



## Cerebral gas embolism associated with central venous catheter: Systematic review



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### ABSTRACT

**Objective:** Cerebral gas embolism (CGE) is a potentially catastrophic complication of central venous catheters (CVCs) manipulation or accidental disconnection, which is rarely reported in the literature. This systematic review aims to characterize the clinical manifestations, imaging features and outcome of CGE associated with CVCs. **Methods:** Systematic literature search of all published cases of CGE associated with CVCs, and identification of previously unreported local cases. Descriptive analysis of all cases, mortality analysis for cases with individualized data.

**Results:** Of the 158 patients with CGE associated with CVCs found, 71.8% were male and mean age was 56.4 years. CGE symptoms frequently occurred while in the upright position. The most frequent neurological manifestation was sudden-onset focal neurological sign (67.7%), followed by coma (59.5%), epileptic seizures (24.7%) and encephalopathy (21.5%). Imaging revealed intracranial air bubbles in 69.1% and cerebral ischemia or edema was demonstrated in 66.7%. Overall mortality was 21.7%, and clinical predictors of mortality were increasing age ( $p < 0.001$ ), coma ( $p = 0.001$ ), cardiorespiratory arrest shortly after symptom onset ( $p < 0.001$ ) and male sex ( $p = 0.035$ ).

**Conclusions:** CGE associated with CVCs may mimic ischemic stroke, but patients frequently present a severe vigilance disturbance and epileptic seizures. Mortality occurs in 1/5 of patients, which substantiates implementation of protocols and measures to prevent this severe complication of CVC use.

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## 1. Introduction

Cerebral gas embolism (CGE) is a known complication of several medical procedures during which air enters the vascular structures. Air embolism may occur in circumstances such as venous catheterization, neurosurgical, vascular and cardiac surgeries, gastroenterology procedures, pulmonary barotrauma and invasive lung procedures (1). The use of central venous catheters (CVCs) in settings outside the intensive care unit, namely in awake and ambulatory patients, increases the risk of accidental catheter disconnection and manipulation by undertrained personnel. However, reports of CGE associated with CVCs in the medical literature are not frequent and largely confined to single case reports, which may be explained by the perception of physicians that this should be a “never event” and possible lack of recognition

of clinical and imaging characteristics (2). CGE associated with CVCs may involve the cerebral arterial vasculature (for which to occur, a right-to-left shunt, even if transient, must exist) or may involve the cerebral venous vasculature by a retrograde mechanism where air ascends through the jugular vein opposite to blood flow (2). Although CGE may be formally considered as an acute stroke according to the World Health Organization definition, neurological manifestations of CGE may be mild and transient or accompanied by a severe disturbance of consciousness, and pathophysiology may include mechanisms other than central nervous system infarction or ischemia. The current systematic review aims to describe manifestations and imaging findings of CGE patients associated with CVCs and to find clinical predictors of mortality.

## 2. Materials and methods

### 2.1. Local cases

Our Neurology Department database for hospitalized patients between January 2008 and May 2015 was reviewed to select patients

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with CGE associated with CVCs. Clinical characteristics, imaging findings, treatment and outcome were collected from patient records.

## 2.2. Literature search

Pubmed search in May 2015, for the following search terms: “air embolism” or “gas embolism” in combination with “catheter” or “line”. Articles written in English, French, German, Portuguese, Spanish and Norwegian were included. Selection of all papers reporting patients with air embolism thought to be associated with a CVC, either presumed by clinical manifestations and circumstances or confirmed by diagnostic tests, with manifestations that could be attributed cerebral dysfunction or with imaging evidence of cerebral air embolism. Reference list of the papers of interest were also reviewed according to this selection criteria. Papers reporting case series of patients with CGE associated with CVCs were included in the descriptive analysis but excluded from the analysis of mortality prediction if individualized data for single patients could not be retrieved. Patients found in our database have not been previously reported and were included in the analysis. Conference proceedings and papers without retrievable information concerning clinical manifestations were excluded.

## 2.3. Statistical analysis

Descriptive analysis, Pearson's chi-square test, Fisher's exact test and Mann–Whitney U test were used according to variables types and test assumptions. Univariate binary logistic regression was used for analysis of predictors of mortality, and odds ratio (OR) and 95% confidence intervals (95% CI) were calculated. IBM SPSS 22 ® with an alpha value set at 0.05 as the statistical threshold for significance.

## 3. Results

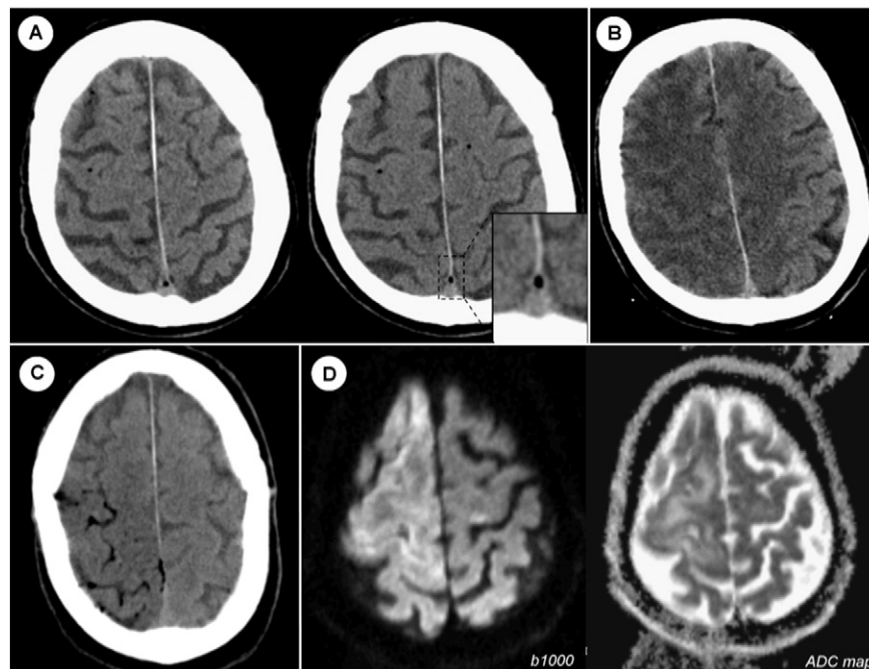
We found 4 patients with CGE associated with CVCs in our database, details can be found in the Supplemental Material. Imaging findings of local cases 1–3 are illustrated in Fig. 1.

Pubmed search originated 899 papers, final selection included 66 papers of interest, with inclusion of 158 patients who met selection criteria, of which 4 patients are previously unreported local cases (Fig. 2).

The majority of papers ( $n = 57$ ) reported single patients. Neurological manifestations of the acute event were available for 158 patients (100%), body position on symptom onset was available for 48 patients (30.4%), computed tomography (CT) was performed in 68 (43.0%) and magnetic resonance imaging (MRI) in 24 patients (15.2%). No reference to treatment was available for 17 patients (10.8%). In one paper, clinical characteristics and outcomes could be obtained, but data was not individually reported for each patient (3). This paper and another paper (4), in which no outcome was reported, were included in the descriptive analysis, but excluded from the mortality analysis. Details of the 158 patients included in this systematic review are provided in Supplemental Digital Content, with accompanying references.

### 3.1. Descriptive analysis

Mean age was 56.4 years and 71.8% of patients were male. CGE occurred after accidental CVC disconnection or leak in 88 patients (61.5%), after CVC removal in 31 (21.7%), after CVC insertion in 10 (7.0%), after CVC manipulation in 10 (7.0%) and with no apparent relation with CVC procedure in 4 (2.8%). Symptom onset occurred in the upright position (standing or sitting upright) in 77.1% and in recumbent position in 22.9%. Median time from CVC event to symptom onset was during the first minute (interquartile range 1–7.5; data available for 37 patients). The most frequent neurological manifestation was sudden-



**Fig. 1.** A–B: Local case 1, accidental disconnection of right subclavian CVC in a 77 year-old man hospitalized for treatment of subphrenic abscess. Acute phase CT (A) showed air bubbles in the parenchyma, subarachnoid space, and venous sinus. Twenty-four hour follow-up CT (B) revealed extensive bilateral supratentorial cortico-subcortical hypodense lesions and no air bubbles. C: Local case 2, apparently uneventful disconnection of right subclavian CVC during a period of out-of-bed mobilization of a patient hospitalized after emergent treatment of mesenteric ischemia. Acute phase CT (C) revealed air bubbles in bilateral fronto-parietal-occipital subarachnoid spaces (right side predominant), in the parenchyma and in the superior sagittal sinus. D: Local case 3, accidental disconnection of right subclavian CVC in an 82 year-old man hospitalized for surgical treatment of urothelial carcinoma. MRI performed 4 h after onset of the neurological manifestations (D) showed a right frontal area of increased diffusion coefficient in diffusion-weighted imaging.

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