

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: The article “Cerebrovascular air embolism during endoscopic esophageal varix ligation under sedation or anesthesia: a case report” is well written though I suggest the following corrections:

(1) For the case report where the procedure was already performed, one should know whether it was sedation or anesthesia. So, remove “or anesthesia” from the title and keep it as “ligation under sedation”

We have removed “or anesthesia” from the title and keep it as “ligation under sedation”

(2) During this procedure, multiple varices were ligated and not just one Varix. Also, there is no clear evidence of cerebral air embolism in the entire script, so the cerebral air embolism was suspected. Hence the correct title would be “A case report of suspected cerebrovascular air embolism during endoscopic ligation of esophageal varices under sedation with fatal outcome”.

As the reviewer’ opinion, we have correct our title. The title is “Suspected cerebrovascular air embolism during endoscopic esophageal varices ligation under sedation with fatal outcome: a case report”.

(3) Key words: Paradoxical air embolism should be one word. Sedation/anesthesia should be removed.

We have removed Sedation/anesthesia as key words. Now the key words are: Cerebral

infarction; Paradoxical air embolism; Endoscopic ligation; Esophageal variceal; Sedation; Case report.

(4) The case summary is totally inadequate. Background and conclusions can be shortened. In a case report, case summary is extremely important.

We have revised the summary. Background and conclusions have been shortened.

Background:

Air embolism is a very rare, yet serious and potentially fatal complication of digestive endoscopic treatment. Air embolism is the result of air directly entering the arteries or veins. However, to recognize neurological dysfunction under sedation can be difficult. Therefore, it is extremely important to identify high-risk groups and take preventive measures.

Case summary:

Herein, we report a 74-year-old female patient with esophageal varices who suffered from consciousness disturbance after the third endoscopic ligation of esophageal varices under sedation. Combined with the patient's imaging examination results and medical history, we highly suspected that the patient had developed paradoxical cerebral air embolism during endoscopic ligation. We learned that the patient died at a later follow-up. In order to be able to identify and prevent the occurrence of air embolism early, we summarize and analyze the risk factors, pathogenesis, clinical manifestations, prevention and treatment options of gastrointestinal endoscopy complicated by cerebral air embolism.

Conclusion:

Electroencephalographic monitoring helps to recognize the occurrence of air embolism in time and increase the patient's chance of survival.

(5) The dosages of the drugs used for during the procedure indicate that it was sedation and not anesthesia.

We agree the reviewer's opinion, and have removed "anesthesia" in some places.

(6) Use of shorter acting narcotics like Fentanyl or remifentanyl infusion are better suited for procedures in high risk patients who already showed cerebral infarction pre-operatively than sufentanyl.

We agree the reviewer's opinion, and have mentioned this in "discussion" part.

(7) During the procedure: it is easy to monitor end tidal CO₂ which should have been monitored and mentioned in the discussion part. Monitoring of end tidal nitrogen is also very useful, if available, Also, for a patient with an existing cerebral infarct, any kind of cerebral function monitoring would have been useful to detect the level of sedation. While BIS is available for many years and should have been used, newer SedLine monitor is desirable.

We agree the reviewer's opinion, and have mentioned this in "discussion"part. In our case, End-tidal carbon dioxide (EtCO₂) monitoring was not used because the patient was not breathing through a mask, endotracheal tube, or laryngeal mask airway, and an EtCO₂ sampling nasal cannula was not available.

(8) In the discussion, need to mention the usefulness of TEE, precordial doppler and transcranial doppler. Precordial doppler would have been appropriate in this particular case considering the patient had an enlarged heart with tricuspid regurgitation. As appropriately mentioned in the script by the authors that the patient was a high risk for air embolism, transcranial doppler would have been useful.

We have mentioned this in the discussion in revised manuscript.

(9) In the discussion, the authors also need to mention the preventive measures of air embolism in high risk patients like the position during the procedure, adequate hydration etc.

We have mentioned this in the last part of the discussion in revised manuscript.

(10) The discussion should also mention that “Air embolism is iatrogenic and preventable”. Lethal volumes of entrained air should be mentioned which is around 200 to 300 ml or 3–5 ml/Kg (Closer the vein of entrainment to the heart, smaller the volume required.)

We have mentioned this in the last part of the discussion in revised manuscript.

(11) Also mention, why the patient was sent to the ward and not to the high dependency unit (HDU) despite not regaining consciousness.

We have explained the reason in the revised manuscript. The CT revealed no obvious bleeding or infarction. The patient's state of consciousness then improved. After consulting the doctor in charge and the patient's family members, the patient was returned to the Gastroenterology High Dependency Unit for continued monitoring and observation.

(12) And the most important, how the diagnosis of cerebral air embolism was concluded in this particular case should be mentioned somewhere.

The patient's previous echocardiography did not find a cardiac shunt or intra-atrial thrombosis; the patient also had no atrial fibrillation, diabetes, hyperlipidemia, or other diseases, and subsequent CTA results suggested the absence of carotid atherosclerotic plaque and intracranial artery stenosis. The patient did not have intraoperative hypotension; therefore, the patient did not have any high-risk factors for cerebral infarction. But the patient had a history of multiple endoscopic esophageal varix ligations or gluing treatments. There was a high risk of

air embolisms in the past; traffic arteries were formed due to past disease. Air may have flowed back into the left ventricle along the injured intestinal artery, and then into the systemic circulation to form an air embolism. The diagnosis of air embolism is usually difficult and complicated because air entering the systemic circulation may be rapidly distributed to various organs; therefore, it is typically necessary to exclude other life-threatening processes. The patient's blood ammonia level was normal, which ruled out the possibility of hepatic encephalopathy, and there was no cerebral ischemia or hypoxia caused by hypotension, hypoperfusion and hypoxia, and brain dysfunction caused by hypoglycemia during the operation. The causes of air embolism are relatively hidden. some air embolisms are found only in postmortem autopsy. Therefore, We think this patient is probably air embolism.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Very well written manuscript. However the author widens at some points