Neuroanesthesia and Intensive Care

Cerebral arterial gas embolism following diagnostic bronchoscopy: delayed treatment with hyperbaric oxygen

[Embolie gazeuse de l'artère cérébrale suivant une bronchoscopie diagnostique : traitement différé avec l'oxygène hyperbare]

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Purpose: To describe a clinical scenario consistent with the diagnosis of cerebral arterial gas embolism (CAGE) acquired during an outpatient bronchoscopy. Our discussion explores the mechanisms and diagnosis of CAGE and the role of hyperbaric oxygen therapy.

Clinical features: A diagnostic bronchoscopy was performed on a 70-yr-old man who had had a lobectomy for bronchogenic carcinoma three months earlier. During the direct insufflation of oxygen into the right middle lobe bronchus, the patient became unresponsive and developed subcutaneous emphysema. Immediately, an endotracheal tube and bilateral chest tubes were placed with resultant improvement in his oxygen saturation. However, he remained unresponsive with extensor and flexor responses to pain. Later, in the intensive care unit, he exhibited seizure activity requiring anticonvulsant therapy. Sedation was utilized only briefly to facilitate controlled ventilation. Investigations revealed a negative computerized tomography (CT) scan of the head, a normal cerebral spinal fluid examination, a CT chest that showed evidence of barotrauma, and an abnormal electroencephalogram. Fifty-two hours after the event, he was treated for presumed CAGE with hyperbaric oxygen using a modified United States Navy Table 6. Twelve hours later he had regained consciousness and was extubated. He underwent two more hyperbaric treatments and was discharged from hospital one week after the event, fully recovered.

Conclusion: A patient with presumed CAGE made a complete recovery following treatment with hyperbaric oxygen therapy even though it was initiated after a significant time delay.

Objectif : *Décrire un scénario clinique caractéristique du diagnostic d'embolie gazeuse de l'artère cérébrale (EGAC) survenue pendant une bronchoscopie réalisée en clinique externe. Notre discussion explore les mécanismes et le diagnostic d'EGAC et le rôle de l'oxygénothérapie hyperbare.*

Éléments cliniques : *Une bronchoscopie diagnostique a été réalisée chez un homme de 70 ans qui avait subi, trois mois auparavant, une lobectomie pour un carcinome bronchique. Pendant l'insufflation directe d'oxygène dans la bronche du lobe droit moyen, le patient est devenu comateux et un emphysème sous-cutané s'est développé. On a immédiatement placé un tube endotrachéal et des drains thoraciques bilatéraux, ce qui a amélioré la saturation en oxygène. Cependant, le patient est demeuré comateux et réagissait à la douleur par des mouvements de décérébration et de décortication. Par la suite, à l'unité des soins intensifs, on a enregistré une activité épileptique qui a nécessité une thérapie anticonvulsive. La sédation, de courte durée seulement, a visé à faciliter la ventilation contrôlée. Les examens ont révélé une tomodensitométrie négative du crâne, un examen normal du liquide céphalo-rachidien, un barotrauma pulmonaire mis en évidence par une tomographie, un électroencéphalogramme anormal. Cinquante-deux heures après l'incident, il a été traité pour une EGAC présumée avec de l'oxygène hyperbare en utilisant une Table 6 modifiée de la Marine américaine. Douze heures plus tard, il a repris conscience et a été extubé. Il a reçu deux autres traitements hyperbares et, une semaine après l'événement, il a quitté l'hôpital complètement rétabli.*

Conclusion : *Un patient, victime d'une EGAC présumée s'est complètement rétabli à la suite d'une oxygénothérapie hyperbare même si ce traitement a été différé de manière significative.*

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CEREBRAL arterial gas embolism (CAGE) is a rare but potentially fatal event. The exact incidence is unknown but neurologic sequelae are thought to occur in one third of patients who experience CAGE after cardiac surgery.[1] In addition to resuscitative and supportive care, hyperbaric oxygen therapy (HBO_2) is a therapeutic option for CAGE. We report a case of severe neurological impairment associated with barotrauma during a diagnostic bronchoscopy. Hyperbaric oxygen was initiated two days following the event.

Case report

A 70-yr-old man underwent a diagnostic bronchoscopy three months following a right upper lobectomy for bronchogenic cancer. He had a history of hypertension, smoking, and chronic obstructive pulmonary disease. In an attempt to expand atelectasis of the right middle lobe, oxygen from the hospital pipeline 12 $L \cdot min^{-1}$ at 50 *psi* (345 kPa) was insufflated into the right middle lobe bronchial orifice. During the procedure, the patient developed severe respiratory distress and acute oxygen desaturation. He became unresponsive and subcutaneous emphysema was noted. The bronchoscopist promptly intubated the patient's trachea and inserted bilateral chest tubes. Gas was found in the left pleural cavity. Oxygen saturation immediately improved. He remained hemodynamically stable throughout the event and was transferred to the intensive care unit (ICU).

Seven hours later, he remained unconscious and withdrew to pain only. Until then he had received fentanyl 50 μg, morphine 4 mg, and midazolam 4 mg. A propofol infusion of 10–15 $\mu g \cdot kg \cdot min^{-1}$ was started at this time to facilitate mechanical ventilation and minimize airway pressures. At this time CAGE was not considered in the differential diagnosis.

The next day there were flexor and extensor responses to pain in the extremities. Brainstem reflexes were intact. The propofol infusion (10 $\mu g \cdot kg \cdot min^{-1}$) was temporarily discontinued. Forty-five minutes later, he had a transient episode of ventricular tachycardia followed by both generalized and right-sided seizures. This occurred during routine endotracheal tube care involving manual ventilation of the lungs. Treatment with thiopentone, midazolam, and dilantin was initiated. The patient was immediately turned on his right side and the head of the bed was lowered, and he was given 100% oxygen. The seizure activity and the ventricular tachycardia resolved. Fundoscopic examination was normal and there were no localizing signs. An electroencephalogram (EEG) showed a diffuse disturbance of cerebral activity and periodic lateralized epileptiform discharges (PLEDS). A computerized tomography (CT) scan of the head was normal. Serum creatine kinase (CK) was elevated at 281 $U \cdot L^{-1}$.

Two days after the bronchoscopy the patient remained unconscious. An examination of the cerebrospinal fluid was done and was normal. CT chest showed a residual loculated right pneumothorax, pneumomediastinum, and subcutaneous emphysema. While the possibility of CAGE had previously been entertained, at this time there was a clear mechanism for CAGE to have occurred and no apparent alternative explanation for the patient's condition. Therefore, hyperbaric oxygen therapy was requested and commenced approximately 52 hr after the respiratory arrest. The chamber is a dualplace, capable of compression to 66 feet of sea water (fsw). Attendants accompany critically ill patients and *iv* medications may be infused from outside the chamber. The patient was treated with a U.S. Navy Table 6[2] with extensions at both 60 fsw and 30 fsw (284 and 193 kPa respectively). Total treatment time was seven hours and 25 min. During the course of the treatment the dose of propofol was increased on several occasions to control patient agitation. There were no adverse effects noted in the patient or attendants.

Ninety minutes after completion of hyperbaric therapy, the patient could obey commands. Ten hours later he was alert and his trachea was extubated. He was oriented to place but not time. He was treated with hyperbaric oxygen two more times at 2.5 atmospheres absolute (253 kPa). One week later he was discharged home. Two weeks later his complete neurologic recovery was verified.

Discussion

CAGE most often occurs in two situations, SCUBA (self contained underwater breathing apparatus) diving or medical procedures. Gas embolization requires the presence of two factors: a portal of entry into a blood vessel and a pressure gradient to drive gas into the blood vessel. The gas can be entrained from the atmosphere by negative pressure within a vein (for example the jugular vein in the sitting position). Gas can also be forced into a vessel by positive pressure. Gas may enter the arterial circulation directly or from the venous circulation *via* a right-to-left cardiac shunt or intrapulmonary shunt. Passage of bubbles through the pulmonary capillaries to the left heart is well recognized. Embolization of even small amounts of gas to the brain can produce neurologic damage thereby producing the syndrome of CAGE.

In SCUBA divers, aside from trauma or other forms of decompression sickness, there are usually no

factors to confound the diagnosis of CAGE. Symptoms typically develop within 20 min of surfacing. As well, there is often accompanying evidence of pulmonary barotrauma (pneumothorax, pneumomediastinum, subcutaneous emphysema, and interstitial emphysema). Iatrogenic gas emboli, however, are more elusive. They tend to occur during diagnostic and therapeutic procedures involving vascular cannulation or intracavitary gas insufflation. Patients experiencing iatrogenic emboli are more likely to have concurrent medical problems such as cerebrovascular disease, cardiovascular disease, and metabolic disorders. These factors, as well as pharmacological sedation, can all produce neurological impairment and therefore expand the differential diagnosis.

The presenting symptoms and signs of CAGE can be generalized or focal. Cardiopulmonary arrest, altered level of consciousness, seizures, hemiparesis, hemianopsia, paresthesiae, pupillary asymmetry, dizziness, nausea, and headache are all reported.[1,3–5] Unfortunately, these features are non-specific and can be attributed to other etiologies. Retinal gas bubbles on retinoscopy and Liebermeister's sign (a blue or pale tongue secondary to lingual artery emboli) are pathognomonic of arterial gas embolism but are extremely rare signs.[6]

A CT scan of the head is usually not helpful. Dexter *et al.*[7] demonstrated that only macroscopic bubbles (1.3 mm radius) would be identifiable and only if the CT cuts, usually at 1-cm intervals, coincidentally intersect the appropriate level. Therefore, absence of air on CT scan does not exclude the diagnosis. Magnetic resonance imaging, single photon emission computed tomography scanning, or Xenon enhanced CT are only helpful in delineating regional blood flow.[8] The finding of gas in an arterial blood sample is specific but infrequent.[6] Elevated CK levels have been noted in divers with CAGE. Elevation of serum gamma-glutamyl transpeptidase, aspartate aminotransferase, and lactate dehydrogenase can also occur in CAGE or decompression sickness.[4]

Initial management of CAGE includes immediate respiratory and hemodynamic support. Trendelenberg positioning may prevent movement of arterial gas cephalad. Although it is frequently recommended, there is no evidence that left lateral decubitus positioning improves outcome with venous gas embolism.[9] Tight control of serum glucose is advocated as this may limit the extent of neuronal damage in areas of ischemia.[8] Lidocaine has been shown in animal models to improve recovery of somatosensory evoked potentials following CAGE.[10,11] There is no proven benefit of steroids and they are not recommended.[12] An experiment in rabbits has shown a protective effect from prophylactic heparin.[13]

There are several proposed beneficial effects of HBO_2 in CAGE. Firstly, increased ambient pressure directly compresses the gas bubbles. Bubble volume and therefore diameter is reduced in accordance with Boyle's Law ($P_1 * V_1 = P_2 * V_2$). Secondly, a resulting increase in the bubble surface area to volume ratio allows more rapid resorption of nitrogen from within the bubble. Finally, volume reduction is hastened by the diffusion of nitrogen down a steeper bubble-plasma partial pressure gradient. All three mechanisms promote restoration of distal blood flow. A reduction of bubble-endothelial interface results in less "foreign body" exposed to the vascular endothelium. This decreases vascular endothelial injury and therefore reduces the "no reflow" phenomenon, which is believed to be a cause of delayed symptom onset or failure of HBO_2 treatment.[5,6] Decreased reperfusion injury is thought to result from reduced leukocyte aggregation.[5] A high dissolved oxygen content allows better oxygen delivery to neural tissue compromised by marginal blood flow (the "ischemic penumbra").[1,5] As well, cerebral edema can be reduced by HBO_2.[6]

Hyperbaric oxygen is recommended for CAGE[12] although there are no randomized controlled trials reported in humans. Studies in cats show significant somatosensory evoked potential recovery following induced CAGE when HBO_2 is given. This compares to a poor recovery in animals kept at atmospheric pressure breathing air.[11,14] In humans, two early studies comparing mortality rates suggest a beneficial effect. Retrospective data published in 1964 showed a decrease in mortality from 93% with no treatment to 33% with conventional aggressive treatment (left lateral decubitus position, vasopressors, and oxygen by positive pressure).[8] A later study showed a mortality rate of only 7% in 30 patients treated when hyperbaric oxygen was utilized.[8]

In our patient, there were two possible mechanisms of CAGE. Firstly, oxygen administered under pressure during the bronchoscopy caused significant barotrauma manifested by pneumothoraces, subcutaneous emphysema, and pneumomediastinum. The oxygen could then have passed into the pulmonary venous circulation, resulting in arterial embolization. As well, the jet of oxygen could have entrained air present in the alveoli. Secondly, the barotrauma may have created a persistent open pathway for gas to travel from alveoli into the circulation. Thus the patient may have experienced ongoing gas embolization during mechanical ventilation after the initial event. Nitrogen gas is more likely than oxygen to persist in the circulation because it is not metabolized or bound by hemoglobin.

The diagnosis of CAGE is primarily based on clinical features. As described, current diagnostic tests for CAGE are likely not sensitive enough, particularly when performed hours after the event. However, in our patient, the following clinical features were consistent with this diagnosis: impairment of consciousness immediately following massive barotrauma, seizures, an EEG with PLEDS which are indicative of acute cerebrovascular dysfunction,[1,3–5] an elevated CK, and the complete recovery of the patient. There were no metabolic, infectious, or structural causes identified that could explain the clinical findings. The patient did not have a cardiac arrest nor was there any evidence of a post anoxic-ischemic encephalopathy. The propofol sedation is a possible confounding factor. However, it was not started until seven hours after the event and was maintained at a relatively low dose that does not account for the patient's degree of neurologic impairment. As well, the EEG did not show the characteristics of propofol sedation.[1 5]

There are several factors that support our impression that HBO_2 was therapeutic in this case. During the course of treatment the dose of propofol had to be increased. This suggests that the patient's level of consciousness improved during treatment, a finding reported by others.[1,3] The patient's neurologic status remained dramatically improved after treatment with no other explanation. There had been no signs of improvement over the preceding two days.

There are several other reports of successful outcomes after late hyperbaric treatment up to 30 hr after CAGE.[2,3,16] An effect of late treatment is supported by evidence that bubbles may persist in the cerebral circulation for 40 hr or longer.[8]

In summary, we present a previously unreported mechanism of pulmonary barotrauma followed by impaired consciousness likely due to CAGE. There was a significant delay in commencing HBO_2 yet the patient made a complete recovery. HBO_2 is the only available treatment that can reverse the underlying pathophysiology of CAGE. We suggest that urgent HBO_2 therapy be considered in any patient when CAGE is suspected, even after a significant time interval of one to two days.

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