CORRESPONDENCE

Fatal Cerebral Venous Air Embolism During Endoscopic Retrograde Cholangiopancreatography—Case Report and Review of the Literature

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Background

Endoscopic retrograde cholangiopancreatography (ERCP) is a routine minimally invasive technique for diagnostic and therapeutic purposes. According to a multicenter study in 1998, the rate of major complications was 1.38 % in diagnostic and 5.4 % in therapeutic ERCPs; fatal complications occurred in 0.21 and 0.49 % respectively [1] and were even lower in centers with high case volumes. Major complications include pancreatitis, cholangitis, duodenal perforation, hemorrhage, and the exceedingly rare event of systemic air embolism.

According to our own analysis of the literature and a review article from 2010 [2], only 10 cases of fatal systemic air embolism during ERCP have been reported so far. Intracranial embolism during ERCP has been reported in eight cases (Table 1) and of these, six had a fatal outcome [2–7].

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Case Description

A 58-year-old female patient (60 kg, 155 cm) with increased cholestase parameters (total bilirubin 173 µmol/l (<21), alkaline phosphatase 359 U/l (35–104)), dilation of the intrahepatic bile ducts, and a lesion suspected to be a cholangiocellular carcinoma located near the hilus of the liver received two unsuccessful ERCPs for papillotomy. For a third ERCP, the patient was transferred to a specialized center. Bilateral biopsy of the hepatic ducts and stenting of the common hepatic duct was performed. The procedure required insufflation of air with high pressure into the duodenum. During ERCP, a temporary abnormal breathing pattern and a decrease of oxygen saturation from 100 to 89 % was observed. After completion of the procedure, the patient did not regain consciousness when anesthesiological medication was stopped (Midazolam 1 mg, Propofol 180 mg, Butylscopolamin 10 mg, Flumazenil 0.25 mg).

The patient showed a persistent Glasgow Coma Scale (GCS) score of 3 and deviation of her eyes to the left indicating an early affection of the brain. Before the intervention, the patient received a central venous catheter in the right jugular vein. No aspiration of air or disconnection of the tubing was noted. Medication on admission had been Ceftriaxon only (2 g/day).

The patient was immediately transferred to the emergency room for further diagnostic evaluation. Auscultation of the heart was normal and oxygen saturation at this point of time was 100 % with high oxygen flow (10 l/min). The patient received a whole body computed tomography (CT) scan. Echocardiography was not performed.

The cranial CT scan revealed massive air embolism including the sinus sagittalis superior with venous congestion and brain swelling (Fig. 1a–d). The CT scan of the chest showed no signs of air embolism within the heart or

Table 1 Published cases of intracranial air embolism during ERCP (Table adapted from [2])

Reference	Age	Sex	Procedure	History	RF	Organs	PFO	CCT[a]	Outcome
Finsterer et al. [2]	59	F	ST-clearing	CHE, CJS, ST	CG, LA, BE	LR, HT, BN	Yes	Nm	Fatal
Nayagam et al. [3]	56	M	ST-clearing	ST	AC	HT, BN	No	Nm	Fatal
Stabile et al. [4]	65	M	BS-extraction	PTHD, BT	HB	LR, BN	No	Nm	Fatal
Tan et al. [5][b]	82	M	ST-exchange	ST	Nm	LR, HT, BN	Nm	Nm	Fatal
Argüelles Garcia et al. [6][c]	82	M	Expl. ERCP	BS extraction	CHP	BN	Nm	Art	Fatal
Bisceglia et al. [7]	78	M	BS-extraction	GDR, CHE, PT, BS extraction	CG, BS	LR, LN, HT, BN	No	Ven	Fatal
Van Boxel et al. [8, 13]	82	M	ST-removal	ST	CG, BS	HT, BN	Nm	Ven	Survived
Rabe et al. [14]	87	M	ST-clearing	ST	A	BN	Yes	Art	Survived

A adenoma, *AC* adenocarcinoma, *BE* bacteremia, *BS* bile stones, *BT* biliary sphincterotomy, *BN* brain, *CHE* cholecystectomy, *CHP* cholecystopancreatitis, *CG* cholangitis, *CJS* choledochojejunostomy, *Expl. ERCP* explorative endoscopic retrograde cholangiopancreatography, *F* female, *GDR* gastroduodenal resection, *HB* hemobilia, *HT* heart, *LA* liver-abscesses, *LR* liver, *LG* lung, *M* male, *Nm* not mentioned, *PFO* persistent foramen ovale, *PT* papillotomy, *PTHD* percutaneous transhepatic biliary drainage, *RF* risk factors, *ST* stenting of bile ducts, *VE* venous embolism

[a]Cranial computed tomography appearance of intracranial air embolism corresponding to arterial (Art) or venous (Ven) structures

[b]Article in French

[c]Article in Spanish

lung, however subsegmental pulmonary embolism could not be ruled out; the abdominal CT scan showed aerobilia and an obstruction of the left portal vein due to the mass near the liver hilus.

Due to the unfavorable prognosis, the patient received comfort therapy only with consent of her relatives. The patient died 1 day after ERCP.

The autopsy examination of the brain revealed multiple acute bilateral supra- and infratentorial infarctions with generalized edema and a concomitant mass effect including a midline shift and a unilateral uncal herniation.

The further macroscopic and histologic autopsy examination showed Echinococcosis of the liver with nodular multicystic tumor-like lesions in the liver segments IVa/b, but no manifestation in other organs. Changes suspicious for a small (3 mm) triangular defect of the wall of the right hepatic duct were observed and the vessels in this region showed perivascular hemorrhage. Examination of the thorax showed peripheral pulmonary embolism. A slit-shaped persistent foramen ovale (PFO) was noted.

Discussion

Air embolism during ERCP can arise when the integrity of the bile ducts and accompanying vessels is disrupted by mechanical damage or preexistent fistulas of these structures are laid open. The findings of the autopsy examination suggest that iatrogenic air inclusions of the bile duct entered the liver veins and portal vein.

Cerebral air embolism derived from venous air inclusions most commonly occurs within arteries as paradoxical
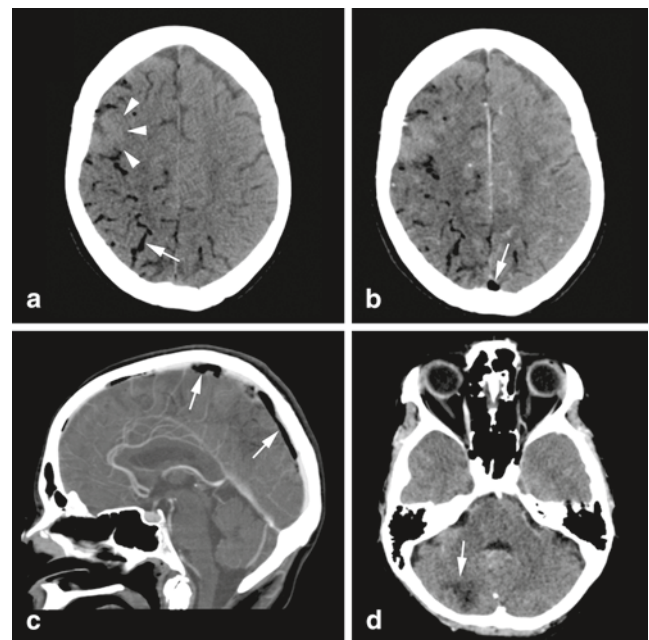

Fig. 1 Native axial cranial CT (**a**) showing inclusions of air within the subarachnoid spaces most likely corresponding to embolism of superficial cortical veins (*arrow*) predominantly within the right hemisphere. Large hypodense areas represent venous congestion with edema. Additional slightly hyperdense areas of the right frontal lobe (*arrowheads*) are due to discrete hemorrhagic transformation. Contrast enhanced axial cranial CT (**b**) focally showing diffuse contrast enhancement of the brain parenchyma as a consequence of the disruption of the blood brain barrier. Beside air inclusions within the subarachnoid space, air within the superior sagittal sinus (*arrow*) is observed. Contrast enhanced sagittal view (**c**) illustrating large inclusions of air within the superior sagittal sinus (*arrows*). Also an infratentorial hypodense lesion (*arrow*) probably due to air embolism of inferior cerebellar veins was observed (*axial view*) (**d**)

embolism, if the patient has a cardiac septal defect like a PFO as observed at the autopsy of the patient described here. If large amounts of air reach the circulation, direct transpulmonal passage of air may be possible [4]. However, both effects require additional pulmonary hypertension to induce paradoxical embolism [8].

A different pathway that has been proposed is retrograde passage of air within the venous system meaning that air would pass the vena cava inferior, the right atrium, the vena cava superior, and vena jugularis interna to reach the brain. Another possible way for venous dissemination of air would be portocaval collaterals.

In the case presented here, the observation of large air emboli within the superior sagittal sinus (*arrows* in Fig. 1b and c) and within the subarachnoid space corresponding to the anatomical structures of the superficial cortical veins (Fig. 1a), argues for a retrograde passage of air via the venous system. In such cases, the right hemisphere seems to be more commonly affected, due to the shorter and anatomically more direct way into the right jugular vein [9], which is consistent with our observations (Fig. 1a and b). Evidence for air inclusions within the circulus arteriosus willisii was neither observed in the native CT scan nor in the contrast-enhanced CT-angiography. However, from our findings (additional) paradoxical arterial embolism cannot be ruled out. The autopsy examination showed multiple intracranial infarctions, but without discriminating if those were of venous or arterial origin.

Regarding the previously published cases of intracranial air embolism during ERCP (Table 1), only two patients showed air inclusions within structures corresponding to the superficial cortical veins [7, 8] and this was only in one case discussed as a possible retrograde passage of air. However retrograde passage of air within veins has been shown in experimental models [10] and has been proposed to be underestimated in cases of intracranial air embolism [11]. Lacking the proof of intracranial arterial or venous embolism in the autopsy examination, it will remain a matter of debate which mechanism (predominantly) occurred in the case reported here.

Beside cardiac auscultation (loud churning sound) and proof of air bubbles with transthoracic echocardiography, CT scans usually provide the most helpful information in cases of systemic air embolism. With this imaging modality, the macroscopic air embolism can be identified within the vessels of the affected organs. Measurement of Hounsfield Units (HU) helps to distinguish air inclusions (HU < -500) from fat (HU about -100). Furthermore, the secondary signs of embolism can be visualized, e.g. infarction pneumonia of the lung and swelling of the brain due to edema. Contrast enhanced CT angiography may be helpful to distinguish venous and arterial air embolism, which can be difficult to discriminate.

Regarding a rapid onset of neurological symptoms in cases of intracranial air embolism, the main differential diagnoses include intracranial hemorrhage and infarctions of other etiology. Tumors or infections may also present with hypodense areas and brain swelling in CT scans, but are unlikely regarding the clinical course. Rarely a prolonged unconsciousness post anesthesia can be caused by a nonconvulsive epileptic state, but which is not accompanied by the imaging findings mentioned above.

Intracranial air embolism typically leads to rapid neurological deterioration. However, during anesthesia signs of intracranial and systemic embolism may be more subtle like a temporary decrease of blood pressure or a decrease of oxygen saturation. If embolism is suspected during ERCP, the intervention needs to be stopped and the patient should receive high flow oxygen and volume expansion. Furthermore, Trendelenburg position to prevent air from reaching the brain and left lateral recumbent position to trap air in the right heart is recommended; in cases of trapping in the right atrium, the aspiration of air can be achieved with the help of a pulmonary artery catheter [8]. For treatment of confirmed systemic embolism, early hyperbaric oxygenation is recommended [12].

The risk factors for systemic air embolism during ERCP are not fully understood. As enhancing pathogenetic factors, the inflammation of the bile duct or surrounding veins, hepatic abscesses or tumors, insufflation of air with high pressure, and previous surgery or interventions of the bile duct system have been proposed [2]. Interestingly, all patients with intracranial air embolism during ERCP showed a history of previous interventions or surgery of the bile duct system (Table 1).

Awareness of these possible risk factors and knowledge of the necessary diagnostic and medical approaches might improve the outcome of these patients.

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