Case and Review

When in Trouble Think of the Bubble: Paradoxical Cerebral Arterial Gas Embolism after Endoscopic Retrograde Cholangiopancreatography

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Abstract

Air embolism (a result of direct communication with the vasculature and an external pressure gradient from the gastrointestinal or the biliary tract), although rare, is a potentially devastating adverse event seen in endoscopic retrograde cholangiopancreatography (ERCP) procedures. Whether venous, arterial, or paradoxical, the clinical presentation ranges from asymptomatic patients to cardiorespiratory arrest. This is of particular importance because it makes the diagnosis of air embolism even more difficult in an already sedated patient. Since early recognition increases the chances of patients' survival, endoscopists should be highly motivated and trained to recognize this complication as early as possible. With only 60 cases of air embolism reported (and even fewer related to paradoxical air embolism), we aimed to report a case of

paradoxical cerebral air embolism in a patient undergoing ERCP due to a common bile duct stricture and to provide a mini-review of this clinical entity that can serve as a bedside quick reference guide for endoscopists worldwide.

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Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) has become the gold standard when treating patients with benign or malignant diseases of the biliary tract [1]. However, any ERCP (as well as all endoscopic procedures) is not without adverse effects. While post-ERCP pancreatitis, bleeding, perforation, and infectious adverse events are amongst the most common, cardiopulmonary adverse events should not be considered negligible, accounting for 4–16% of ERCP-related adverse events. Amongst the latter, air embolism, although rare, is a potentially devastating adverse event [2, 3].

Air embolism can take the form of venous air embolism (where the embolus reaches the pulmonary circulation), systemic arterial air embolism (where the embolus reaches the coronary or the cerebral arteries), and paradoxical air embolism (where the venous embolus reaches the systemic circulation). A recent prospective cohort study over a 15-month period of patients who underwent ERCP monitored for venous arterial embolism reported an incidence of 2.4% (20 out of 843 ERCP procedures) [4]. The United States of America National Inpatient Sample from 1998 to 2013 reported the occurrence of air embolism in 3.32 per 100,000 ERCP procedures [5]. With only 60 cases of air embolism reported (and even fewer related to paradoxical air embolism) [6–58], we aimed to report a case of paradoxical cerebral air embolism in a patient undergoing ERCP due to a common bile duct (CBD) stricture and to provide a mini-review of this clinical entity that can serve as a bedside quick reference guide for endoscopists worldwide.

Case Presentation

A 79-year-old male was admitted to our department for a programmed ERCP session for a mid-CBD stricture. His past medical history included hypertension and type 2 diabetes mellitus. He was given 8 mg midazolam premedication as well as 50 mg pethidine (both intravenously). The patient was placed in a left lateral decubitus position while receiving oxygen (O₂) through a nasal cannula. Monitoring included noninvasive arterial blood pressure monitoring by cuff, pulse oximetry, and three-lead electrocardiography. 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.

We reported the following ERCP findings: after CBD cannulation, contrast material was injected with the cholangiography revealing a 10-mm mid-CBD stricture with concomitant intrahepatic duct and suprapapillary dilation up to 17 mm; no filling defect was noted (Fig. 1). An endoscopic sphincterotomy was performed using a wire-guided pull-type sphincterotome.

Afterwards, a balloon catheter was inserted in the CBD via the wire-guided technique and inflated according to the CBD diameter. Under strict fluoroscopic guidance, the inflated balloon catheter was pulled several times from the CBD into the lumen of the duodenum; no stones were expelled. Balloon occlusion cholangiography at the end did not reveal any additional radiographic findings. Brushing of the stenotic CBD part was performed and a 10-Fr, 7-cm plastic stent was inserted into the CBD so as to secure bile drainage.

Up to that point, the procedure duration was 30 min, during which the patient's vital signs and hemodynamic parameters were unremarkable. Due to the suprapapillary concomitant dilation noted before, we decided to terminate the ERCP by taking biopsy samples from the papilla; afterwards, the endoscope was withdrawn. While repositioning the patient from the left lateral decubitus to the supine position, he developed marked desaturation and hypotension. Flumazenil and naloxone were administered so as to reverse any remaining benzodiazepine and opioid effect, respectively, and high-flow O₂ was also administered. Shortly after, the patient's hemodynamic parameters were restored, but he failed to regain consciousness (Glasgow Coma Scale score 7).

The patient was intubated within the following minutes and transported to the intensive care unit for further management. A bedside transesophageal echocardiogram bubble study was undertaken that demonstrated a patent foramen ovale (Fig. 2a, b). An emergency head computed tomography followed revealing no air but an extensive hypodense lesion in the right parieto-occipital lobe, indicating an extensive ischemic infarction (Fig. 3).

After a few days, the patient slowly regained consciousness and was extubated. However, he exhibited left hemiparesis. In that context, in our department we have been using EtCO₂ monitoring ever since in all ERCP procedures.

Discussion

Pathophysiology and Risk Factors

Since air embolism is the end result of the direct communication between a source of air and the arterial or venous vasculature, its pathophysiology is twofold. On the one hand, an increased pressure gradient (insufflated air during any endoscopic procedure) must be present so as to favor the passage of air into the circulation. On the other hand, a disruption of a mucosal-vascular barrier (a direct vasculature defect per se or an organ wall defect) is also implicated [59–62].

During ERCP, the endoscopist controls the intermittent flow of pressurized air (or carbon dioxide [CO₂]) so as to distend the bowel, the biliary tree, and the pancreatic duct. Both air amount and velocity play a crucial part in the severity of the embolus. However, in most cases this is not enough; for the air embolus to reach the regional veins or the arterial bed, a disruption of a mucosal-vascular barrier must take place. These disruptions may involve (1) endoscope (or its accessories)-induced mechanical irritation of the bile duct wall, (2) biliary-venous fistulas, (3) air transgression into adjacent veins from mucosal and/or muscular wall inflammation, (4) intramural dissection of air into the portal venous system via injured duodenal vein radicles, (5) portal vein cannulation, and (6) portocaval or transhepatic collaterals

[59–62]. Table 1 depicts the risk factors for developing air embolism (not only for ERCP patients).

Semiology

The effect and the corresponding sign(s) of an air bubble depend on both the flow and the volume of air introduced into the circulation. Therefore, the clinical presentation ranges from asymptomatic patients to cardiac arrest, with many cases only being diagnosed postmortem or due to the endoscopist's high clinical suspicion that triggers the undertaking of special diagnostic procedures [59–62].

What is characteristic regarding ERCP-related air embolism is that, most often, the symptoms appear or get significantly worse upon repositioning the patient from the prone to the supine position after the procedure has ended. The small hydrostatic gradient created between the pancreatic/biliary ducts and the draining veins in the prone or semiprone position (typical for any ERCP procedure) renders the appearance of a venous air embolus more likely. Endoscopists should have an increased clinical suspicion of an air embolus in any ERCP patient that deteriorates abruptly upon position change at the end of the procedure [59, 63].

In the case of venous air embolism, the embolus travels from the superior vena cava to the right heart, leading to right ventricular strain and pulmonary hypertension, ending in cardiovascular collapse. In the case of systemic arterial air embolism, the embolus enters the aorta with the end result being myocardial ischemia, arrhythmias, congestive heart failure, cardiac arrest (in case of coronary emboli), or cerebral ischemia and increased intracranial pressure (in case of cerebral emboli). In the case of paradoxical air embolism, the venous embolus reaches the systemic circulation through, most commonly, an intracardiac shunt (patent foramen ovale), with the end result depending on the appearance of a cardiac or cerebral embolus. Other shunts implicated include (1) intrapulmonary right to left shunts, (2) arteriovenous shunts, (3) an atrial septal defect, (4) air passage into the left atrium via the pulmonary veins, (5) Thebesian veins, (6) insertion of the caval veins directly into the left atrium, and (7) retrograde flow into cerebral veins via the superior vena cava [59–61].

However, the absence of such an abnormality does not rule out paradoxical air embolism in patients undergoing ERCP, perhaps having to do with the fact that the differences in gases' partial pressures, bubble sizes, surface tensions, and vascular pressure influence emboli passage across the lungs [14, 41, 44, 46, 60, 64].

Diagnosis

Since early recognition increases the chances of patient survival, endoscopists should be highly motivated and trained to recognize this complication as early as possible, differentiating it from any sedation-related neurologic and/or cardiopulmonary problems due to central nervous system ischemia or hemorrhage. Since air may be rapidly absorbed from the circulation while diagnostic tests are being arranged, imaging or invasive procedures are sometimes inaccurate. Needless to say, all invasive diagnostic tests should be done after the patient's initial hemodynamic stabilization or while cardiopulmonary resuscitation takes place [59–62].

Possible clinician tools, studies, and their findings that can help diagnose air embolism during and after ERCP are summarized in Table 2.

Treatment

Initial Measures

In any ERCP patient showing signs of rapid hemodynamic compromise raising the suspicion of air embolism, the first step requires terminating the procedure so as to prevent further gas entry; if possible, the endoscopist should opt for decompressing the upper gastrointestinal tract while withdrawing the side viewing endoscope (decompression via the nasogastric tube can follow at a later time).

Earlier reports advocated putting the patient in a Trendelenburg position to minimize cerebral air emboli. However, recent reports strongly object to this practice as it can increase intracranial pressure and worsen cerebral edema (in cerebral air embolism patients). In arterial air embolism, the supine decubitus position should be preferred. Overall, the left lateral decubitus position (Durant maneuver) is preferred. This helps to prevent air from traveling through the right side of the heart into the pulmonary arteries, leading to right ventricular outflow obstruction (air migrates superiorly into the right ventricular making it less likely to embolize as the right ventricular outflow tract is placed inferior to the right ventricular cavity) [65].

Hemodynamic and respiratory stabilization are the next steps. In cardiac arrest patients, cardiopulmonary resuscitation should start immediately. Cardiopulmonary resuscitation can, also, break large air bubbles into smaller ones and, through the increased intrathoracic pressure produced, can force air out of the right ventricular into the pulmonary vessels. The patient should be put on high flow O₂ (beneficial for eliminating gas bubbles through a diffusion gradient as well as for treating hypoxia). If the patient was not intubated beforehand, in cardiac arrest patients or in patients exhibiting signs of cerebral hypoperfusion, an endotracheal tube should be secured as quickly as possible so as to protect the airway and provide adequate oxygenation [59].

Immediate volume expansion through fluid resuscitation is necessary so as to increase central venous pressure and thereby prevent further entry of gas into the venous circulation. Whether colloids or crystalloids should be administered remains a matter of debate. However, for cerebral air embolism patients with signs of increased intracranial pressure or cerebral edema, one must choose hyperosmolar solutions. Administration of vasotropes is essential for hemodynamically collapsed patients unresponsive to fluid resuscitation [60–62, 66, 67].

If bedside echocardiography confirms air in the right heart, a central venous catheter can be inserted so as to evacuate up to 50% of entrained air, but also for central venous pressure monitoring [61, 68].

Specific Treatment

Isolated venous air embolism usually requires no specific treatment; arterial air embolism should be treated as if treating patients with decompression sickness – first-aid O₂ followed by hyperbaric O₂ [69]. Timely hyperbaric O₂ therapy is the definitive treatment as it may decrease the size of air emboli by facilitating gas reabsorption, therefore minimizing air bubbles, reducing cerebral edema, reducing platelet aggregation due to bubble-induced endothelial damage, accelerating nitrogen reabsorption, preventing release of free O₂ radicals, and

increasing O₂ concentrations in the blood (improving tissue oxygenation and reducing ischemic reperfusion injury). Timely hyperbaric O₂ therapy administered within the first 5 h increases the chance for full recovery by 50% [70–72].

Prophylaxis

Since specific treatment modalities for air embolism are not always at hand, much interest has been drawn to recognize high-risk patients and implement specific prophylactic measures so as to reduce the severity (or even the incidence) of the disease.

Firstly, the importance of performing ERCPs only when clinically indicated cannot be overstated enough; by not overperforming ERCPs, the incidence of peri-ERCP adverse effects is kept to a minimum. Regarding patients per se, optimizing their volume status and maintaining normovolemia can prevent air embolism during the endoscopy [70].

Nowadays, CO₂ has replaced air as the “gold standard” for distension in any gastrointestinal endoscopic procedure. CO₂ markedly increases the safety margin of unintended gas migration into the circulation, even though CO₂ embolization has also been reported [73–75]. As mentioned in earlier reports relating to air (and not CO₂), reducing the maximum air pressure has also been found to decrease the risk of developing cerebral air embolism. Insufflated air and the rate of infusion are decisive for the outcome [76]. Some endoscopists favor water/saline irrigation to distend the biliary tree when performing direct retrograde cholangioscopy [77].

Researchers advocate the use of bedside precordial Doppler ultrasound for quick air detection within the heart and pulmonary vasculature, even before clinical symptoms appear, although real-time clinical data are lacking [59]. Other go even further by suggesting the use of echocardiography to rule out the presence of right-to-left shunt in all patients scheduled for ERCP [58].

Statement of Ethics

We have not submitted an ethical institutional review board statement. The patient gave his written informed consent for publication of his case.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

K. Ekmektzoglou, G. Alexandrakis, and P. Apostolopoulos designed the study. K. Dimopoulos, P. Tsibouris, C. Kalantzis, and E. Vlachou collected the clinical data. K. Ekmektzoglou, G. Alexandrakis, and P. Apostolopoulos analyzed the data and wrote the manuscript.

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Fig. 1. Endoscopic retrograde cholangiopancreatography cholangiogram revealing a 10-mm mid-common bile duct stricture with concomitant intrahepatic duct and suprapapillary dilation; no filling defect was noted.

Fig. 2. **a** Transesophageal color Doppler showing the interatrial shunt due to the presence of patent foramen ovale. **b** Transesophageal bubble study confirming the interatrial shunt due to the presence of patent foramen ovale.

Fig. 3. Head computed tomography revealing an extensive hypodense lesion in the right parieto-occipital lobe, indicative of an extensive ischemic infarction.

Table 1. Risk factors for developing air embolism (not only for endoscopic retrograde cholangiopancreatography patients)

Previous interventions/surgeries
Percutaneous transhepatic biliary drainage
Sphincterotomy
Stent insertion
Endoscopic papillary balloon dilation
Pre-cut papillotomy
Choledochoduodenostomy
Choledochojejunostomy
Hepaticojejunostomy
Status post Whipple's operation
Billroth II
Roux-en-Y
Kasai procedure (hepatopertoenterostomy)
Cholangioscopy
Insufflation of air with high pressure
Transhepatic portosystemic shunts/cholangiopathy
Bilio-venous fistula
Bilio-duodenal fistula
Portal cavernoma/splenomes-enteric portal shunt
Choledochal varices
Extrahepatic portal vein obstruction/Budd-Chiari syndrome
Splenomesenteric portal shunt
Blunt/penetrating liver trauma
Bile duct/surrounding veins inflammation
Cholangitis
Pylephlebitis
Biliary atresia
Gastrointestinal tumors
Gallbladder carcinoma
Cholangiocarcinoma
Hepatocellular carcinoma
Hepatic abscesses
Liver biopsy
Alcoholic liver cirrhosis
Transjugular intrahepatic portosystemic shunt
Recurrent/chronic pancreatitis
Mesenteric ischemia
Necrotizing enterocolitis
Gastric ulcer
Inflammatory bowel disease
Pneumatosis cystoides intestinalis

Table 2. Possible clinician tools, studies, and their findings that can help diagnose air embolism during and after endoscopic retrograde cholangiopancreatography

Vital signs and altered monitoring readings

Hypoxia
Hypotension
Capnography
End-tidal carbon dioxide decrease
Nitrogen seen among the expired gases if air used for insufflation

Inspection and physical examination

Cardiac auscultation
“Mill-Wheel” murmur
Cyanosis
Skin mottling

Standard diagnostic tests

Electrocardiogram
Pulmonary artery hypertension
Right ventricular strain
Nonspecific ST and T wave changes
ST-segment depression/elevation
Arterial blood gas
Hypoxemia
Hypercarbia
Complete blood count
Increased Hct (due to endothelial injury leading to leakage of intravascular fluid and elevated Hct)
Decreased platelet count with increased creatine kinase (due to air bubble and platelet binding, and platelet aggregation because of complement activation)
Increased creatine kinase (due to skeletal/cardiac/cerebral air embolization)
Brain natriuretic peptide
Troponin

Imaging

Chest X-ray
Air in pulmonary artery
Pulmonary edema
Adult respiratory distress syndrome
Diminished vascularity in the upper lobes
Intracardiac air
Atelectasis
Cardiac echocardiography (transthoracic echocardiogram or transesophageal echocardiogram)
Air in cardiac chambers
Intracardiac shunts
Acute right ventricle dilation
Decreased systolic function
Pulmonary artery hypertension
Global hypokinesis with mobile echogenic densities in the right atrium and right ventricle
Thoracic computed tomography
Air in the pulmonary artery and heart
Abdominal computed tomography
Air in the portal vein (if portal vein is cannulated)
Head computed tomography
Intraparenchymal gas
Midline shift
Cerebral edema
Uncal herniation
Head magnetic resonance imaging
Acute infarcts
Ventilation-perfusion lung scan
Pulmonary angiography

Precordial Doppler ultrasound

In cases where the air infusion rate is low and cardiac auscultation is inconclusive

Pulmonary artery catheter

Increased right heart and pulmonary artery pressures

Central venous pressure

Increased central venous pressure

Post mortem findings/autopsy

Fistulas
Air in the heart