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DOI: [10.1159/000348656](https://doi.org/10.1159/000348656)**Nonaccidental Arterial Cerebral Air Embolism:
A Ten-Year Stroke Center Experience**Spyridoula Tsetsou^a, Eric Eeckhout^b, Salah Dine Qanadli^c,
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Lausanne, Switzerland*Introduction*

Arterial air embolism can result from the introduction of air directly into the arterial system, incomplete filtration of venous air emboli by the pulmonary capillaries, or paradoxical right-to-left embolization [1]. It is a medical emergency as it can lead to cerebral ischemic events (CIE) such as ischemic stroke or transient ischemic attack (TIA), or to acute coronary syndrome. The incidence of cerebral air embolism (CAE) in a stroke population remains unknown [2–5].

We aim to present the incidence, causes, treatment and course of nonaccidental CAE-related CIE in an academic center over a 10-year period.

Methods

We retrospectively identified all CIE-related CAE from July 2002 to June 2012 from the prospective Acute Stroke Registry and Analysis of Lausanne (ASTRAL) and its companion registry for other cerebrovascular events (ASTRAL-E) [6]. The institution's discharge diagnoses database was also searched for air embolism, stroke and TIA. The diagnosis of CAE was made in patients with a CIE and either (1) presence of air bubbles in cerebral parenchyma on acute imaging or (2) circumstances allowing air entry into the arterial system immediately before the CIE, without simultaneous evidence of thromboembolism. Patients with CAE due to accidents, diving and surgery were excluded. In suspected cases, medical charts, neuroimaging and complementary exams were reviewed and 3 months follow-up was obtained. Acute cerebral imaging was carried out in all patients.

The institutional ethics committee has approved the scientific use of ASTRAL and ASTRAL-E and the present analysis. It does not require the consent of individual patients for the present study.

Results

During the observation period, 3,726 patients with a main diagnosis of ischemic stroke, and 831 with TIA were admitted to our center. Among them, we identified 5 CAE-related CIE (table 1), resulting in an incidence of 0.1%.

Patient 1: A 77-year-old woman was diagnosed with platypnea-orthodeoxia syndrome due to massive patent foramen ovale (PFO). During the control transthoracic echocardiography (showing moderate residual shunt) the day after PFO closure, immediately after the microbubble injection (bubbles produced by injecting 0.5–1.0 ml of ambient air in 10 ml of a mixture of a 0.9% saline/5% glucose solution which is shaken manually for 1 min; residual visible air on top of the solution was evacuated before injection), the patient developed mutism, somnolence and right hemiparesis. The patient improved rapidly with hyperbaric oxygen therapy (HOT) and became asymptomatic 2 days later.

Patient 2: A 49-year-old man had a right middle cerebral artery TIA 14 years earlier, attributed to a massive PFO with atrial septal aneurysm. The patient now decided to close the PFO. Thirty seconds after the microbubble injection (for method, see patient 1) during a transthoracic echocardiography to confirm the PFO, the patient presented with bilateral transient visual loss and a left hemisindrome. HOT was started immediately after hospital arrival and before neuroimaging. After HOT, only a left-sided hyperreflexia was present and the MRI taken 7 h after stroke onset was normal. The PFO was closed 3 weeks later.

Patient 3: A 67-year-old woman with chronic superior vena cava syndrome was dialyzed for diabetic nephropathy through a central venous catheter (CVC). Fifteen minutes after the beginning of a dialysis session, she developed acute right eye deviation and left hemiparesis. Right frontal intracortical air bubbles were found on acute CT, and focal cerebral edema was found 5 days later (fig. 1a, b). A moderate-sized PFO was detected. She initially had partial recovery but died 6 weeks later from sepsis.

Patient 4: A 34-year-old man with Rendu-Osler-Weber disease had multiple pulmonary arteriovenous malformations (PAVMs) embolized 13 years earlier. Over a period of 5 days he now experienced multiple episodes of transitory left hemiparesis, followed by a stroke with a left hemisindrome. After partial improvement over 2 days, he developed multiple episodes of chest pain and secondarily generalized seizures. Ischemic ECG changes and cardiac enzyme elevation occurred, but coronary angiography was normal. After partial embolization of the PAVMs, he developed another acute left hemisindrome, followed by cardiorespiratory arrest, cardiac massage and intubation. Cerebral CT showed parenchymal air emboli (fig. 2b), MRI revealed ischemic strokes (fig. 2c), and transcranial Doppler detected multiple spontaneous embolic signals. More PAVMs were embolized (fig. 2a), and the patient recovered progressively.

Patient 5: A 74-year-old man with chronic liver cancer developed syncope 30 min after a needle biopsy of a lung nodule, followed by dysarthria and gait ataxia. The thoracic CT at the end of the biopsy retrospectively showed air bubbles in the left ventricle (fig. 3a). MRI confirmed ischemic strokes. A minor-sized PFO was also detected (fig. 3b). The patient recovered completely spontaneously within 48 h.

Table 1. Clinical and radiological information

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Vascular risk factors	hypertension hypercholesterolemia	ex-smoker	diabetes type II hypertension hypercholesterolemia	smoker	diabetes type II hypertension hypercholesterolemia
Clinical diagnosis related to CAE	left MCA stroke	multifocal TIA	right MCA stroke	multiple TIAs, strokes, ACS, seizures and cardiorespiratory arrest	bilateral MCA stroke
NIHSS (acute → 24 h → 7 days)	11 → 5 → 1	4 → 0 → 0	23 → 23 → 11	13 → 13 → 5 (most severe episode)	2 → 1 → 0
Cause of air emboli	diagnostic injection of bubbles during TTE	diagnostic injection of bubbles during TTE	dialysis through CVC with presumed air emboli through PFO	air entry directly into PAVMs	air entry into pulmonary veins during lung biopsy
Right-to-left shunt	incompletely closed PFO	PFO with massive shunt	PFO with moderate shunt	PAVMs with massive shunt; no PFO	PFO with minimal shunt
Acute neuroimaging (median delay 150 min, range 30 min to 9 h)	CT: chronic cerebellar stroke	MRI: normal	CT: air bubbles in right MCA cortex CTP: right MCA hypoperfusion	CT after most severe stroke: normal CTP: left MCA hypoperfusion CT after cardiorespiratory arrest: air bubbles in left MCA cortex	CT: chronic lacunes
Subacute neuroimaging	MRI: chronic cerebellar stroke		CT: anterior right MCA edema	MRI: bihemispheric ischemic lesions	MRI: bihemispheric ischemic lesions
Treatment	acute HOT	acute HOT	PFO closure	embolization of PAVMs	–
mRS at 3 months	1	0	6	2	1

NIHSS = National Institute of Health Stroke Scale; mRS = modified Rankin scale; MCA = middle cerebral artery; ACS = acute coronary syndrome; TTE = transthoracic echocardiography; CTP = perfusion CT.

Fig.1. CTs of patient 3. **a** Air bubbles in frontal brain parenchyma. **b** 5 days later: focal edema.

Fig. 2. Patient 4. **a** Thoracic CTA: residual PAVM (white arrow), PAVM embolized with device (yellow arrow; color in online version only). **b** Cerebral CT: air bubbles in brain parenchyma. **c** Diffusion MRI: bi-hemispheric ischemic lesions.

Fig. 3. Patient 5. **a** Thoracic CT at the end of the lung biopsy: air in the left ventricle (arrow). **b** Diffusion MRI: ischemic lesions (arrows).

Further work-up showed no other potential embolic stroke sources in all patients.

Discussion

Over a 10-year period, we found 5 nonaccidental CAE-related CIEs in our center, representing only 0.1% of all CIEs. Other reported frequencies are 0.1–2% with the use of central catheters [2] and 0.06% with the use of microbubbles in echocardiography [3]. Like others, we cannot exclude an underascertainment due to possible missed diagnosis.

For the diagnosis of air embolism in clinical practice, it would be desirable to demonstrate air bubbles within intracerebral vessels. This has been found in several cases [7], whereas no case has been described showing air on an MRI, admitting that this exam tends to be performed less acutely. Very rapid imaging (preferably CT) is therefore crucial if one wants to demonstrate intracranial air. However, given the rapid resolution of small air bubbles in the human tissue, air may be impossible to be demonstrated in many cases. Therefore, it is likely that the air embolism will have to be diagnosed in most patients based on clinical examination together

with the anamnestic temporal relationship of circumstances facilitating air entry into the systemic circulation.

Most nonaccidental causes of arterial CAE are iatrogenic and related to microbubble studies [3], manipulations of a CVC [2, 7] or surgery. Causes in our patients were often related to right-to-left shunt. In both our patients with CAE related to injection of microbubbles for PFO diagnosis, neuroimaging was normal, which is consistent with small-sized air emboli. The use of a small needle held in a vertical position may decrease the risk of such a complication [3]. Thorough agitation of manually produced microbubble solutions for testing of PFO and evacuation of visible air on top of this solution may decrease the risk of CAE in this situation [3]. Paradoxical air embolism through the PFO was also the likely cause in our patient with a CAE shortly after starting hemodialysis through a CVC. This may be prevented by avoiding deep inspiration and by using the Trendelenburg position, all of which may prevent air aspiration into the CVC [2].

In the patient with PAVM, direct demonstration of cerebral intracortical air led to the diagnosis of CAE, although we initially suspected paradoxical embolization of venous thrombi [8]. This is only the third reported patient with PAVM and spontaneous CAE, and the first with simultaneous CIE and acute coronary syndrome due to air emboli [4, 5].

CAE is a rare complication of needle lung biopsy [7, 9] by direct air entry in the pulmonary veins. Detection of air in the left ventricle just before the CIE made this diagnosis very likely.

The recommended treatment of CAE includes high concentration oxygen therapy, flat supine position and immediate HOT [1]. It was associated with rapid recovery in 2 of our patients. In PAVM-associated CAE, however, HOT could increase the risk of CAE by inducing more air entry from alveoli into the PAVM.

Limitations of our study are the small number of patients, its retrospective analysis, and exclusion of accidental CEA.

In summary, nonaccidental CAE should be suspected in patients with acute focal neurological deficits in the setting of right-to-left shunts and iatrogenic manipulations of the vascular system. It is a rare, preventable and treatable condition.

Disclosure Statement

None.

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