Cerebral Gas Embolism Caused by Pleural Fibrinolytic Treatment

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Background and Purpose—Intrapleural fibrinolytic therapy is a technique used to treat empyemas and parapneumonic effusions. Cerebral air embolism is an unusual potentially severe complication of this technique.

Summary of Case—A patient with parapneumonic pleural effusion underwent pleural lavage with streptokinase when he suddenly demonstrated focal neurological signs and seizures. The CT revealed multiple air-isodense spots in right hemisphere of the brain, suggesting cerebral air embolism. As a result of early diagnosis and emergency hyperbaric oxygenation, the patient recovered without delayed sequelae.

Conclusions—Air embolism is a potentially severe complication which can occur during fibrinolytic pleural lavage, and clinicians should be aware of this risk. In this context, the onset of acute focal neurological signs or seizures should suggest the possibility of air embolism and lead to the transfer of the patient close to a hyperbaric facility within a few hours. (Stroke, 2007;38:000-000.)

Key Words: air embolism ■ fibrinolytic therapy ■ hyperbaric oxygenation ■ stroke

Parapneumonic effusions and empyema may complicate lower respiratory tract infections. In this condition, loculation of fluid is a major problem, and therapeutic options include conventional surgical drainage, video-assisted thoracoscopic surgery and the use of intrapleural fibrinolytic agents (urokinase and streptokinase) to break down fibrin bands that may cause loculation.1–4 Although many physicians use fibrinolytic agents, the technique of instillation has not yet been standardized.5 A Cochrane Systematic Review6 evaluated the benefit of adding intrapleural fibrinolytic therapy to intercostal tube drainage in the treatment of complicated parapneumonic effusions and empyema. Controlled trials conducted up to 2003 were reviewed, concluding that intrapleural fibrinolytic therapy conferred significant benefits when compared with normal saline control. However, the routine use of fibrinolytic therapy cannot be recommended because the trial numbers were too small. A recent meta-analysis raised the same conclusions.7 Remarkably, complications attributable to therapy were not observed at all in these trials, although several case reports of cerebral air embolism have been published.8–10 Herein we report a new case.

Case Reports

A 50-year-old male patient, with a previous history of intestinal adenocarcinoma and resection of colorectal liver metastases developed a right purulent pleural effusion (Figure, A). He was admitted to hospital for daily pleural lavages with saline associated with streptokinase and for antibiotic treatment. During the third lavage he suddenly developed a generalized tonic-clonic seizure. Neurological examination showed a drowsy patient, with a conjugated gaze deviation toward the right, lower left facial paralysis, left hemiplegia and left Babinski sign. He immediately underwent a CT scan of the brain which revealed multiple air-isodense spots in the right hemisphere suggesting cerebral air embolisms (Figure, B). He received hyperbaric oxygen therapy (a 135-minute session at 2.8 ATA, followed by 70 minutes at 2.3 ATA) with a favorable outcome within 24 hours.

Discussion

Gas embolism is a known complication of various invasive procedures. Air bubbles circulating in the blood stream obstruct the blood flow, causing tissue ischemia. There are 2 broad categories of gas embolism, venous and arterial, which may be differentiated by the mechanism of gas entry and the site where the emboli ultimately lodge. In venous gas embolism, the air is transported to the lungs through the pulmonary arteries, causing interference with gas exchange, cardiac arrhythmias, pulmonary hypertension, right ventricular strain, and, eventually, cardiac failure. Furthermore, retrograde cerebral venous gas embolism (CVGE) is possible.11 Arterial gas embolism is caused by the entry of gas into the pulmonary veins or directly into the arteries of the systemic circulation. The systemic passage of air from the pleura is possible by different theoretical mechanisms. A direct communication between the pulmonary vasculature and either the pleural cavity (pleuromedullary fistula) or the bronchial tree (bronchovascular fistula) is necessary. An accidental lesion of

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the pulmonary tissue can also be caused by chest drain, which may have led to a breach, as happens in lung trauma or in iatrogenic pneumothorax. In this case it would be expected that the symptoms occur during the first lavages, or at least that the patient refers from the beginning some symptom of discomfort such as coughing. Whatever the source of air, the fibrinolytic agent might dissolve fibrin membranes of the visceral pleura and vasculature and thereby open a passage for air, especially in the presence of a favorable pressure gradient. Although obstruction is possible in any artery, obstruction of arteries of the brain (CAGE) is especially serious and may be fatal because of the vulnerability of the brain to short periods of hypoxia. In CAGE, the cerebral distribution of bubbles will depend on the corporal position. When the patient is laid on the left side most bubbles will lead to the right hemisphere.\textsuperscript{12}

Although the hypothesis of an enzyme-induced fistula to explain gas embolism by pleural fibrinolytic treatment is very attractive, a perforation caused by the tools used during the procedure cannot be excluded. Nevertheless, this patient had undergone 2 previous lavages without complications, which makes the enzyme-induced mechanism more plausible. This procedure is usually performed in our hospital, and no similar complications had ever occurred. Other complications of this procedure have previously been reported, such as cardiac arrest of secondary distress respiratory syndrome\textsuperscript{8} but no signs or symptoms suggesting embolisms in different organs were observed in this patient.

The temporal relationship between this procedure and the onset of acute focal neurological signs is the most important clue for diagnosing cerebral gas embolism. CT scan and MRI of the brain are usually confirmatory tests. In CAGE, CT demonstrates intraarterial air in 1 or both cerebral hemispheres,\textsuperscript{8,14} but only macroscopic bubbles (1.3-mm radius) are identifiable and only if the CT slices, usually at 1-cm intervals, coincidentally intersect the appropriate level.\textsuperscript{15} Therefore, absence of air on CT scan does not exclude the diagnosis. MRI provides a higher sensitivity.\textsuperscript{16} In CVGE, brain CT is diagnostic only if obtained immediately because air is rapidly resorbed from the brain arterioles. Diffusion-weighted MRI shows multiple areas of restricted diffusion in a gyriform pattern affecting predominantly cortical areas in both hemispheres.\textsuperscript{17}

Oxygen should be administered at as high a concentration as possible.\textsuperscript{13} Administration of oxygen is important not only to treat hypoxia and hypoxemia but also to eliminate the gas in the bubbles by establishing a diffusion gradient that favors the egress of gas from the bubbles. In patients requiring mechanical ventilation, ventilatory pressures and volumes should be kept as low as possible to maintain adequate oxygenation and to limit a pressure gradient which would favor gas entry in the pulmonary circulation.\textsuperscript{18} The improvements in the oxygen-carrying capacity of plasma and in the delivery of oxygen to tissues offset the embolic insult to the microvasculature. Several CAGE published cases\textsuperscript{8,19,20} have also reported very good outcomes when treated with hyperbaric oxygenation.

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Disclosures

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References

10. Neugebauer W. Cerebral air embolism following irrigation in empyema. 
11. Schlimp CJ, Loimer T, Rieger M, Lederer W, Schmidts MB. The 
   potential of venous air embolism ascending retrograde to the brain. 
12. Dutka AJ. A review of the pathophysiology and potential application of 
   experimental therapies for cerebral ischemia to the treatment of cerebral 
13. Annane D, Troche G, Delisile F, Devauchelle P, Hassine D, Paraire F, 
   Raphael JC, Gajdos P. Kinetics of elimination and acute consequences of 
14. Yang CW, Yang BP. Massive cerebral arterial air embolism following 
15. Dexter F, Hindman BJ. Recommendations for hyperbaric oxygen therapy 
   of cerebral air embolism based on a mathematical model of bubble 
16. Reuter M, Tetzlaff K, Hutzelmann A, Fritsch G, Steffens JC, 
   Bettinghausen E, Heller M. MR imaging of the central nervous system 
   in diving-related decompression illness. Acta Radiol. 1997;38: 
   940–944.
17. Caulfield AF, Lansberg MG, Marks MP, Albers GW, Wijman CA. MRI 
   characteristics of cerebral air embolism from a venous source. Neurology. 
   2006;66:945–946.
18. Chiu CJ, Golding MR, Linder JB, Fries CC. Pulmonary venous air 
   cerebral air embolism: importance of an early hyperbaric oxygenation. 
20. Murphy BP, Harford FJ, Cramer FS. Cerebral air embolism resulting 
   from invasive medical procedures: treatment with hyperbaric oxygen. 
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