umfst.ro

(DM), and micro- and macrovascular complications, including lower extremity artery disease and triple vessel coronary artery disease is reported.

He presented at a private ambulatory clinic in Târgu Mureş, Romania, where he had been scheduled to undergo a diagnostic coronary angiography.

As per the institute's protocol, he received 100 ml of contrast fluid, ioversol (Optiray 350™, Guerbet, Lanester, France), a hyperosmolar non-ionic contrast media. There were no immediate intra- or peri-procedural complications. He was placed in the observational ward, and five hours after the procedure, he complained of a throbbing headache.

Symptomatic treatment was administered, which consisted of a 75 mg dose of intravenous non-steroidal anti-inflammatory drug Refen (S.C. STADA M&D S.R.L., Timișoara, România). Ten hours after the procedure the patient presented with intense behavioural changes, aggressive tendencies and severe, pulsating headache. He was transferred to the emergency department, and an urgent neurological consultation was ordered.

A neurological examination performed eleven hours after the procedure revealed no meningeal signs or motor deficits. The patient was in an acute confused state. He was verbally and physically aggressive and uncooperative. Apart from a mildly elevated blood pressure of 160/70 mmHg, the clinical and para-clinical parameters were unremarkable. The native cerebral computer tomography (CT) effectuated 15 hours after the procedure revealed a mild hyper-density in the frontal lobes (Figure 1 A).

A contrast enhanced cerebral CT scan with 50 ml of contrast fluid (Optiray 350™, Guerbet, Lanester, France) was effectuated immediately after the native CT.

The contrast scan was unremarkable, with no pathological changes observed.

Following a second dose of contrast agent administration, the patient's condition worsened, presenting with severe psychomotor and behavioural disturbance. He exhibited a sudden onset of hetero-aggressive behaviour towards the medical personnel and caregivers, associated with confusion and intense delirium that rendered him unable to recognise any family members.

At this point, a diagnosis of CIE was suspected given the worsening of the clinical pictures and symptoms compatible with higher function impairment following the administration of the contrast agent. Therefore, on second day after the coronary angiography, the patient was hospitalised in the neurology ward.

In the neurology ward, to facilitate contrast agent elimination, the patient was administered 20 mg/2 ml, furosemide (Zentiva, Bucharest, Romania), 75 mg of Refen, (S.C. STADA M&D S.R.L., Timișoara, România) once a day, 200 mg carbamazepine LPH, (Labormed Pharma S.A., Bucharest, Romania) for seven days, with progressive tapering thereafter, 100 mg Aspirin, (Bayer, Leverkusen, Germany), once a day, and 5 mg Prestarium (Servier, Gidy, France), once a day), 0.5 mg, Frontin (EGIS PHARMACEUTICALS PLC, Körmend, Hungary) two times daily for five days, and 3x10 oral drops, of the antipsychotic, haloperidol (Gedeon Richter Romania S.A., Târgu-Mureş Romania) for five days.

On Day one, post-admission, a cerebral MRI was performed, which was unremarkable (Figure 1 B, C).

By three days post-admission, the patient's condition had gradually improved with resolution of the behavioural symptoms and a partial recovery of retrograde memory.

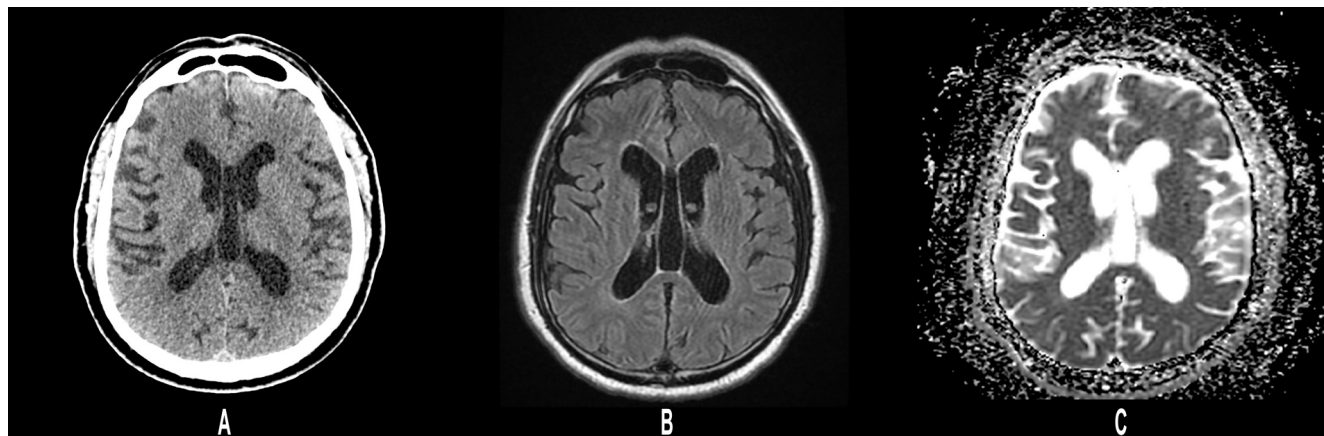


Fig. 1. A. Axial, native cerebral CT scan showing bilateral frontal hyperdensities; B. Axial T2 FLAIR; C. Axial ADC map sequences revealing the absence of lesions in the frontal lobe.

He was discharged ten days after the initial onset, with no neurologic sequelae.

■ DISCUSSION

The underlying mechanism of CIE is still a controversial subject of debate amongst medical specialists. The pathophysiology behind CIE relies on the temporary disruption of the BBB secondary to the administration of the iodinated contrast media [1]. CNS homeostasis is dependent on the integrity of the BBB, which is composed of endothelial cells joined together by tight junctions residing on a basal membrane [5]. Under normal circumstances, the BBB is impermeable to contrast agents. The osmotic balance of the BBB is disturbed as a consequence of contrast agent administration, leading to hyper-osmolarity which in turn causes dehydration of the endothelial cells, leading to shrinkage and tight junction disruption [6, 7, 8].

It is uncertain whether neurotoxicity and secondary brain oedema are solely secondary to the disturbance of the osmotic balance following the administration of contrast agent, or whether the toxic potential of said agents should also be considered. Several studies performed on animal subjects compared the administration of contrast agents, non-ionic monomers, and dimers with mannitol at a higher or similar osmolarity than the contrast agents. Researchers assessed the BBB damage after direct exposure to the selected agents. They found that almost no damage was noted after mannitol administration, which indicated that osmolarity alone is not a risk factor for BBB disruption, with the damage most likely being secondary to the chemotoxicity of the agent or a combination of hyperosmolarity and toxicity [9, 10]. Previous studies have reported that non-ionic agents are less likely to produce BBB disruption [11]. However, several CIE cases were reported after administration of iodixanol, a non-ionic iso-osmolar substance, reinforcing the suspicion that a series of occurrences must be entwined to disrupt BBB permeability [8]. Both ioversol and iodixanol are iodinated, non-ionic water-soluble contrast agents. From a chemical standpoint, both molecules are highly hydrophilic, exhibiting numerous hydroxyl groups. Therefore, these molecules are freely distributed, with only a very small fraction bound to plasmatic proteins. This may have a significant impact when a hyperosmolar solution is administered.

Moreover, the two molecules' chemical similarities are numerous, except that iodixanol is structured as a "dimer". In contrast, ioversol is structured as a monomer [12, 13]. Several predisposing factors for CIE have been previously described. The most common factors include male sex, chronic, poorly controlled hypertension, diabetes mellitus, and chronic kidney disease. The latter factors are associated with insufficiency in cerebral and vascular system autoregulation; together with a large contrast volume (between 80–400 mL) [14]. Overcoming self-regulatory mechanisms by toxic and chemical factors, oxidative stress, neuroinflammation, mitochondrial disorders, and axonal transport disorders ultimately causes cell death [15]. Our patient, having poorly controlled hypertension associated with large vessel disease and microvascular complication, was at risk due to vascular autoregulation's alteration, both at a cerebral and a renal level. It has been documented that chronic uncontrolled hypertension is one of the most significant risk factors for the development of CIE, due to the induction of the contrast agent's extravasation by impairment of the BBB [3].

The paradox of dose-effect has not been noted. There is contradictory data regarding the association between fluid volume and the onset of CIE [16]. This pathology was also triggered in cases where low volumes of contrast agents were administered [17]. Nonetheless, a higher volume leads to more prolonged exposure. Suppose there is an underlying renal disease present. In that case, this can increase the time needed for elimination and therefore favour the onset of CIE.

The usual presentation of CIE is subacute, including transient focal neurological signs such as motor deficits, visual field defects ranging from hemianopia to cortical blindness, seizures, behavioural changes and an acute confusional state. However, in rare and severe untreated cases, the evolution may be towards an altered conscious state, coma and death [1, 14, 18, 19]. Due to a non-specific array of symptoms, the differential diagnosis of encephalopathy should include various CNS infections, subarachnoid haemorrhage, vasculitis, stroke and other possible reversible causes, such as posterior reversible encephalopathy syndrome and hypertensive encephalopathy (PRES) [20, 21, 22]. PRES syndrome requires a particular set of risk factors (female sex, pregnancy). In this case, it was overruled rapidly, together with the vascular causes, given that the MRI and CT scan were unremarkable.

When the suspicion of CIE is addressed, cerebral imaging is of utmost importance. Although a normal CT scan has been reported in some cases, CT changes resembling oedema, focal cortical enhancement, and subarachnoid hyperdensity mimicking subarachnoid haemorrhage have also been reported in the literature [19, 23]. Typically, the MRI findings include T2, fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted images (DWI) hyperintensities, but with normal apparent diffusion coefficient (ADC) sequence, thus differentiating cerebral ischemia from contrast agent extravasation and supporting the non-ischemic nature of this pathology [3, 14, 24, 25]. In the present case, the cerebral CT scan revealed a minor diffuse hyperdensity in the frontal lobe that was non-specific, but which could have explained the acute behavioural changes. The MRI performed at more than 24 hours following the onset of symptoms described no pathological changes, which is unremarkable given that CIE is a regressive pathology. Once the contrast agent is eliminated, there are no indications on cerebral imaging.

The symptoms of CIE typically resolve spontaneously within two days. However, some cases have been reported to last over a week, especially in renal disease patients [3, 16, 20]. The chance of re-occurrence after a new procedure involving contrast fluid is variable. In most cases, if preventive measures are taken, such as adequate hydration and the use of a lower contrast volume, the patients present only with a slight sensitivity to contrast agent or develop no symptoms at all [4]. Law et al. (2015) reported a recurrent CIE case after contrast agent administration, which was resolved under 24 hours [26]. The patient had no epileptic seizures and overall had a satisfying behavioural evolution.

The treatment of CIE has to be tailored to the patient's clinical status and symptoms. Intravenous hydration, diuretics and steroidal agents are mandatory to facilitate the elimination of the contrast agent. If the risk of epileptic seizures is high, anticonvulsants should be administered [20].

■ CONCLUSION

CIE is a possible complication secondary to contrast fluid administration and should be considered, especially in high-risk patients. Therefore, the profile of a male patient with chronic, poorly controlled hypertension with micro and macrovascular complications that

undoubtedly impact the autoregulatory mechanisms should be adequately managed when undergoing catheterisation or contrast imaging. Even if the most typical clinical scenario involves transitory focal neurological deficits, the sudden onset of behavioural changes and memory disorders should not be ruled out of the diagnosis protocol. CIE represents a diagnostic challenge that should not be overlooked, given that when rightfully addressed, the majority of cases are associated with an excellent outcome.

■ CONFLICT OF INTEREST

None to declare.

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