

Subarachnoid Hemorrhage Mimicking Leakage of Contrast Media After Coronary Angiography

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We report a patient who developed subarachnoid hemorrhage (SAH) just after coronary angiography (CAG) with non-ionic contrast media (CM) and minimal dose of heparin. The 55-year-old man had a history of acute ST elevation myocardial infarction that had been treated with primary percutaneous coronary intervention and was admitted for a follow-up CAG. The CAG was performed by the transradial approach, using 1000 U of unfractionated heparin for the luminal coating and 70 mL of iodixanol. At the end of CAG, he complained of nausea and rapidly became stuporous. Brain CT showed a diffusely increased Hounsfield unit (HU) in the cisternal space, similar to leakage of CM. The maximal HU was 65 in the cisternal space. No vascular malformations were detected on cerebral angiography. The patient partially recovered his mental status and motor weakness after 2 days. Two weeks later, subacute SAH was evident on magnetic resonance imaging. The patient was discharged after 28 days. (**Korean Circ J 2012;42:197-200**)

KEY WORDS: Subarachnoid hemorrhage; Iodixanol; Coronary angiography.

Introduction

Bleeding is a common complication of antithrombotic treatments of acute coronary syndrome (ACS), and invasive procedures are one of the important risk factors of bleeding.^{1,2} Contrast media (CM) and heparin are used during coronary angiography (CAG) and play a role as anticoagulants.³ The reported overall bleeding rate in patients with ACS undergoing percutaneous coronary intervention (PCI) is 18.1%, and that of major bleeding after CAG is 2.7%.⁴ In patients with ACS, bleeding is usually associated with increased mortality, risk of ischemic events and myocardial infarction.⁵ Although sub-

arachnoid hemorrhage (SAH) is one of the major bleeding events that can but rarely occur after CAG, extravasation of the CM by disruption of the blood-brain barrier (BBB) after CAG can sometimes mimic acute SAH on brain computed tomography (CT).⁶ We report a patient who developed SAH just after CAG with non-ionic CM and a minimal dose of heparin.

Case

A 55-year-old man with a history of acute ST elevation myocardial infarction (STEMI) was admitted for a follow-up CAG. He was taking antihypertensive medication and did not have a history of neurologic disease or hemorrhagic disorder. He was admitted to the hospital due to STEMI of inferior wall which was 1 year before. Emergent CAG showed total occlusion of the right coronary artery at the middle portion (Fig. 1A). Primary PCI was performed, and intracoronary thrombi were aspirated during the PCI. A TAXUS Liberté paclitaxel-eluting coronary stent® (3.0×24 mm, Boston Scientific Co., Natick, MA, USA) was implanted in the middle portion of the right coronary artery. During the procedure, we injected 100 mL of iodixanol (Visipaque®, GE Healthcare Co., Ireland Cork, Ireland), which is a nonionic CM, and 3000 IU of unfractionated heparin. There were no side effects of the CM. Laboratory data showed no coagulation

Received: April 9, 2011

Revision Received: August 2, 2011

Accepted: September 21, 2011

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• The authors have no financial conflicts of interest.

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abnormalities as well. He was started on aspirin, clopidogrel, carvedilol, cilazapril, pitavastatin and isosorbide mononitrate.

After 15 months, the patient was readmitted for the follow-up CAG. He had an alert mental state, without any symptoms or signs at admission. His blood pressure was 130/80 mm Hg and his heart rate was 80 beats per minute. Flattened T wave and pathologic Q wave were identified on the inferior leads of the electrocardiography (ECG), and isolated ventricular premature complex was seen on ECG. Complete blood count indicated 15.5 gm/dL of hemoglobin and 153000/mm² platelets. The prothrombin time (international normalized ratio 1.06) and the activated partial thromboplastin time (36.1 seconds), serum creatinine (0.9 mg/dL), aspartate aminotransferase and alanine aminotransferase (18 IU/L and 18 IU/L, respectively) were all within normal range. Right radial arterial puncture was performed

for the CAG, and no evidence of in-stent restenosis was demonstrated (Fig. 1B). Unfractionated heparin (1000 IU) was used for the luminal coating of the 5 French Judkin catheters and 70 mL of iodixanol was used for CAG. At the end of the CAG, the patient complained of neck stiffness and nausea with vomiting. He showed an alert mental state, and the pupil reflexes were prompt and isocoric. However, weaknesses in both lower extremities (motor grade IV) was noted.

Emergent non-contrast brain CT was performed. Diffusely increased density (maximum 65 Hounsfield units) was found in all cisternal spaces, including the Sylvian fissure (Fig. 2A). Small amount of intraventricular and intracranial hemorrhage of the left posterior lobe and the periventricular white matter were also seen. Additionally, cerebral angiography was performed using 100 mL of iodixanol. Vascular malformation or aneurysm was not detected

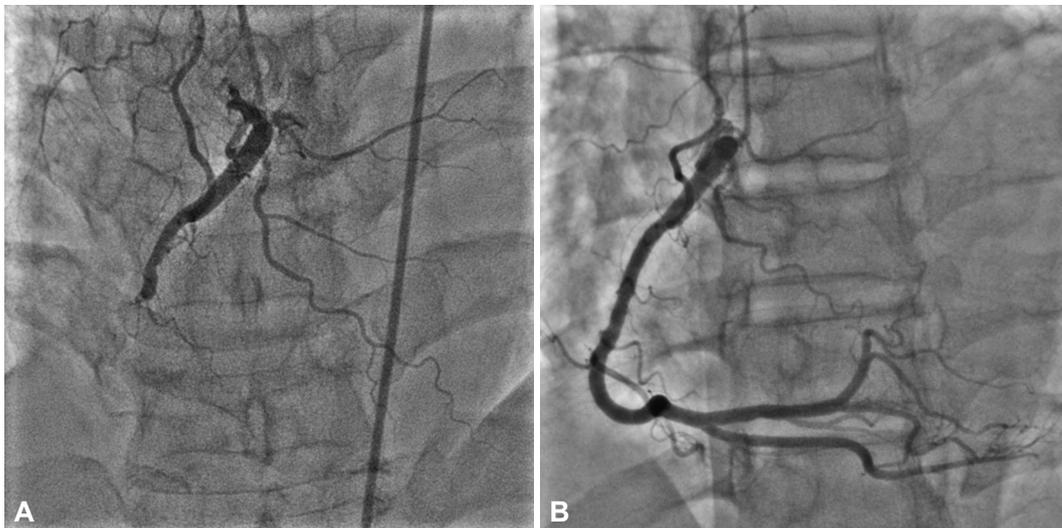


Fig. 1. Angiographic findings of the right coronary artery. A: totally occluded right coronary artery at the initial coronary angiography for primary percutaneous coronary intervention. B: patent previous TAXUS Liberté stent on follow-up coronary angiography performed 15 months later.

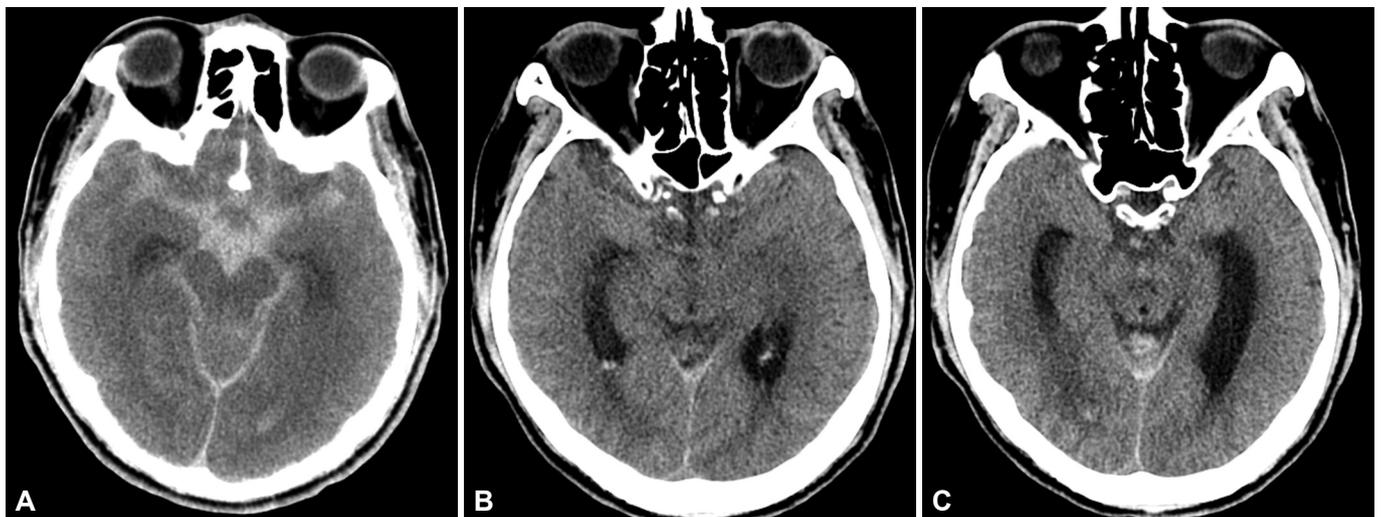


Fig. 2. Initial brain CT shows. A: diffuse acute subarachnoid hemorrhage (maximum 65 HU) in the basal, interpeduncular, ambient and both lateral cisterns. B and C: CT scan shows almost complete resolution of the acute SAH after 2 days. SAH: subarachnoid hemorrhage.

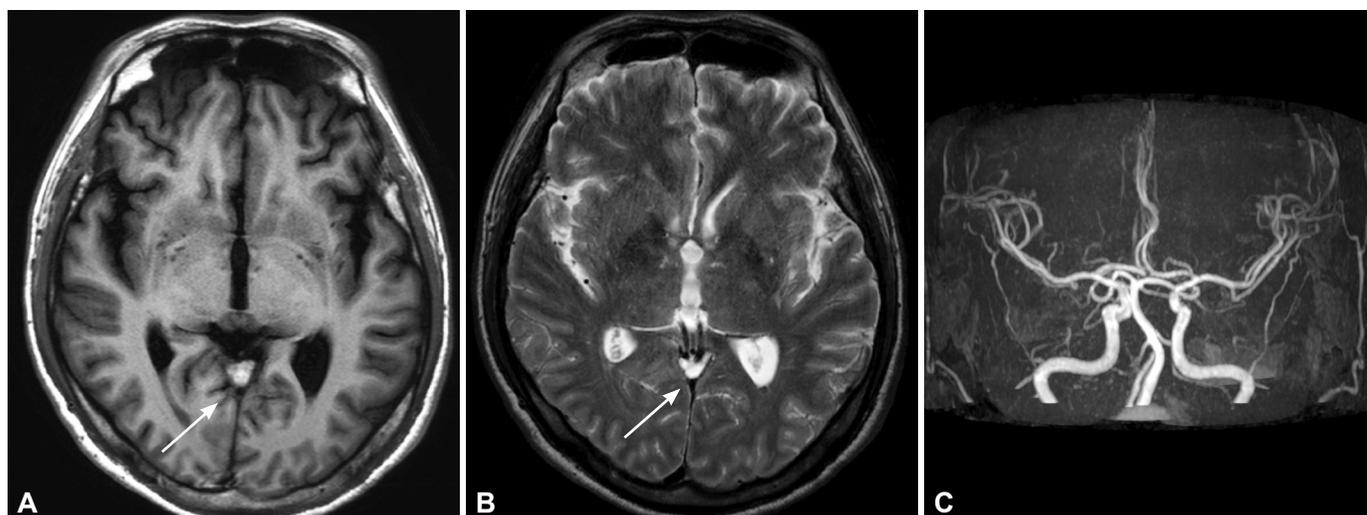


Fig. 3. Two weeks after the SAH, magnetic resonance (MR) image shows hyperdense material in the supravermian cistern on both T1 (A) and T2 (B) weighted images (arrows), suggesting remnant subacute SAH. The MR angiogram reveals no evidence of aneurysm in the major intracranial vessels (C). SAH: subarachnoid hemorrhage.

on the digital subtraction angiography. However, the patient became stuporous and showed sluggish pupil reflexes. He was transferred to the neurosurgery ward and was referred to the surgical intensive care unit (SICU). We discontinued aspirin and clopidogrel, and intravenous sodium valproate, tranexamic acid, mannitol and nicardipine were administered. After 24 hours in the SICU, the patient was in lethargic mental state with dysarthria and motor weakness was partially recovered. Transcranial Doppler ultrasound examination failed, due to a poor acoustic window. Follow-up brain CT (48 hours after the CAG) showed that the SAH had improved remarkably (Fig. 2B and C).

Two weeks after the event, brain magnetic resonance imaging (MRI) with angiography was performed. A remnant subacute stage SAH (high signal on both T1- and T2-weighted images) in the supravermian cistern, the posterior fossa (medulla level), the right central sulcus and a small amount of intraventricular hemorrhage remained, but were shrunken compared to previous images. A steno-occlusive lesion or aneurysm was not detected on MR angiography (Fig. 3). The patient was returned to the general ward and aspirin was restarted on the 21st day. He was improved to an alert mental state and dysarthria was recovered gradually. The patient was discharged from the hospital on the 28th day after admission and is still alive after 12 months. However, mild sensory impairment in his right arm still exists.

Discussion

Subarachnoid hemorrhage is a life-threatening major bleeding after angiography associated with multi-systemic symptoms.⁷⁾ However, neurotoxicity of the CM (i.e. leakage of CM in the subarachnoid

space) can sometimes mimic an acute SAH.⁶⁾ We report a case of SAH after CAG that was initially confused with neurotoxicity of CM.

Clotted blood may have a slightly higher attenuation in the range of 45-100 Hounsfield unit (HU).⁴⁾ Blood typically has a maximal range of 40-60 HU (100% blood by volume has an attenuation of 66 HU.)⁸⁾ Only 50% or less is reabsorbed from the subarachnoid space within 24 hours in SAH.⁹⁾ The maximal HU of CM is more than 90 on a brain CT.¹⁰⁾

Contrast media-induced neurotoxicity has been reported as transient and rapidly reversible.⁴⁾ The disruption of the BBB may cause extravasation of the CM after CAG, which may mimic acute SAH.⁵⁾ The neurotoxicity of CM can occur especially when using ionic high osmolar agents, but does not happen frequently.¹¹⁾ In general, non-ionic CM has a lower incidence of neurotoxic events than ionic CM.¹²⁾ Non-ionic CM, such as iodixanol, has been reported to cause transient cortical blindness, confusion and amnesia, but no focal deficits, whereas ionic CM develops more severe complications, including seizures and motor and speech deficits.³⁾¹³⁾¹⁴⁾ Although it is hard to discriminate CM leakage clinically, hyperdense signal on both T1 and T2 weighted MRI images can be helpful in the diagnosis of late subacute SAH.¹⁵⁾

In this presented case, equivocal HU on the initial brain CT and rapid clearance of the hyperdensity on follow-up images were not diagnostic. Similarly, sustained neurologic symptoms were not consistent with direct neurotoxicity of CM. Subacute SAH was confirmed on MRI images 2 weeks after the initial event.

When using CM, the pathophysiology of bleeding is not clear in patients. CM has been shown to act as anticoagulant through prolongation of the *in vitro* bleeding time;²⁾¹⁶⁾ however, non-ionic CM has a smaller effect on bleeding tendencies than ionic CM.¹⁶⁾ The ad-

ministered CM dosage and concentration did not exceed those recommended for CAG (as indicated by the manufacturer) and the patient had no renal function impairment. In addition, the total amount of heparin used during the CAG was minimal; therefore, the possibility of a heparin-induced SAH was relatively low. The anticoagulatory effects of iodixanol may play an additional role in the cause of SAH. The anticoagulation effects of both heparin and iodixanol may have been summative in this case.

Most cases of SAH are caused by rupture of an intracranial aneurysm. The incidence of SAH was 15 to 20% in patients without a vascular lesion on cerebral angiography, and up to 24% of all SAH patients with initial negative angiography have an aneurysm found on repeat angiography.¹⁷⁾ Sickle cell disease, bleeding disorders, pituitary apoplexy, trauma, cocaine abuse, spinal aneurysm, brain tumor, reversible vasoconstriction syndrome and reversible posterior leukoencephalopathy syndrome have been reported as possible causes of SAH, rather than vascular lesion.^{11,18)} Although vascular cause was ruled out by MR angiography and conventional cerebral angiography, we could not exclude the microaneurysm and vasoconstriction syndrome in this case. A cerebrospinal fluid analysis might be helpful to distinguish blood from CM.^{6,19)}

Acute SAH is a rare but possible complication after coronary artery intervention with a minimal dose of heparin and CM.

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