A Delayed Fatal Septic Cerebral Infarction after Endoscopic Retrograde Cholangiopancreatography

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Endoscopic retrograde cholangiopancreatography (ERCP)-related complications should be promptly and properly managed in accordance with the type and severity of the complication and the comorbidity of the patient. Neurologic complications occur very rarely, but despite of the prompt management, the patient status can severely deteriorate and sometimes result in fatality. A female patient visited SAM Medical Center for abdominal pain and yellow skin. She has taken a current medication for essential hypertension since 10 years ago. Initial laboratory findings showed obstructive jaundice and abdominal computed tomography (CT) showed two common bile duct stones with moderate dilation of bile duct. Her vital sign with oxygen saturation was stable until the first attack of seizure 12 hours later after removal of stones through the ERCP. Emergent brain CT and magnetic resonance imaging revealed multiple cerebral infarctions of both hemispheres with right predominance of middle cerebral artery territory and no evidence of air emboli. She died four days later despite of intensive care including high oxygen therapy and intravenous broad spectrum antibiotics with antiplatelet drug. We report a rare, delayed occurrence of a fatal multiple cerebral infarctions 12 hours after ERCP.

Keywords: Cerebral infarction; Fatal; Complication; Endoscopic retrograde cholangiopancreatography

INTRODUCTION

Relatively common adverse events related to endoscopic retrograde cholangiopancreatography (ERCP) include pancreatitis, cholangitis and bleeding. The more severe but rare and sometimes fatal complications include sedation-related cardiopulmonary compromise, bowel perforation, necrotizing pancreatitis, and systemic air embolism [1,2]. These severe complications necessitate prompt rescue intervention or surgery because delayed recognition and management can lead to catastrophic morbidity and mortality. Sedation-related hypoxia sometimes resolved slowly with simple oxygen supply without neurologic sequelae. The ERCP procedure duration is relatively longer than other simple endoscopic examinations and the patient usually experiences delayed recovery from deep sedation after ERCP, despite use of the sedative reversal agents such as flumazenil. Because the endoscopist can consider deep sedation to be simply due to excessive dose of the sedative and long procedure time especially in a patient without abnormal neurologic sign and vital sign after ERCP, they may not be aware of the possible occurrence of post-procedure neurologic complications such as air embolism or ischemic cerebrovascular accident [3,4]. This is a case report of a rare occurrence of fatal multiple septic cerebral infarctions in which diagnosis was made 2 hours after ERCP in a patient with cholangitis because the patient’s vital signs were stable and exhibited no abnormal neurologic sign before the onset of seizures.

CASE REPORT

A 74-year-old female patient visited the emergency center for abdominal pain over 10 days with yellow skin. She had hypertension and hyperlipidemia for 10 years and has been taking current medication of amlodipine 10 mg and atorvastatin 10 mg once a day. There was no previous history of arrhythmia or cerebrovascular disease. Initial vital signs included blood pressure 110/70...
mm Hg, pulse rate 74 beats per minute, respiratory rate 20/min, and body temperature 36.8°C. On physical examination, she was mentally alert but had abdominal tenderness in the right upper quadrant but no rebound tenderness and chest auscultation was unremarkable. Laboratory findings included: hemoglobin 13.0 g/dL, white blood cell (WBC) 16,930/μL, C-reactive protein (CRP) 4.7 mg/L, blood urea nitrogen 18 mg/dL, creatinine 0.9 mg/dL, aspartate aminotransferase/alanine aminotransferase 261/181 IU/L, total bilirubin 3.5 mg/dL, alkaline phosphatase 339 IU/L, amylase/lipase 48/62 IU/L, creatine kinase MB isoenzyme (CK-MB) 2.1 ng/mL, and troponin-I 0.3 ng/mL. The initial electrocardiography (ECG) revealed normal sinus rhythm and normal axis. Chest and abdominal X-ray were unremarkable. Abdominal computed tomography (CT) scan revealed two stones in the common bile duct (CBD) with moderate dilation (Fig. 1A-C).

Intravenous administration of ceftriaxone with metronidazole was started. Intravenous premedication of 2 mg midazolam, 30 mg propofol, 25 mg meperidine, and 5 mg cimetropium before ERCP was injected. After biliary sphincterotomy, yellow stones were removed by basket (Olympus, Tokyo, Japan) but the removal of the last stone in CBD was difficult because it was not captured. Therefore, after dilation with controlled radial expansion balloon (12-13.5-15 mm; Boston Scientific, Natick, MA, USA), the stone was removed by retrieval balloon (Fig. 1C-E). Total procedure time was approximately 50 minutes and during the procedure, vital signs were stable, except for two episodes in which oxygen saturation dropped below 80% in the last third of the procedure but slowly recovered after approximately 2 minutes of oxygen therapy given by nasal prongs at 5 L/min. The procedure was continued except the two short rests for 90 seconds without endoscopic withdrawal and no position change of the patient was performed during the hypoxic episodes. After ERCP, the patient appeared deeply sedated and the vital signs, including oxygen saturation over 90% with 2 L/min via nasal prongs, remained stable in recovery room for 10 minutes and the patient was discharged to the general ward. Total sedative dose included the initial dose of the above drugs plus additional 100 mg intermittent propofol injections on demand. There was no free air on the post-ERCP chest X-ray. A complete neurologic examination was not performed due to unconscious mental status, but withdrawal movement to pain was examined. Intravenous flumazenil, 0.5 mg, was injected two times at 5 minutes intervals but her mental status was not improved. During the stay of the general
ward after ERCP, there was only one call by his family’s concern for his drowsy mental state 2 hours after ERCP. And then the neurologic examination by attending physician was non-specific without further aggravation compared to the time just after ERCP and no other additional change was notified from rounding nurse in late night and dawn. During the overnight, her vital signs and oxygen saturation with nasal prongs at 1-2 L/min was stable. Then the first seizure occurred 12 hours after ERCP and the seizure was generalized tonic-clonic type for about 2 minutes with high blood pressure (180/100 mm Hg), tachypnea (30/min) and tachycardia (120/min) while oxygen saturation decreased to 80%. Increasing oxygen by facemask (more than 8 L/min) was required to maintain oxygen saturation greater than 90%. Emergency non-enhanced brain CT showed no hemorrhage and no air emboli, but a low-density area of right middle cerebral artery territory at right parietotemporal and occipital lobes (Fig. 2 arrows). Subsequent brain magnetic resonance imaging (MRI) showed clear evidence of widespread acute cerebral infarctions in both cerebral hemispheres with right-sided predominance (Fig. 3). Neurologic examination revealed normal pupil reflex to light with no nystagmus and poor gag reflex. Motor response in the right upper extremity was grade IV with hypotonia in the other extremities and no limb response to pain. Two more seizures with similar pattern then developed during the intensive care unit (ICU) stay. Blood tests showed WBC 46,000/μL, CRP 144.7 mg/L, CK-MB 18.3 ng/mL, troponin-I 0.75 ng/mL, brain natriuretic peptide 131.6 pg/mL, and D-dimer 3,193 ng/mL. Trans-thoracic echocardiogram was proposed for the evaluation of infective endocarditis, intracardiac shunt or air embolism but her family refused the examination due to the cost. We changed intravenous antibiotics to nafcillin 2 g every four hours, ceftriaxone 2 g every 12 hours, ampicillin/sulbactam 3 g every six hours after 3 separate blood cultures due to possible multiple cerebral infarctions from infective endocarditis, and subcutaneous enoxaparin 1 mg/kg every 12 hours was given. On the second day, vital sign showed blood pressure 170/100 mm Hg, pulse rate 120/min, respiratory rate 28/min, body temperature 37.8°C, and oxygen saturation 90% to 95% with oxygen nasal cannula at 3-5 L/min. Neurologic response revealed coma comparable to that of the first day. On the third day, she showed persistent high blood pressure, tachycardia, tachypnea and intermittent high body temperature. On the fourth day, both the heart rate and blood pressure decreased excessively to less than 50/min and 60/40 mm Hg, respectively and oxygen saturation was difficultly maintained at 80% to 85% by non-rebreathing mask at 15 L/min. The patient deteriorated rapidly and died despite intravenous inotropic infusions. No cardiopulmonary resuscitation was performed based on family preference. In the meantime, there was still no growth in the sets of blood cultures.

**DISCUSSION**

Neurologic complication after gastrointestinal (GI) endoscopy is uncommon but sometimes severe and even fatal. Sedation-related complications after GI endoscopy are relatively common, generally transient and easily treated by conservative management except for few cases accompanied with hemodynamic compromise. The recognition and diagnosis of neurologic complications,
such as air embolism or hemorrhagic stroke, after complex therapeutic GI procedures is sometimes difficult to recognize because the clinical symptoms and signs are initially similar to that after deep sedation [3,5]. The sedated patient after endoscopy, especially complex procedures, should be monitored by blood pressure, heart rate, pulse oximetry and ECG and should be admitted to the recovery room until at least 30-60 minutes before discharge [1,4]. But this patient was observed to monitor vital signs and oxygen saturation in recovery room for only 10 minutes.

Aldrete scoring system is commonly used for the assessment of discharge and a patient with score 8 or higher can be considered for discharge [6]. Although this patient scored approximately 7 on Aldrete scoring at the time of discharge from the recovery room, it likely doesn’t matter from our experience of previous ERCP in the fact that his saturation with vital sign was spontaneously recovered only through oxygen supply via nasal prong without help of other specific maneuver and there was some response to pain after ERCP with stable vital sign including respiration. But there was unsatisfied missing in that the patient would not be monitored in the ICU for deep drowsy state after ERCP due to the lack of our experience of rare severe neurologic complication after sedative endoscopy.

Other potentially severe complications such as severe necrotizing pancreatitis, massive bleeding, and GI perforation after therapeutic procedures such as ERCP could be recognized early by real-time endoscopic view and post-procedure laboratory findings and promptly managed by endoscopic or surgical treatment according to the clinical characteristics and severity [7]. The cases of severe neurologic complication such as air embolism accompanied with cerebral infarction or intracranial hemorrhage after various endoscopic procedures have been previously reported [8,9].
Air embolism which is a result of direct communication between air and blood vessels by pressure gradient favoring the passage of air into the circulation has been previously reported. Risk factors for air embolism include previous interventions or surgeries of bile duct system, blunt or penetrating trauma to liver, biliary atresia, and interventional techniques including cholangiography and biliary sphincterotomy. Like the occurrence of air embolism after ERCP, hematogenous spread of septic emboli through the sphincterotony and bile duct injury site attributable to repeated manipulations of accessories for stone removal may cause the development of delayed multiple septic cerebral infarctions in this patient.

The treatment includes left lateral decubitus position to trap air in the nondependent right atrium, Trendelenburg position to allow air in pulmonary outflow tract, and hyperbaric oxygen therapy to promote the resorption of nitrogen from the bubbles and reduction of the size of bubble [3]. The risk of air embolism in this patient was considered low during the ERCP because of spontaneous recovery of the oxygen saturation with low oxygen supply without position change of the patient, no evidence of hemodynamic compromise and lack of apparent air in brain CT and MRI.

One previous intracerebral hemorrhage after gastric polypectomy was believed to be associated with the combination of the procedure-induced stress and the administration of adrenaline [8]. Another subarachnoid hemorrhage after screening colonoscopy was related to the increased intracranial hypertension accompanied by increased intra-abdominal pressure during colonoscopy [9].

A possible infective endocarditis complicated with current cholangitis was less likely, but could be a differential diagnosis. Neurologic events such as cerebral infarction, cerebral hemorrhage, and cerebral encephalopathy in the infective endocarditis frequently require admission to ICU [10]. Complications occur early during the course of infective endocarditis in up to 40% of the patients. Cardiac valvular abnormality is a well-known risk factor and other host-related factors include chronic alcoholism, meningitis, and autoimmune disease. Procedure-related risk factors are thought to be secondary infection of a heart valve through the bacteremia following the procedure. Prophylactic antibiotics are often considered in the patients with current infection [11,12]. In this patient, the infective endocarditis could be excluded based on no prior history of heart problems except for essential hypertension and no other medical history, as well as non-specific initial ECG and cardiac enzyme results. These test results also had no specific changes after the seizure and there was no growth of microorganisms in blood cultures.

In summary, we report that a very rare delayed diagnosis of fatal cerebral infarctions 12 hours later after ERCP occurred in a patient with CBD stones, who experienced two prolonged hypoxic events about 2 minutes during ERCP but slowly recovered with oxygen therapy by nasal prong. The endoscopist should keep in mind that if the patient undergoes complex endoscopic procedure such as ERCP, experiences relatively prolonged hypoxic events during the procedure and has not recovered by the use of the antidote of sedative more than two times, close observation of the patient is very important in recovery room over 30 minutes. And the consideration of ICU stay for 1 day is advisable for the patient to discover a possible delayed occurrence of fatal cerebral infarction.

REFERENCES