Case Report

Development of acute ischemic stroke in two patients with acute upper gastrointestinal bleeding

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Abstract: Acute ischemic stroke is one of the leading causes of death in the world. Major risk factors include behavior, metabolism, and environment-related factors. To our knowledge, no study has reported the association between acute ischemic stroke and acute upper gastrointestinal bleeding. Herein, we presented two cases of acute upper gastrointestinal bleeding who developed acute ischemic stroke during their hospitalizations. The potential mechanisms for explaining their association were preliminarily discussed.

Keywords: Bleeding; gastrointestinal; stroke; cerebral; infarction

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Introduction

Stroke is characterized as the focal neurological function is suddenly lost due to the infarction or hemorrhage in the brain, retina, or spinal cord (1,2). It is mainly divided into ischemic stroke (i.e., cerebral infarction) and hemorrhagic stroke. According to the Global Burden of Disease study 2010, there were 16.9 million people with first stroke and 33 million stroke survivors (3). According to the Global Burden of Disease study 2013, it became the 3rd cause of global years of life lost (4). Potential risk factors of stroke include behavior-related factors (smoking, poor diet, and low physical activity), metabolism-related factors (arterial hypertension, obesity, diabetes, high total cholesterol, and renal dysfunction), and environment-related factors (air pollution and lead exposure) (5). To our knowledge, no study reported the potential association of cerebral infarction with acute upper gastrointestinal bleeding. In this report, we introduced two cases admitted with acute upper gastrointestinal bleeding who developed cerebral infarction during their hospitalizations.

Case presentation

Case 1

On the afternoon of January 26, 2016, a 53-year-old male patient was admitted to our department due to intermittent haematemesis and melena for 3 days. He underwent duodenopancreatectomy for duodenal neoplasms 8 years ago. He had a long-term history of aspirin use. Before his admission, a regular blood test demonstrated that hemoglobin concentration was 140 g/L (normal range: 110–170 g/L), red blood cell was 4.77×10^{12}/L (normal range: 4.0×10^{12}–5.5×10^{12}/L), white blood cell was 9.8×10^{9}/L (normal range: 4.0×10^{9}–10.0×10^{9}/L), and platelets count was 325×10^{9}/L (normal range: 100×10^{9}–300×10^{9}/L). Hepatitis B or C virus infection was negative. Levels of tumor markers (e.g., CEA, CA-50, CA199, and CA24-2) were within the normal range. Liver function was within the normal range. An intravenous infusion of esomeprazole and octreotide was continuously given.

On January 27, 2016, a regular blood test demonstrated

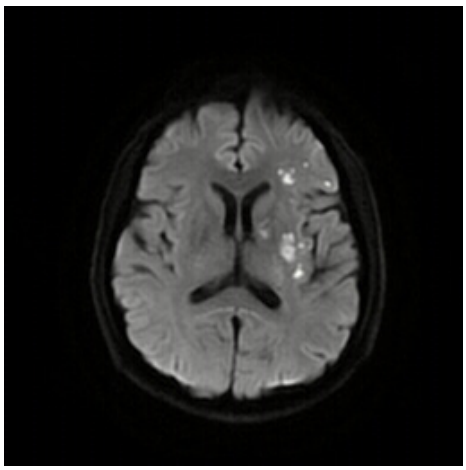

Figure 1 DWI examination in the first patient. DWI, diffusion weight imaging.

that hemoglobin concentration was 108 g/L (normal range: 130–175 g/L), red blood cell was 3.63×10^{12}/L (normal range: 4.3×10^{12}–5.8×10^{12}/L), white blood cell was 9.0×10^{9}/L (normal range: 3.5×10^{9}–9.5×10^{9}/L), and platelets count was 267×10^{9}/L (normal range: 125×10^{9}–350×10^{9}/L). On the morning of January 28, 2016, after a written informed consent from this patient and his relatives was obtained, an upper gastrointestinal endoscopy was performed. Endoscopy showed active bleeding in the stomach, but no source of bleeding was identified. On the afternoon of this day, there was a significantly decreased hemoglobin concentration of 88 g/L (normal range: 130–175 g/L). And then, a superior mesenteric arterial angiography did not identify any source of bleeding. Pharmacological therapy was continued.

On the evening of January 29, 2016, he was found confused and faint. A regular blood test demonstrated that hemoglobin concentration was 70 g/L (normal range: 130–175 g/L), red blood cell was 2.38×10^{12}/L (normal range: 4.3×10^{12}–5.8×10^{12}/L), white blood cell was 9.7×10^{9}/L (normal range: 3.5×10^{9}–9.5×10^{9}/L), and platelets count was 253×10^{9}/L (normal range: 125×10^{9}–350×10^{9}/L). Thus, a continued bleeding was considered. He received two units of red blood cell and 170 mL of fresh frozen plasma.

On the morning of January 30, 2016, the strength of his right extremities was remarkably weakened. Hemoglobin concentration was 68 g/L (normal range: 130–175 g/L). Cranial MR, MRA, and diffusion weight imaging (DWI) examinations showed multiple cerebral infarction in the left frontal lobe, nucleus basalis, and corona radiata, obstruction of left arteria cerebri media, and stenosis of right arteria cerebri anterior and left arteria cerebri posterior (*Figure 1*). A consultation of neurologist was performed. Rosuvastatin was prescribed. After that, the activity of right extremities gradually recovered. No bleeding was further observed. On February 14, 2016, a regular blood test demonstrated that hemoglobin concentration was 83 g/L (normal range: 130–175 g/L), red blood cell was 3.15×10^{12}/L (normal range: 4.3×10^{12}–5.8×10^{12}/L), white blood cell was 8.1×10^{9}/L (normal range: 3.5×10^{9}–9.5×10^{9}/L), and platelets count was 291×10^{9}/L (normal range: 125×10^{9}–350×10^{9}/L). On February 14, 2016, he was discharged without any further complaint of haematemesis and melena.

Case 2

On the evening of October 21 2016, a 46-year-old male patient was admitted to our department due to haematemesis and melena for 2 days. He had a 2-year history of arterial hypertension and lacunar infarction. Long-term use of aspirin, clopidogrel, and atorvastatin was prescribed. He also had a 28-year history of smoking and alcohol abuse. At his admission, the blood pressure was 97/77 mmHg, the pulse was 126 b.p.m., no remarkable abdominal tenderness or rebound was observed, and the mobility of extremities was normal. A regular blood test demonstrated that hemoglobin concentration was 84 g/L (normal range: 130–175 g/L), red blood cell was 2.69×10^{12}/L (normal range: 4.3×10^{12}–5.8×10^{12}/L), white blood cell was 16.5×10^{9}/L (normal range: 3.5×10^{9}–9.5×10^{9}/L), and platelets count was 241×10^{9}/L (normal range: 125×10^{9}–350×10^{9}/L). Blood glucose was 10.56 mmol/L (normal range: 3.9–6.1 mmol/L). No remarkable abnormality of the liver and renal function was observed. Prothrombin time, INR, and APTT were within the normal range. Hepatitis B or C virus infection was negative. Levels of serum tumor markers (e.g., alpha-fetoprotein, CEA, CA-50, CA199, CA24-2, and PSA) were within the normal range. Except for fluid infusion, an intravenous infusion of pantoprazole and somatostatin was continuously given.

On the morning of October 22, 2016, he presented with melena again. After a written informed consent from this patient and his relatives was obtained, an emergent upper gastrointestinal endoscopy was performed. Endoscopy demonstrated an ulcer with active bleeding at the angular notch and duodenal bulb (*Figure 2*). Thus, a diagnosis of peptic ulcer related upper gastrointestinal bleeding was established. At the same time, hemoglobin concentration

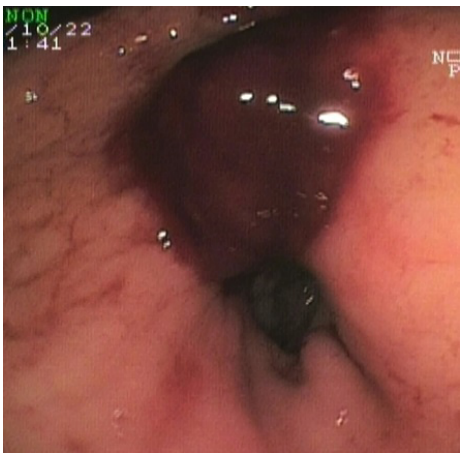

Figure 2 Upper gastrointestinal endoscopy at his admission in the second patient.

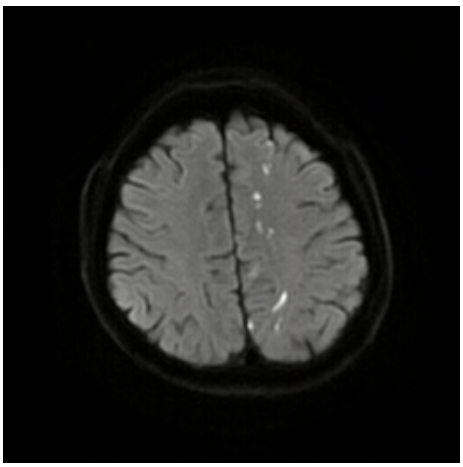

Figure 3 DWI examination in the second patient. DWI, diffusion weight imaging.

was 69 g/L (normal range: 130–175 g/L), red blood cell was 2.18×10^{12}/L (normal range: 4.3×10^{12}–5.8×10^{12}/L), white blood cell was 10.9×10^{9}/L (normal range: 3.5×10^{9}–9.5×10^{9}/L), and platelets count was 205×10^{9}/L (normal range: 125×10^{9}–350×10^{9}/L). A 1.5-unit of red blood cell was further infused. After that, neither haematemesis nor melena recurred. On October 23, 2016, hemoglobin concentration was 84 g/L (normal range: 130–175 g/L), red blood cell was 2.63×10^{12}/L (normal range: 4.3×10^{12}–5.8×10^{12}/L), white blood cell was 10.3×10^{9}/L (normal range: 3.5×10^{9}–9.5×10^{9}/L), and platelets count was 210×10^{9}/L (normal range: 125×10^{9}–350×10^{9}/L).

On the early morning of October 24, 2016, he presented

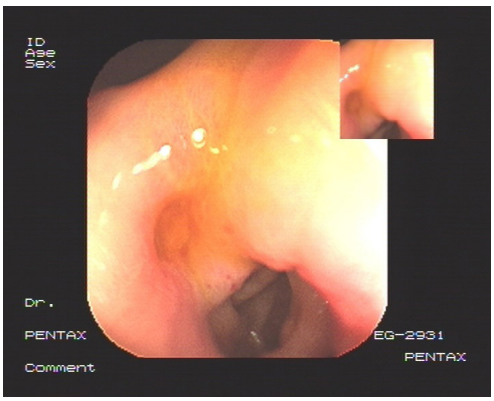

Figure 4 Upper gastrointestinal endoscopy after treatment in the second patient.

with the right lower extremity swelling pain. An emergent color Doppler ultrasound did not show any thrombus in both lower extremities. And then, the symptoms were alleviated. However, on the evening of this day, he could not move the right lower extremity. On physical examinations, the algesthesia of the right lower extremity was normal, and Babinski's sign was positive. Cranial CT scans demonstrated multiple lacunar cerebral infarctions. A consultation of neurologist was performed. Cranial MR, MRA, and DWI examinations showed acute infarction in the left frontal lobe, parietal lobe, corpus callosum, nucleus basalis, and corona radiata, multiple lacunar cerebral infarctions, stenosis of left arteria basilaris and arteria cerebri anterior, media, and posterior (*Figure 3*). Considering a recent history of gastrointestinal bleeding, thrombolytic or antiplatelet drugs were not considered. Intravenous use of edaravone and cinepazide maleate and oral use of citicoline sodium capsules and atorvastatin were given. After that, the activity of right lower extremity gradually recovered. On October 31, 2016, an upper gastrointestinal endoscopy showed that peptic ulcer was at the healing phase (*Figure 4*). On November 2, 2016, he was discharged without any further complaint of haematemesis and melena.

Discussion

Nowadays, acute upper gastrointestinal bleeding, which refers to a fresh bleeding from a lesion proximal to the ligament of Treitz, still represents a common emergency condition in the digestive diseases (6-8). In the United States, there are 160 hospital admissions with acute upper

gastrointestinal bleeding per 100,000 population per year (9). In the United Kingdom, there are 6,750 patients admitted with acute upper gastrointestinal bleeding during a 2-month period (10). According to the findings of population-based studies, the incidence of acute upper gastrointestinal bleeding is 90–108/100,000 inhabitants per year (11-14). Peptic ulcer is the major cause of acute upper gastrointestinal bleeding. Indeed, a history of aspirin use has been clearly recorded in both cases. Unfortunately, in the first case, endoscopy did not find any clear sources of bleeding. This might be because an abnormal anatomy after duodenopancreatectomy precluded from a more accurate endoscopic finding.

The overall mortality of acute upper gastrointestinal bleeding is 3–14%. But not all death events are attributed to the bleeding episodes. Thus, the conditions that result in a high risk of death but are not directly related to bleeding should be further explored. In our cases, cerebral infarction, which carries a high risk of mortality and morbidity worldwide, was followed by acute upper gastrointestinal bleeding episodes. The images showed poor cerebral vascular conditions in both cases, and a previous history of arterial hypertension and lacunar infarction and long-term history of cigarette smoking was clearly recorded in the second case. These conditions might indicate a potential risk of embolism or stenosis. In addition, we proposed two hypotheses for explaining their association as follows: (I) acute massive blood loss results in systemic vasoconstriction, especially cerebral vessels, thereby increasing the risk of ischemic stroke; and (II) cerebral ischemia and reperfusion injury is caused by acute blood loss and subsequent blood transfusion. Regardless of the potential mechanisms, the brain protection might be necessary to decrease the risk of acute ischemic stroke. Continuous hemodynamic monitoring is warranted to avoid hypotension, and special care in sedation should be applied for patients having had acute blood loss. Certainly, randomized controlled trials should explore the clinical benefits of brain protection in patients with acute upper gastrointestinal bleeding and a high-risk of cerebral infarction.

In addition, we should not neglect a possibility of ischemic stroke as a complication of endoscopic examination. Cerebrovascular accidents, including both transient ischemic strokes and ischemic strokes, have been rarely reported during or following endoscopic procedures (15,16). In a prospective audit of 14,149 upper gastrointestinal endoscopies, six cerebrovascular accidents were reported, with attributable fatality in at least one case; therefore, a risk of cerebrovascular accident can be estimated as high as approximately 1 in 2,300 for gastroscopy (15). Acute severe hypovolemia in patients with upper gastrointestinal bleeding and possible hypotension due to sedation have been acknowledged as the main causes of such complications (15,16).

In conclusion, we found a unique phenomenon that cerebral infarction might be secondary to acute upper gastrointestinal bleeding. Due to the nature of our case report, we could not arbitrarily establish an absolute association between acute ischemic stroke and acute upper gastrointestinal bleeding. In future, well-designed case-control studies or prospective cohort studies should be warranted to explain the association between them.

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Footnote

Conflicts of Interest: The authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/amj.2017.02.05). Dr. Qi serves as an Editor-in-Chief of AME Medical Journal. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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