Contrast-enhanced encephalopathy and massive cerebral edema after endovascular coiling of cerebral aneurysm. A case report

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Abstract

Contrast-induced encephalopathy (CIEP) is a rare complication after endovascular therapy. The etiology of CIEP is still a matter of debate. We present a rare occurrence of CIEP in a known hypertensive and type 2 diabetic patient after endovascular coiling of cerebral aneurysm with oculomotor nerve palsy.

A 68-year old female presented with seven days history of headache and left ptosis or blepharoptosis with mild mydriasis. The headaches were localized mainly at the left side of the nose, orbit, and upper forehead while the left ptosis was associated with blurred vision. Computed tomography angiography revealed an aneurysm in between the C4 segment of the left internal carotid artery (ICA) and the bifurcation of the left posterior communicating artery. Digital subtraction angiography further confirmed the aneurysm. We used the transarterial approach to assess the aneurysm and subsequent coiling. Iohexol (Omnipaque) contrast agent was used during the endovascular procedure. The patient's condition deteriorated into acute confusion state with cardinal symptomology of CIEP immediately after the operation. Computed tomography scan revealed cortical contrast enhancement in the vascular territory of the ICA as well as edema. Her symptomatology resolved 48 hours after treated with anticonvulsants, intracranial pressure reduction and hydration.

Chronic hypertension as well as type 2 diabetics may be critical predisposing factors to CIEP. CIEP should be suspected in patients presenting with acute confusion state after endovascular therapy. Massive edema with ischemic brain changes in white matter of the brain before endovascular procedure should rise suspicion of CIEP.

Introduction

Contrast-induced encephalopathy (CIEP) is a rare complication after endovascular therapy.[1-5] The precise etiological mechanisms via which this occur is still a matter of debate.[2,4] Nevertheless, osmotic disruption of the blood-brain barrier (BBB) arising from repeated contrast injections into a single vessel has been speculated as a cause of this complication.[3,4,6] Chronic hypertension, transient ischemia attack, compromised cerebral autoregulation, renal failure, enormous contrast volumes, selective vertebralbasilar arteriography (VAG) and male gender have been implicated as predisposing factors of CIEP.[5,7-10] The symptomatology of CIEP often commence during the procedure but become apparent few hours after the procedure.[5] Most symptoms are typically self-limiting, resolving within 2-4 days of onset.[3,11,12] Nevertheless, full recovery may take as long as few weeks in a few patients.[3,12]

Anomalous cortical contrast enhancement with mild to severe edema, subarachnoid contrast enhancement, as well as striatal contrast enhancement are the typical postprocedural CT findings.[2,9,12] Adequate hydration with intravenous crystalloids as well as anticonvulsants are the supportive treatment modalities for this post procedural complication.[5,13] The observation of CIEP in a known hypertensive and type 2 diabetic patient after endovascular coiling of aneurysm is very rare and has not been reported in literature. We present a case of CIEP after endovascular coiling of cerebral aneurysm in a hypertensive and type 2 diabetic patient with left oculomotor nerve palsy (OMNP).

Case Report

We present a 68-year old female, with seven days history of headache and left ptosis or blepharoptosis with mild mydriasis. Her headaches were severe and localized mainly at the left side of the nose, orbit, and upper forehead. Her left ptosis was associated with blurred vision with no nausea and vomiting. She is a known hypertensive as well as type 2 diabetic detected 30 years prior to the current presentation. Her hypertensive and diabetics were poorly controlled prior to the above symptomatology. She was on felodipine 2.5 mg twice daily and subcutaneous insulin 9 units before breakfast, lunch and dinner, plus enteric-coated oral metformin 1g twice daily. She had no history of trauma or signs of meningitis. Cranial nerve examination revealed an acute left OMNP. All other cranial never and peripheral never were grossly intact. General neurological examination did not yield much. Ophthalmic examination did not show any retinal microangiopathy. Routine laboratory investigation most especially renal function test and chest X-ray were grossly at normal ranges. Her presentation was initially misdiagnosed as an acute cerebral infarction and treated for 3 days with aspirin, clopidogrel, fluvastatin and mecobalamin with no improvement which led to her referral to our department. Computed tomography angiography (CTA) done at our institution revealed an

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Ethics approval and consent to participate: this case was reported or written in according to ethical committee of the Affiliated Hospital of Jiangsu University's criteria for reporting or writing case reports. The patient and relatives were informed about our intension to involve him in a case study and they agreed to partake in the study.

Patient consent for publication: the patient and relatives were dually informed about our intention to publish his case and they fully concerted to the use of these documents. A written informed consent was obtained. A written concern for publication was signed. The hospital also concerted to the use of this information for publication.

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aneurysm in between the C4 segment of the left internal carotid artery (ICA) and the bifurcation of the left posterior communicating artery (PCA) (Figure 1). The aneurysm was large in size measuring about 3.0×5.3 mm diameter. Massive edema with ischemic brain changes in white matter of the brain with paranasal sinus inflammation were also observed during CTA evaluation. Digital subtraction angiography (DSA) further confirmed the parameters of the aneurysm (Figure 2). Therefore, a diagnosis of left OMNP as a result of compression by an aneurysm at the bifurcation of PCA in a known hypertensive as well as type 2 diabetic patient was made.

After comprehensive evaluation of her co-morbid conditions and current illness, we opted to treat her aneurysm via endovascular coil instead of surgical clipping of the aneurysm. Iohexol (Omnipaque) contrast agent was used during the endovascular procedure. We used the trans-arterial approach to assess the aneurysm and subsequently coiling. After positioning her on the surgical table, we insert the 6F arterial sheath through the right femoral artery according to the Seldinger method. Using a 5F single-curved angiography tube under the guidance of the ultra-sliding guide wire, via the left ICA, we identified the aneurysm at the bifurcation of the PCA and left ICA. The PCA was however not visible. The left anterior choroidal artery was slightly dilated. A total of seven coils (MicrVention Inc, California, USA) were used to completely occlude the aneurysm during the operation (Figure 3). Post-operative CT scan showed no intracranial hemorrhage, air embolism as well as cerebral infarction. Nevertheless, we observed cortical contrast enhancement in the vascular territory of the left ICA as well as edema (Figure 4).

The patient's condition deteriorated into acute confusion state immediately after the operation and become apparent 2hour after the procedure. She also showed symptoms of motor and sensory disturbances; vision disturbances, such as cortical blindness, ophthalmoplegia, aphasia; as well as seizures which lasted for 24 h. After thorough evaluation of the patient's condition, we arrived at conclusion that, she developed a post contrast-enhanced encephalopathy. She was treated with anticonvulsants, intracranial pressure reduction and hydration. The above symptomatology resolved 48 hours after the operation. A repeated CT scan done a week later revealed a resolution of the cortical contrast enhancement in the vascular territory of the left ICA as well as edema (Figure 5). The patient was discharged home two weeks later after scheduled post-operative visits were arranged

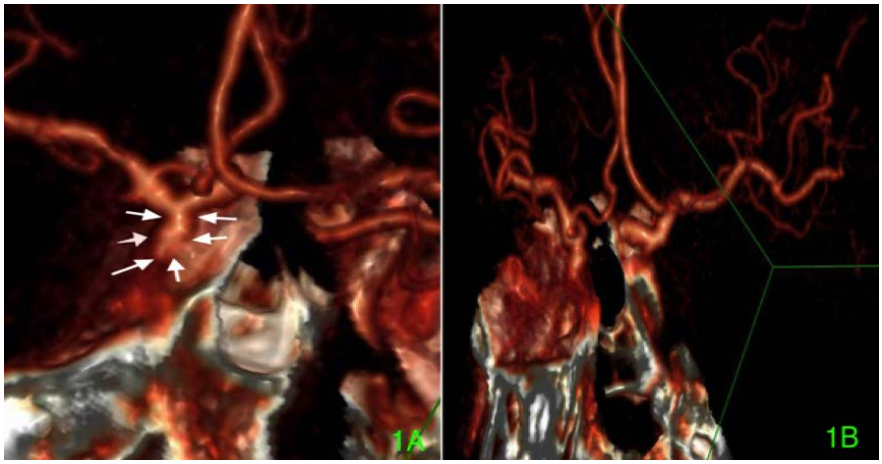

Figure 1. A-B) Computed tomography angiography images showing an aneurysm in between the C4 segment of the left internal carotid artery and the bifurcation of the left posterior communicating artery. White arrows = aneurysm.

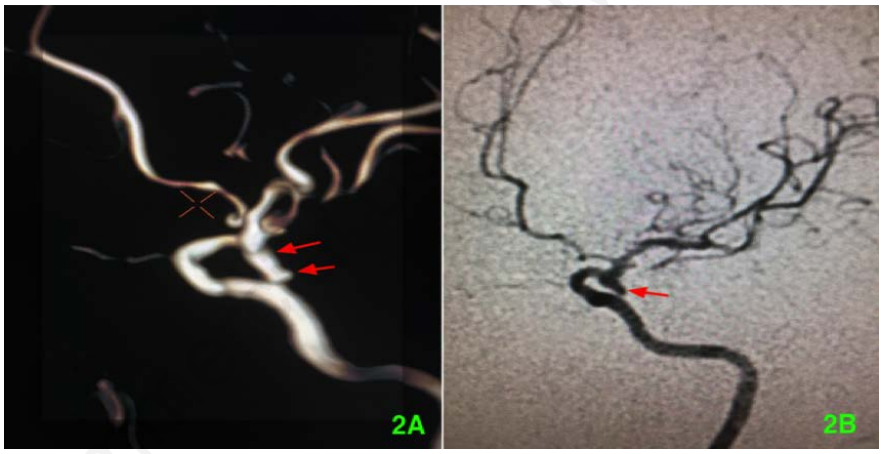

Figure 2. A-B) Digital subtraction angiography images confirming the aneurysm in between the C4 segment of the left internal carotid artery and the bifurcation of the left posterior communicating artery. Red arrow = aneurysm.

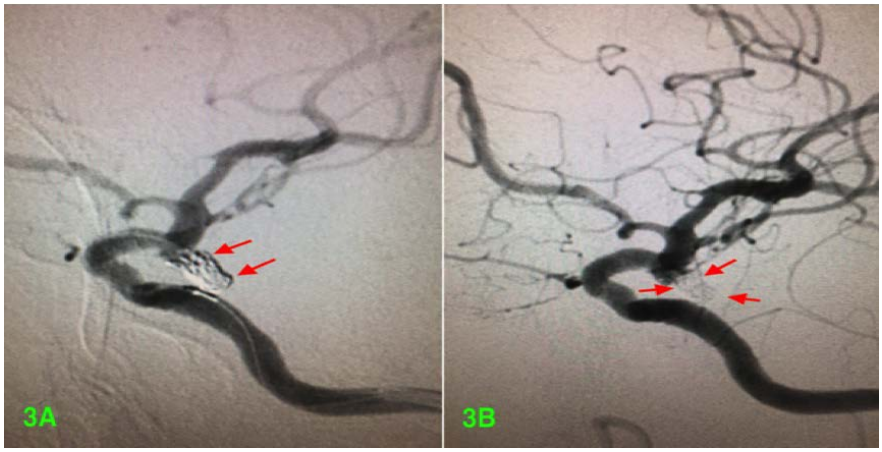

Figure 3. A-B) Intraoperative digital subtraction angiography images showing coils *in situ* and disappearance of the aneurysm. Red arrow = casted view of the aneurysm.

every six months. She was also referred to hypertension as well as diabetic clinics for further assessment and management. We observed massive improvement in her condition during the first six months scheduled visit. Two years follow-up revealed no recurrence of symptomatology and massive improvement of quality of life.

Discussion

PCA aneurysms are the most common types of aneurysms to form in the basal cistern and frequently involves in isolated OMNP due to their anatomical location.[14,15] The oculomotor nerve originates from the midbrain on the medial side of the cerebral peduncles and extends forward and laterally between the posterior cerebral artery and superior cerebellar artery.[15] Our patients presented with OMNP as result of compression by an aneurysm at the bifurcation of PCA. She is a known hypertensive as well as type 2 diabetic patient. Apart from the intraocular muscular involvement during OMNP, pupillary involvement is also higher suspicion of compression because the pupillomotor fibers and their vascular component originates from overlying pia course along the superficial as well as superomedial aspect of the oculomotor nerve.[14,16] Also, trauma, stroke, post-surgical inflammation, neoplasms as well as microvascular damage from chronic disease have been implicated as cause of OMNP.[14,17]

Our patient condition was initially misdiagnosed as an acute cerebral infarction and treated with aspirin, clopidogrel, fluvastatin and mecobalamin with no improvement. We utilized CTA to detect the aneurysm between the C4 segment of the left ICA and the bifurcation of the left PCA. The gold standard radiological evaluation modality for aneurysms compressing on the OMNT are CTA, magnetic resonance angiography (MRA), and digital subtraction angiography (DSA).[18] It essential to note that, CTA, MRA, DSA necessitates the use of iodinated contrast material as well as ionizing radiation.[18] The massive edema with ischemic brain changes in white matter of the brain with paranasal sinus inflammation observed during CTA evaluation may have contributed to the development of post-operative CIEP. We successfully treated the aneurysm via endovascular coil instead of surgical clipping after a comprehensive evaluation of her co-morbid conditions and her current presentation. Endovascular coiling is an effective technique for treating unruptured, ruptured aneurysms as well as preventing the rupture of cerebral aneurysms.[1]

Studies have shown that, after endovascular interventions, a few patients experience complications such as thromboembolic events, aneurysm rupture, and peri-aneurysmal edema, which may be suggestive of symptomatic inflammatory responses.[1,19,20] Also, reversible encephalopathy syndrome has been observed in patients after endovascular interventions.[1,21,22] The possible mechanism of CIEP is as a result of disruption of the BBB leading to leakage of contrast agent into the cortex as well as subarachnoid space. This event causes neurotoxicity as well as cortical edema.[6,23] Furthermore, the cause of BBB disruption is associated with hyperosmolality as well as chemotoxicity of contrast agent.[13,24] Iodinated contrast agents have been implicated in CIEP related neurotoxicity as a result of temporary BBB disruption.[23,24] Temporary break of CIEP related BBB was first observed by Uchiyama et al who detected elevated concentration of iodine contrast agent in cerebrospinal fluid of their index cases and not in 4 control cases.[25]

Studies have showed that a compromised BBB may lead to brain edema, resulting in the influx of proteins, electrolytes, as well as water across the anomalous perme-

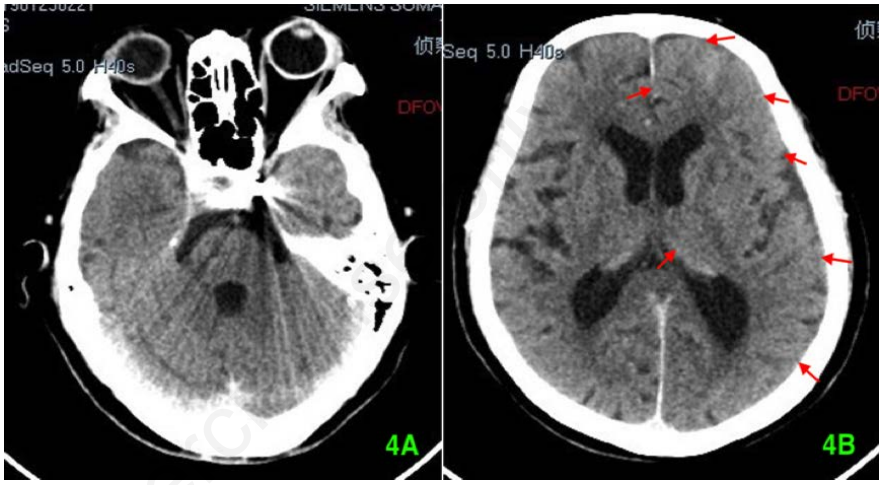

Figure 4. A-B) None contrast post-operative computed tomographic scan images showing cortical contrast enhancement in the vascular territory of the left internal carotid artery as well as edema. No intracranial hemorrhage, air embolism as well as cerebral infarction were observed. Red arrows show the demarcations or margins and the extent of contrast-induced encephalopathy.

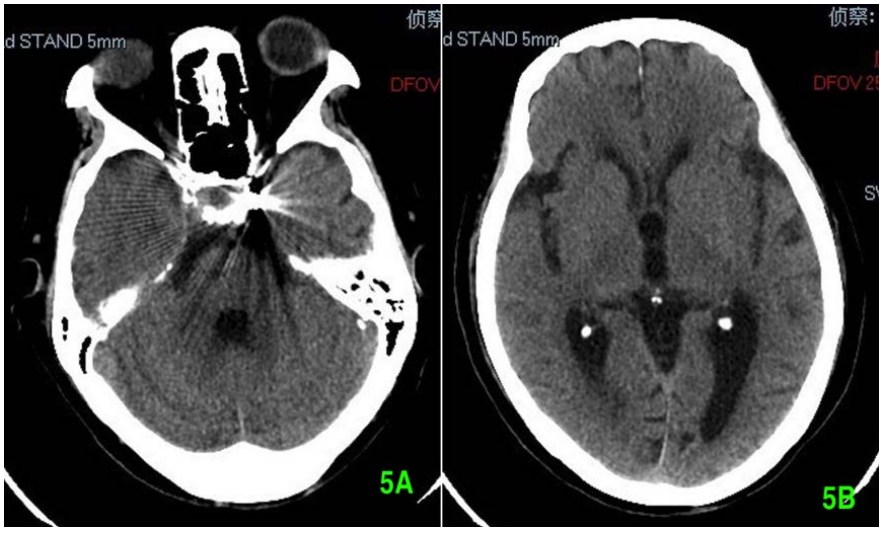

Figure 5. A-B) None contrast post-operative computed tomographic scan images take a week later showing resolution of the cortical contrast enhancement in the vascular territory of the left internal carotid artery as well as edema. Mild dilatation of the ventricles which signify mild hydrocephalus.

able cerebral vessels into the extracellular space.[26,27] The clinical presentation of CIEP often starts immediately after endovascular procedure with symptoms such as transient cortical blindness, depicted with unilateral or bilateral amaurosis fugax, normal pupillary light reflexes, and extraocular dysfunction.[3,11,28-30] Also, patient present with headache, hemiparesis, aphasia, memory loss, as well as decrease in advanced mental functions like agraphia, loss of coordination, confusion, seizures, and coma.[3,5,31] Most often the patient is misdiagnosed as acute stroke after the procedure.[3] Our patient's condition deteriorated into acute confusion state with the above symptomology immediately after the operation.

In our index case, post-operative CT scan showed no intracranial hemorrhage, air embolism as well as cerebral infarction. Nevertheless, we observed cortical contrast enhancement in the vascular territory of the ICA as well as edema. It is fundamental to exclude embolic or hemorrhagic complications so as to initiate the right treatment early.[5,8,11] Studies have shown that, approximately half of all patients with transient CIEP after intra-arterial contrast administration have histories of chronic hypertension.[5,7] Our patient had chronic hypertension as well as type 2 diabetics. We are of the view that, the initially misdiagnoses of her condition as an acute cerebral infarction and the long-standing compromise of the vascular territory of the ICA as well as edema contributed to the CIEP.

Long exposure and reduced clearance of contrast agent has been associated with CIEP in patients with impaired renal function.[5,10] Our patient's routine laboratory investigations, most especially renal function tests were grossly at normal ranges. Furthermore, selective VAG has been implicated as a high risk of CIEP due to the association of the arterial supply to the brain stem, medulla oblongata, cerebellum, as well as basal parts of the temporal and occipital lobes.[5,9] A study revealed that, the volume of contrast agent capable of triggering CIEP ranged from 80-400 mL while another study revealed that, a local injection of 25 mL contrast agent into the carotid artery may result in CIEP.[5,7] CT scan without contrast agent is the most suitable radiological modality for the evaluation of CIEP because it is capable of showing diffuse cortical hyper-attenuation similar to subarachnoid hemorrhage.[5] However, normal CT scans have been observed in some CIEP cases.[5] Magnetic resonance imaging (MRI) is also crucial in excluding differentials as well as affirming the diagnosis of CIEP.[3,11] MRI may show hyperintensity in the cortex on T2, FLAIR, as well as DWI.[5,20,32] Nevertheless, a trustworthy image modality that can differentiate CIEP from cerebral ischemia is apparent diffuse coefficient (ADC), which often reveal no anomalous intensity in patients with CIEP.[5,32] The management of CIEP involves aggressive intravenous hydration as well as daily hemodialysis with a short course of corticosteroids.[3,4,30] Also, symptomatic treatments, such as anticonvulsant therapy for seizures, are mostly advocated.[3,11,13] Zhao *et al.* reported patient who suffered irreversible fatal CIEP after DSA using iopamidol.[27] Autopsy involving 8 CIEP related decease patients revealed fatal cerebral edema due to contrast neurotoxicity.[27]

Conclusions

Chronic hypertension as well as type 2 diabetics may be critical predisposing factors to CIEP. We are of the view that, the initially misdiagnosis of the patient condition as an acute cerebral infarction and the long-standing compromise of the vascular territory of the ICA as well as edema led to the CIEP. The diagnosis of CIEP should be based on both clinical and radiological evaluation of patients who received endovascular therapy. Nevertheless, in some cases, radiological evaluation may be negative and thus, diagnosis will solely rely on clinical findings.

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