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Case Report

Reversible Acute Onset Coma Following Iodinated Contrast Agent During Carotid Angioplasty And Stenting: Unusual Case Report

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Abstract

Contrast-induced encephalopathy (CIE) is a rare complication of angiographic contrast use that occurs during or after in various angiographic procedures and can result in a range of neurological symptoms. Important diagnostic radiological signs include brain edema and cortical enhancement. Neurotoxicity appears to be due to disruption of the blood-brain-barrier by the high osmolarity of the contrast agent. Here, we present a case of transient contrast encephalopathy "coma of unknown etiology" following carotid angioplasty and stenting (CAS). A 78-year-old right-handed man soon after the procedure of CAS, he developed rapidly aphasia and right faciobrachial hemiparesis. Immediately following neurological focal event, the patient developed psychomotor agitation and delirium. The patient subsequently developed a state of coma. The total amount iomeprol intravascular administered during the procedure was of 190 ml. An emergency nonenhanced CT showed bilateral cortical enhancement and edema in the left cerebral hemisphere. On the second post-procedure day, the patient was transferred to the intensive care unit. Fortunately, her clinical manifestations disappeared gradually, and the patient recovered with complete resolution of contrast enhancement after seven days of conservative treatment. The patients received IV hydration, IV mannitol as part of is treatment protocol. Urgent neuroimaging is important to obtain the correct diagnosis and treated with supportive management as soon as possible. This is an unusual report of neurotoxicity mimicking massive vascular causes of coma clinically. The findings suggest that CIE should be considered in the differential diagnosis if any acute neurological symptoms are noted during and immediately after of angiography examinations. To our knowledge, the development of prolonged coma by neurotoxicity cause, after application of intravascular radiographic contrast is a rare complication of endovascular treatment. This case highlights that severe symptom can persist for many days after endovascular intervention. A high index of suspicion should be maintained for patients with angiographic procedures and rapidly developing neurological deterioration post-procedure. We herein report a case of prolonged coma following procedure of CAS. This case illustrates the diagnostic challenges for a patient that they fall into a coma because of angiographic procedures and raises awareness for CIE as an exclusion diagnosis.

Introduction

Carotid angioplasty and stenting (CAS) have emerged as an alternative treatment of carotid stenosis for patients poorly suited for endarterectomy. The basic indications for CAS as an emerging technique in the treatment of carotid stenosis, do not differ from those for standard surgical carotid endarterectomy (CEA). However, CAS is being used widely to treat severe carotid obstructive disease, and it is now accepted as a less invasive technique that provides an alternative for some patients, with carotid stenosis who are high risk for CEA or who cannot undergo surgery. CAS procedure is indicated and remains cost-effective for high-risk patients [1]. This later procedure is a minimally invasive, in which a very small hollow tube, or catheter, is advanced from a blood vessel in the groin to the carotid arteries. Once the catheter is in place, a balloon may be inflated to open the artery and a stent is placed. Stroke is an uncommon but feared complication of carotid revascularization, and in comparison, with CEA, CAS is associated with a greater odd of stroke and a lower odd of myocardial infarction [2]. Patients under investigation have widespread atherosclerotic disease and are prone to the complications of angiography. Catheter-related vasospasm, intimal tears, or emboli occasionally cause focal deficits during arteriography. Indeed, mechanisms of injury, during endovascular carotid intervention, include embolic and hemodynamic events, and the relatively rare contrast-induced encephalopathy (CIE). This later is a rare neurological complication following the administration of injectable

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intravascular contrast media. Patients with CIE present a wide spectrum of symptoms such as headache, transient cortical blindness, seizure, and other focal neurological deficits. In recent years there has been an increase in the number of endovascular examinations in the study of cerebrovascular diseases. Currently, although nonionic contrast agents have been used, some cases of CIE resulting from coronary angiography or cerebral endovascular therapy have been reported [3]. Nonionic iodinated contrast medium (ICM) is widely used in neuroangiography and intravascular neurointerventional procedures. Contrast-induced neurotoxicity, also known as contrast-induced encephalopathy (CIE), is a known but rare complication following percutaneous carotid intervention resulting in a usually temporary neurological deficit that can mimic acute strokes. Symptoms typically begin within minutes to hours of contrast administration and resolve within one to two days [4]. In CIE important diagnostic radiological signs include brain edema and cortical enhancement. Neuroimaging is important diagnostic tests to exclude hemorrhage, thromboembolic processes, residual contrast enhancement, cerebral edema, or diffuse cortical hyper-attenuation. The incidence of CIE ranges between 0.3% and 1.0% [5]. Although pathophysiology and potential risk factors leading to CIE remain unclear, it is suspected that temporary disruption of the blood-brain barrier integrity leads to the neurotoxic effects [3]. The neurotoxicity caused by ICM depends on its chemical and physical properties, e.i., osmolarity, lyposolubility, and viscosity [6-7]. CIE is extensively reported as a transient and reversible phenomenon, and occurrence of fatal cerebral oedema due to iodinated contrast agents is very rare. However, Zhao et al. reported one case of irreversible fatal cerebral edema [8]. 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 [9-10]. The use of corticosteroids in severe cases to induce anti-inflammatory effects has been reported, but corticosteroid therapy for CIE is controversial [11]. However, steroids are also commonly used to improve cerebral edema by stabilizing the BBB [12]. A high index of suspicion is necessary when evaluating these patients. We herein report a case of prolonged coma during CAS with contrast agents. The patient recovered without any intervention after 6 days of conservative treatment.

Case report

A 78-year-old right-handed Italian man was admitted to the division of vascular and endovascular surgery in our Institute for treatment of a right internal carotid artery stenosis (ICA) detected carotid ultrasound, which was confirmed by computed tomography angiography (CT angiography). Stenosis on carotid ultrasound scan was 70% with a peak systolic velocity of 150 cm/s. CT angiography revealed an 66% stenosis of the right ICA. Brain computed tomography (CT) was normal. On admission to the division of vascular surgery, there was no prior history of stroke, seizure, substance abuse or allergies. The patient's past clinical history was characterized by insulin dependent diabetes, arterial hypertension, and chronic obstructive pulmonary disease (BPCO). Her blood pressure stabilised at 130/70 mmHg. Her current medication included ASA 100 mg, and ramipril 5 mg. Regular insulin was prescribed. The laboratory tests were normal apart from evidence of glucose 242 mg/dL. Indeed, laboratory investigation showed normal serum electrolytes, coagulation profile, renal function, and hepatic function. Chest X-ray (CXR) showed features of BPCO. He was in sinus rhythm. His cardiovascular examination was normal. Her mental status and neurological examination were normal. Two days after his admission, he underwent interventional procedure of the right ICA stenosis. CAS was performed under local anesthesia and are supplemented with little sedation with antithrombotic therapy and vigilance for bradycardia and hypotension. He underwent an angiography of the cervical and intracranial vasculature, reiceiving a total 190 mL of iomeprol contrast (a monomeric nonionic CM, Iomeron 350 mg/ml, Bracco, Italy), which was a standard in our hospital. While still on the table, immediately following the procedure, the patient developed rapidly aphasia and right faciobrachial hemiparesis (3/5). Immediately following neurological event, the patient developed psychomotor agitation and delirium. Clinically, he was agitated, but not verbalizing or obeying simple commands. Urgent computed tomography (CT) without contrast performed approximately thirty minutes after the patient developed neurological event, shoved enhancement in both hemisphere and edema of left cerebral hemisphere in the distribution of the anterior and middle cerebral arteries, there were no mass effects or sign of hemorrhage (Figure 1). After CT the patient became unresponsive with Glascow coma score of 4. He was unresponsive except deep pain, with disconjugate gaze, no spontaneous movements, symmetrically increased reflex, and extensor plantar responses bilateral. The exact timing of his acutely altered state of consciousness is somewhat unclear because he had received sedation with a bolus of midazolam 2 mg injected intravenously (delirium with agitation), for performed an urgent head CT scan. Because patient was in a coma state, was underwent electroencephalogram (EEG) recording, which showed persistent diffuse slowing with no epileptiform abnormalities. EEG recording showed persistent diffuse slowing, and these findings indicates acute non-specific pathologies which may be metabolic or structural disorders. He was acutely managed with intravenous Mannitol (20%) 125 ml 6 time die, hydration and oxygenation. Heart rate, blood pressure, oxygen saturation, sensory and motor functions were regularly monitored. Subsequently, the patient developed respiratory insufficiency. A new laboratory parameter performed one day later, did not identify the aetiology of his coma. Blood glucose was 249 mg/mL, white blood cell counts 14,49 10.3/mmc, creatine kinase 678 U/L and the remainder of his blood test, including those for renal and liver functions, were normal. Follow-up CT was performed approximately 12 hours later the first examination, revealed no evidence of intracranial contrast media, with no evidence of underlying infarction, and the grade of edema in the left hemisphere had decreased compared to that on the CT performed the day before. A brain non contrast MRI taken approximately twenty hours from the onset of neurological event showed a gyriform signal increase in the right cerebral hemisphere, normal sulci, and no cortical edema on fluid-attenuated inversion recovery (FLAIR) image (Figure 2). The patient remained in a continuous coma state and exhibited progressive worsening in her respiratory status and oxygen saturation dropped. Two days after the procedure, after discussion with the hospital's anesthesiologists, it was decided to transfer the patient to the intensive care unit (ICU) for further treatment. When being transferred to the ICU of our institute he had a typical self-limiting, generalized tonic-clonic seizure. Despite treatment with anti-oedema medications, her clinical status was

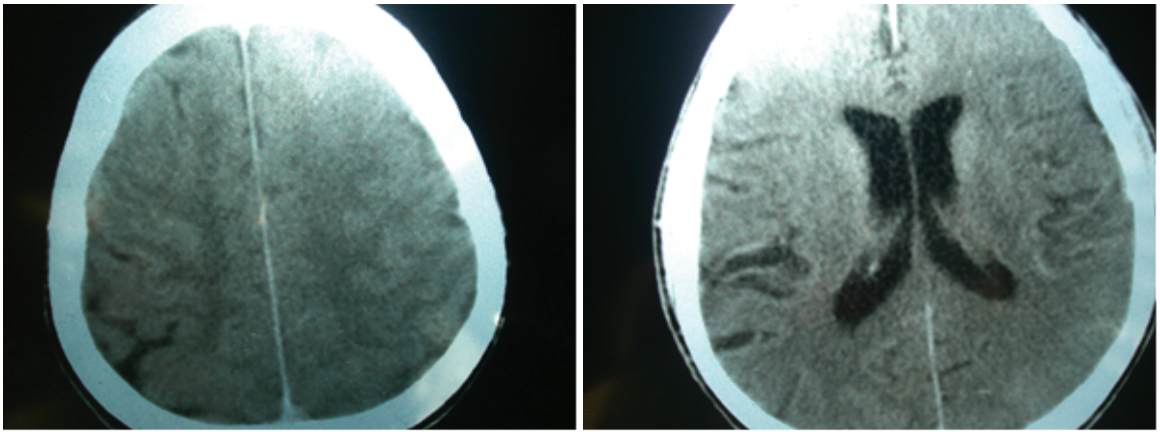

Figure 1. *Noncontrast CT (axial) scan immediately following (approximately thirty minutes) after the initial neurological event shows gyriform enhancement and effacent of the sulci in the left cerebral hemispheres (abnormal cortical contrast enhancement and edema in the left hemisphere).*

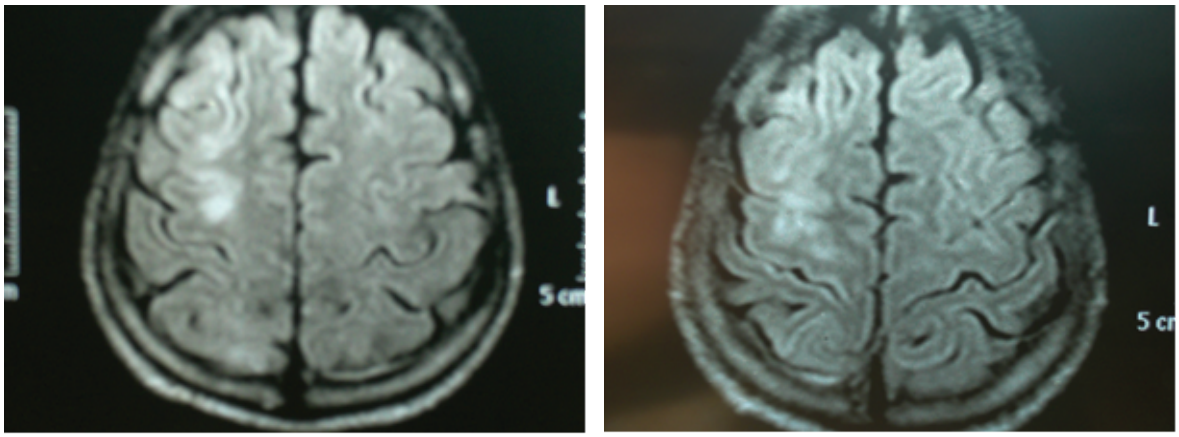

Figure 2. *Axial MRI FLAIR image taken 20 h from the onset symptoms showed a gyriform signal increase in the right cerebral hemisphere.*

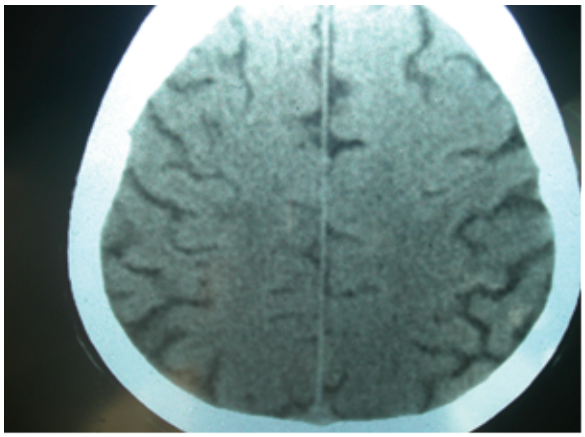

Figure 3. *Follow-up TAC brain scan taken four days later, with resolution of gyral contrast and no cortical edema.*

gradually deteriorating, and endotracheal intubation and mechanical ventilation were applied because of impending respiratory failure. Follow-up carotid duplex ultrasonography was satisfactory, revealing brisk flow in the right carotid artery, without evidence of any vessel occlusion. The following days, in the ICU, the patient became responsive, and he was extubated about three day his intubation. A repeated TC brain scan four day later was now normal (Figure 3). The patient was transferred to regular vascular surgery ward with neither sign of any focal neurological nor overt cognitive deficit. He improved gradually over the next 6 days, returning to baseline status. The neurological event was interpreted as a transitory coma caused by iomeprol that was used during endovascular surgery procedure. He was discharged clinically well, without any neurological deficit with a plan for long-term outpatient follow up.

Discussion

CIE is a rare disease, whose etiology and risk factors remain unclear and need investigation. CIE can occur in the context of diagnostic and therapeutic endovascular procedures. The manifestations of CIE are several, and include cortical blindness, hemiparesis, aphasia, loss of coordination, confusion, seizure, and coma [13]. Transient cortical blindness was first reported in 1970 [14]. The current literature suggests that CIE can occur irrespective of the contrast agent administered [15]. However, the most common manifestation is transient cortical blindness, which can easily masquerade as a stroke. Indeed, CIE may mimic cerebral ischaemia or subarachnoid haemorrhage (SAH). Initially, we suspected the presence of an acute ischemic injury, or the possibility of hyperperfusion syndrome as the patient had undergone CAS for critical carotid artery stenosis. We hypothesized that cerebral embolic risk arising from periprocedural right carotid artery manipulations was a possibility, but contralateral hemispheric focal neurological disturbance with sudden onset (aphasia and right faciobrachial hemiparesis), ruled out this possibility. It is well-known that initial diagnosis of CIE is challenging and requires a temporal correlation between neurological dysfunction and administration of iodinated contrast. Diagnosis is challenging mostly due to its close resemblance to acute stroke. Only 20 cases previously reported global aphasia and/or hemiplegia or mimed anterior circulation strokes [16]. Our report mimicked the stroke symptoms, the timing of symptom onset and clinical progression was characteristics to stroke. Indeed, immediately after the completion of the surgery the patient developed rapidly aphasia, right faciobrachial hemiparesis, psychomotor agitation, and coma clinical syndrome mimicked a left middle cerebral artery occlusion. It is important to differentiate between stroke and CIE as the administration of tPA can increase vascular permeability of the BBB. Typical CT findings include abnormal cortical and subcortical contrast enhancement, cerebral edema, and subarachnoid contrast enhancement like subarachnoid hemorrhage (SAH) [17]. The imaging manifestation of extravasation of contrast media can mimic SAH on CT imaging, including the brain edema, hyperdensity of the subarachnoid space, cortical and subcortical local enhancement [18]. SAH could be considered as the differential diagnosis of CIE, however, in CIE resolution of the sulcal hyperdensity on CT within few hours and absence of xanthochromia, favors the diagnosis of CIE [4]. Radiological signs such as cerebral oedema and cortical enhancement are of great importance in the diagnosis of CIE [19]. Abnormal imaging findings coincide with temporary neurologic deficit attributable to disruption of the BBB and have been thought to be related to use of nonionic ICM [20]. However, rarely neuroimaging can be normal in the face of a florid clinical deterioration [21]. Contrast agents are believed to cause osmotic disruption of the BBB, thus resulting in increased levels of the contrast agent in the blood, which may be a risk factor for neurotoxicity. We reiterate the concept that CIE is a diagnosis of exclusion and is an important clinical entity to consider in the differential diagnosis of stroke. Physicians should be aware of it and consider it prior to initiating thrombolysis. Determining the cause of an acutely depressed level of consciousness following iodinated contrast agent during CAS is a difficult clinical challenge. Our case the combination of agitated delirium and coma suggest that not only the occipital, but also left and right cortical mantle were involved. In these instances, intra-arterial contrast apparently penetrates the BBB by opening tight capillary junctions or enhancing endothelial pinocytosis. Among patients with neuroimaging changes for neurological endovascular procedures who underwent follow-up, complete regression of the abnormalities was shown in 81.5% at a median time of 5 days [22]. Furthermore, neurotoxicity due to ICM, after carotid interventions must be differentiated from nonconvulsive status epilepticus (NCSE). Because NCSE was clinically suspected, EEG was performed. EEG is useful as an objective electrophysiologic assay of cortical function in patients who do not respond to normal sensory stimuli. The EEG may be help differentiate NCSE from other brain diseases causing coma. NCSE comprises a range of conditions in which prolonged (>30 minutes) or recurrent electrographic seizure activity results in nonconvulsive clinical symptoms [23]. Thus, the EEG is most helpful in diagnosing impairment of consciousness due to NCSE [24]. To confirm NCSE, an EEG must show electrographic seizure activity, but EEG performed in our case during the coma state demonstrated diffuse slow wave activity with no lateralizing or paroxysmal features. Finally, we also suspected hyperperfusion syndrome (CHS) due to the failure of normal cerebral autoregulation secondary a CAS. CHS is defined as cerebral blood flow that exceeds the metabolic requirements of brain tissue and/or an increase in cerebral perfusion of 100% compared to preinterventional values. The diagnosis of hyperperfusion syndrome was also a possibility, but the clinical characteristics of CHS, including ipsilateral headaches, vomiting, seizures, confusion, focal neurological deficits, parenchymal hemorrhage, subarachnoid hemorrhage, fluctuation of blood pressure, and even cognitive function impairment [25], were not observed in our patient. Symptoms of CHS can appear 6 h to 4 days after CAS [26]. We think that our patient's coma and respiratory depression are attributed exclusively to nonionic ICM. The temporal relationship between the time of the dose of contrast media and the witnessed deterioration of his level of consciousness, associated with all laboratory parameters within normal limits, support this diagnosis.

Conclusion

CSA is performed on patients with minimal to no symptoms. However, several types of brain injury incurred during carotid revascularization have been previously reported such as embolic injury, hemodynamic events, and hemorrhage. We reported a case of CIE following CAS with the use of an ICM, which resulted in cerebral oedema and coma. However, in some cases, it can pose a diagnostic dilemma. This case highlights a difficult diagnostic dilemma that has profound implications for patient management. Early after selective cerebral angiography, this form of transient neurotoxicity must be differentiated from massive cerebral infarction, SAH, and CHS. Non-contrast CT head and magnetic resonance imaging examinations are essential in ruling out other diseases such as acute cerebral infarction or intracranial hemorrhage. CIE is devastating for the patient, the family and the person carrying out the procedure when coma complicates endovascular procedures. 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 normal volume of contrast administered during percutaneous carotid interventions. Bear in mind that CIE is a rare complication of contrast media use during angiographic procedures, but with the growing use of endovascular interventions as a diagnostic and a

therapeutic means, this complication is likely to become more common. Fortunately, our patient did not lead to permanent neurological deficits. No specific therapeutic strategy exists for CIE. Management is conservative (intravenous fluid therapy, mannitol infusion, dexamethasone and additionally anticonvulsants). Further research is needed in this field for the establishment of safety limits of contrast dosing in angiographic procedures for the overall safety of our patients.

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