Hyperbaric oxygen therapy of iatrogenic cerebral arterial gas embolism

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Benson J, Adkinson C, Collier R. Hyperbaric oxygen therapy of iatrogenic cerebral arterial gas embolism. Undersea Hyperb Med, 2003; 30(2): 117-126 - We describe our experience using HBO$_2$ therapy for iatrogenic cerebral arterial gas embolism (CAGE) in this retrospective review of nineteen patients treated for iatrogenic CAGE, from 1987 to 1999. Immediately after treatment, five patients completely resolved all signs and symptoms, eleven had improvement, one had no change, and two were not assessable. Within two months post treatment, three additional patients completely resolved and six had further improvement. Patients with a venous source all experienced pulmonary signs or symptoms, with eight of nine chest x-rays demonstrating pulmonary edema. Patients with an arterial source had no pulmonary symptoms; all chest x-rays were clear. Imaging studies prior to HBO$_2$ therapy demonstrated gas in six of 23 exams; five of the remaining 17 exams showed secondary changes consistent with gas embolism. Iatrogenic CAGE patients improved with HBO$_2$ therapy, and improvement for some continued for several months. Patients with CAGE from a venous source have pulmonary signs or symptoms. Diagnosis of CAGE should be made on clinical suspicion without reliance on imaging studies.

hyperbaric oxygenation, air embolism, embolism, gas, neurologic manifestations, diagnostic imaging, iatrogenic disease

INTRODUCTION

Iatrogenic gas embolism occurs after many types of invasive procedures in the hospital (1-4). Often iatrogenic cerebral arterial gas embolism (CAGE) is unrecognized, untreated, or treated late, resulting in severe and permanent deficits (5). The diagnosis of CAGE is clinical, but there may be definitive evidence of gas on imaging studies. Hyperbaric oxygen (HBO$_2$) therapy is the treatment of choice in CAGE (5-16) and studies support improvement in clinical outcome with the possibility of full recovery to pre-insult status (4, 6, 7).

There has not been a previous case series that correlates mode of gas entry and outcome. Our purpose was to describe our experience with patients who were diagnosed with iatrogenic CAGE and referred for HBO$_2$ at our institution. We were interested in the mechanism by which gas was introduced into the circulation. We hypothesized the mechanism and location of gas entry affects the presenting signs and symptoms of the patient. We then reviewed the cases to determine if the mechanism and location of gas entry predicted patient outcome in our series. We reviewed the imaging studies performed to determine their usefulness in making the diagnosis of CAGE. We reviewed the responses and outcomes of the patients to HBO$_2$ therapy to provide insight into which factors help identify patients most likely to benefit from treatment.
MATERIALS AND METHODS

We reviewed all patients diagnosed with iatrogenic CAGE and treated with HBO$_2$ therapy at Hennepin County Medical Center (HCMC) from September 1987 through December 1999. The information was obtained from Hyperbaric Medicine facility records and hospital patient records. This included information from referring hospitals and follow-up clinic visits. All patients had a documented exam immediately after HBO$_2$ therapy. Follow up was obtained on all patients for at least two months, unless the patient had died. Long term follow up data was not available for all patients, and available records did not always provide detailed neurological assessment. Results of imaging studies were obtained from the radiology report when available, otherwise from notes by doctors involved in the patient care. The Institutional Review Board approved this study and waived the need for informed consent.

RESULTS

Patient population: Nineteen patients with iatrogenic CAGE were treated at HCMC’s hyperbaric chamber with HBO$_2$ therapy. These included twelve females and seven males, age range 7-81, (see Table 1). All nineteen patients received HBO$_2$ therapy in a Class A, four-lock multiplace chamber (Vacudyne, Inc. Chicago Heights, IL) using US Navy Treatment Tables 6 or 6A, as modified by the US Air Force.

Table 1. Patient Data

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Cause of Embolism</th>
<th>A/V</th>
<th>Initial signs and symptoms</th>
<th>Time to HBO$_2$</th>
<th>CXR</th>
<th>EKG</th>
<th>Diagnostic imaging</th>
<th>Treatment table</th>
<th>Response to HBO$_2$</th>
<th>Final outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>F</td>
<td>CV catheter leak</td>
<td>V</td>
<td>Headache, chest pain, dyspnea</td>
<td>5.5 hrs</td>
<td>No</td>
<td>T wave inversions</td>
<td>Head CT negative</td>
<td>6A</td>
<td>Complete recovery</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>49</td>
<td>M</td>
<td>CV catheter leak</td>
<td>V</td>
<td>Confusion, tachycardia, dyspnea</td>
<td>4.5 hrs</td>
<td>Yes</td>
<td>NSR</td>
<td>None</td>
<td>6A</td>
<td>ARDS improved, dyspnea and tachycardia resolved</td>
<td>ARDS resolved, neurological deficit from prior ICH vs. CSGE</td>
</tr>
<tr>
<td>50</td>
<td>F</td>
<td>Cardiac bypass canalizing aorta</td>
<td>A</td>
<td>Posturing, clonus no verbal response</td>
<td>30 hrs</td>
<td>No</td>
<td>NSR</td>
<td>Head CT negative EEG deep coma</td>
<td>4 modified</td>
<td>Eyes open to voice, moving all extremities, follows simple commands</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>43</td>
<td>F</td>
<td>Cardiac bypass w/PFO</td>
<td>A</td>
<td>Obtunded clonus</td>
<td>6 hrs</td>
<td>No</td>
<td>ST-T elevation</td>
<td>None</td>
<td>#1, 6A, #2, 6, #3-10, 2.4ATA$^e$ for 90 min.</td>
<td>Arouses to verbal stimuli, clonus resolved, extremity movement, follows simple commands</td>
<td>Answers questions, follows commands, improved movement</td>
</tr>
<tr>
<td>34</td>
<td>F</td>
<td>Carotid artery injection</td>
<td>A</td>
<td>Decreased mental status, occasional movement, withdraws</td>
<td>1.5 hrs</td>
<td>No</td>
<td>Sinus tachy$^f$</td>
<td>None</td>
<td>#1, 6A, #2 6, 2.4ATA for 90 min.</td>
<td>Triggering ventilator, spontaneous extremity movement</td>
<td>Talking some, hemiparesis, ambulates independently, lives at home with aide</td>
</tr>
<tr>
<td>24</td>
<td>F</td>
<td>Carotid artery injection</td>
<td>A</td>
<td>Decreased mental status, dysarthria, weakness</td>
<td>6.25 hrs</td>
<td>No</td>
<td>N/A$^g$</td>
<td>Head CT negative</td>
<td>6A</td>
<td>Increased alertness, verbalizes spontaneously</td>
<td>Speech improvement, fine motor deficit</td>
</tr>
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<tr>
<td>48</td>
<td>F</td>
<td>Cardiac bypass with septal defect</td>
<td>A</td>
<td>Cardiopul. Arrest, ventricular tachycardia, GCS'3</td>
<td>8 hrs</td>
<td>No</td>
<td>NSR</td>
<td>TTE#1+gas, shunt, TTE#2 no gas</td>
<td>6A</td>
<td>Cardiovascular stability</td>
<td>Died</td>
</tr>
<tr>
<td>26</td>
<td>F</td>
<td>Carotid artery injection</td>
<td>A</td>
<td>Inappropriate affect, hemiparesis, aphasia, seizure, weakness</td>
<td>5.5 hrs</td>
<td>No</td>
<td>NSR</td>
<td>None</td>
<td>6</td>
<td>Complete recovery</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>81</td>
<td>M</td>
<td>CT guided lung biopsy</td>
<td>A</td>
<td>Seizure, unresponsive GCS3</td>
<td>4.5 hrs</td>
<td>No</td>
<td>NSR</td>
<td>Head CT+gas</td>
<td>6A</td>
<td>Withdraws to pain</td>
<td>Died</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>Cardiac bypass w/atrial septal defect</td>
<td>A</td>
<td>Not awakening from anesthesia GCS3</td>
<td>3.25 hrs</td>
<td>No</td>
<td>NSR</td>
<td>Head CT focal decreased attenuation</td>
<td>6A</td>
<td>Withdraws to stimulation, flexion posturing, eyes open</td>
<td>Died</td>
</tr>
<tr>
<td>67</td>
<td>F</td>
<td>CT guided lung biopsy</td>
<td>A</td>
<td>Confusion, obtunded weakness, dysarthria, posturing</td>
<td>22 hrs</td>
<td>No</td>
<td>NSR</td>
<td>MRI negative EEG left delta activity</td>
<td>6</td>
<td>orientedx1, follows commands, moves extremities, talking</td>
<td>Only mild decrease in higher cortical function</td>
</tr>
<tr>
<td>80</td>
<td>F</td>
<td>Venous dialysis cath. open to air</td>
<td>V</td>
<td>Cardiopulmonary arrest, GCS3</td>
<td>5 hrs</td>
<td>Yes</td>
<td>a-fib tachy</td>
<td>none</td>
<td>6</td>
<td>No change</td>
<td>Died</td>
</tr>
<tr>
<td>73</td>
<td>M</td>
<td>CV line removal</td>
<td>V</td>
<td>Obtunded, posturing, ARDS</td>
<td>9 hrs</td>
<td>Yes</td>
<td>Sinus tachy</td>
<td>Head CT negative, TTE#1+gas, TTE#2 no gas</td>
<td>6</td>
<td>Stable blood pressure, mouthing words</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>CV line removal</td>
<td>V</td>
<td>Syncope, seizure, obtunded, hypotension, chest pain, dyspnea</td>
<td>4.75 hrs</td>
<td>Yes</td>
<td>NSR</td>
<td>Head CT-gas</td>
<td>6</td>
<td>Complete recovery</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>56</td>
<td>M</td>
<td>Pulmonary overpressure</td>
<td>A</td>
<td>Profound right sided weakness</td>
<td>0 hrs</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>6</td>
<td>Complete recovery</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>42</td>
<td>M</td>
<td>Venous dialysis cath. open to air</td>
<td>V</td>
<td>Dizzy, weak, numbness, sleep disturbance, dyspnea</td>
<td>6 hrs</td>
<td>Yes</td>
<td>NSR</td>
<td>None</td>
<td>6</td>
<td>Complete recovery</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>42</td>
<td>M</td>
<td>CV line removal</td>
<td>V</td>
<td>Cardiopulm. arrest, seizure, GCS3</td>
<td>10.75 hrs</td>
<td>Yes</td>
<td>Sinus tachy</td>
<td>Head CT negative</td>
<td>6</td>
<td>Not assessable, chemical paralysis</td>
<td>Died</td>
</tr>
<tr>
<td>38</td>
<td>F</td>
<td>CV line removal</td>
<td>V</td>
<td>LOC1, dizziness, disoriented, mental status change, ARDS</td>
<td>28 hrs</td>
<td>Yes</td>
<td>Sinus tachy</td>
<td>Head CT #1 negative 6 Head CT #2 decreased attenuation TTE negative infarcts</td>
<td>6</td>
<td>Following commands</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>49</td>
<td>F</td>
<td>CV cath. leak</td>
<td>V</td>
<td>Headache, confusion, anxiety, weakness, chest pain, hypotension, dyspnea</td>
<td>6 days</td>
<td>Yes</td>
<td>Q waves inferior leads</td>
<td>Head CT#1 negative 6A, Head CT#1+gas MRI bilateral infarcts, TTE+gas, no shunt, TTE no gas, no shunt</td>
<td>6A</td>
<td>Not assessable, chemical paralysis</td>
<td>Spontaneous respiration, answering questions, increased movement</td>
</tr>
</tbody>
</table>

Footnotes: A/V- arterial/venous; CXR - chest x-ray; CV-central venous; NSR - normal sinus rhythm; ATA - atmospheres absolute; tachy - tachycardia; N/A - non-applicable; GCS - Glasgow Coma Scale; LOC - loss of consciousness
Gas entry mechanism: We identified seven events in our patients that accidentally allowed gas introduction into the circulation. Four patients experienced gas introduction into the venous system during central venous line removal. Three patients had a cut or leak in a central venous access line. Two patients had venous dialysis catheters inadvertently opened to air. Four patients experienced gas entry into the arterial system upon initiation of cardiac bypass. Three patients suffered gas introduction during carotid artery dye injection for radiological procedures. Two patients had gas introduced into the pulmonary capillary system during CT guided lung biopsy. One patient suffered pulmonary overpressure during ascent after routine HBO$_2$ therapy, which allowed gas into the pulmonary venous circulation. Therefore, nine of the nineteen patients had gas introduced into the venous circulation, and ten patients had gas introduced into the arterial circulation.

Signs and symptoms: All patients exhibited neurological signs and symptoms. Some patients also exhibited cardiac and pulmonary signs and symptoms. Neurological signs and symptoms included headache, anxiety, confusion, dizziness, somnolence, speech disturbance, decreased vision, extremity weakness, dyspnea, decreased mental status, focal neurological deficit and unresponsiveness. Cardiac signs and symptoms included cardiac rub, tachycardia, chest pain, syncope, and cardiopulmonary arrest. Pulmonary signs and symptoms included tachypnea, dyspnea, adult respiratory distress syndrome, and cardiopulmonary arrest. All patients with venous introduction of gas had pulmonary signs or symptoms, whereas no patients with an arterial source had pulmonary signs or symptoms.

Diagnostic tests: Chest x-rays were performed on eighteen of the nineteen patients prior to HBO$_2$ therapy. Of the nine patients with gas from a venous source, eight had chest x-ray evidence of pulmonary edema, and one had a normal chest x-ray. Of the ten patients with gas from an arterial source, nine had chest x-rays performed, and none showed pulmonary edema. One patient with gas from an arterial source had a pneumothorax after lung biopsy, and one showed focal changes from lung biopsy. The patient who did not have a chest x-ray was in the chamber when CAGE occurred and was recompressed without delay.

Electrocardiograms (EKG) were performed on seventeen of the nineteen patients prior to HBO$_2$ therapy. All nine of the patients with venous introduced gas had EKGs performed. Three patients had normal EKGs, two had ischemic or ST-T changes, three had sinus tachycardia, and one had atrial fibrillation with a rapid ventricular response. Of the ten patients with arterially introduced gas, six had gas introduced proximal to the coronary arteries. Of these six, four patients had normal EKGs and one had ST-T elevation, and one patient had no EKG performed. Of four patients with arterial gas introduced distal to the coronary arteries, two had normal EKGs, one had sinus tachycardia, and one did not have an EKG performed.

Further imaging studies were performed on twelve patients prior to HBO$_2$ therapy, totaling 23 studies. Seven patients had no imaging studies prior to therapy. These tests included twelve computerized tomography (CT) of the head, two magnetic resonance imaging (MRI) studies of the brain, two electroencephalograms (EEG), six transthoracic echocardiographs (TTE), and one transesophageal echocardiography (TEE). Six of the 23 diagnostic tests (26%) performed demonstrated gas in the circulation: three head CTs and three TTEs. Of the seventeen exams that did not demonstrate gas, five had secondary changes consistent with gas embolism: two head CTs, one MRI, and two EEGs (29%). Of the twelve patients that had imaging tests, five patients had at least one exam demonstrating gas prior to therapy (42%).

Treatment: The mean time from event of gas introduction to HBO$_2$ therapy in eighteen patients was 8.9 ± 8.6 hours (range 0-30 hours); the nineteenth patient suffered repetitive
embolism over six days. All nineteen patients were treated in a multiplace hyperbaric chamber with a physician in attendance. Dive profiles were the US Navy Treatment Tables 6 or 6A. Nine patients were treated on a Table 6A and nine on a Table 6. One patient was started on a Table 6A then continued on a modified Table 4 in accordance with US Navy procedures. Two of the nineteen patients underwent repetitive treatments (see Table 1).

Complications: One patient was dependent on an aortic balloon pump at the beginning of the HBO\textsubscript{2} treatment. The balloon pump stopped functioning at 2.8 ATA (atmospheres absolute); however, the patient’s cardiovascular status stabilized with HBO\textsubscript{2} therapy. One patient suffered pulmonary oxygen toxicity after an unusually long treatment (modified Table 4), which prevented further HBO\textsubscript{2} therapy but the patient’s recovery was excellent. In accordance with established procedures, all twelve intubated patients underwent prophylactic myringotomy. One non-intubated patient required myringotomy after initiation of HBO\textsubscript{2} therapy due to inability to equalize ear pressure, and two non-intubated patients experienced minor middle ear barotrauma. There were no complications of myringotomy.

Outcomes: Immediately upon completion of HBO\textsubscript{2} therapy, five patients (26%) resolved all signs and symptoms, eleven (58%) had improvement, one (5%) had no change and two (11%) were not assessable secondary to medically-induced paralysis. Within two months post HBO\textsubscript{2} therapy, three additional patients had resolved completely and six showed further improvement (Table 1). Therefore, eight patients (42%) had complete recovery, six (32%) had partial recovery, and five patients (26%) died of complications of CAGE. Complete recovery was defined as the patient reporting resolution of all symptoms and the doctor reporting resolution of all signs. Partial recovery was defined by objective improvement of pre-treatment signs and symptoms and is detailed for each patient in Table 1.

Outcome for patients with venous source for CAGE was complete recovery in five, partial recovery in two, and death in two. Outcome for patients with arterial sources for CAGE was complete recovery in three, partial recovery in four, and death in three. The mortality in our series was 26%. Recovery was not significantly different for patients with CAGE from venous introduced gas versus arterial introduced gas. All patients in our study who had a Glasgow Coma Scale (17) (GCS) of 3 upon initiation of HBO\textsubscript{2} treatment died from complications of CAGE.

The time from insult to HBO\textsubscript{2} therapy was recorded for eighteen patients, mean 8.9 hours (standard deviation 8.6, range 0 to 30 hours). One patient excluded from the mean was undiagnosed and therefore untreated for 6 days. The mean time from insult to HBO\textsubscript{2} therapy for patients with complete recovery was 11.1 ± 11.3 hours. In patients with partial recovery mean time to therapy was 8 ± 8 hours, and time for patients who died or exhibited no change was 6.3 ± 3 hours respectively. Of the eleven patients who were treated within 6 hours or less of their insult, five (45%) had complete recovery. Of the seven patients who were treated greater than 6 hours after their insult, three (42%) had complete recovery.

Exceptional case: One patient in this series suffered recurrent iatrogenic CAGE over six days and a serious delay in diagnosis and treatment. She was a 49-year-old female, who had a Swan-Ganz line exchanged with a CVP line in the right internal jugular vein. The first evidence of air embolism occurred with chest pain that resolved and an elevation of Troponin-I from 0.8 to 1.1ng/ml the day after the line change. This was interpreted as post-op cardiac enzyme leak, ischemia, or indigestion. The next day, upon standing, she experienced transient dizziness, orthostatic hypotension, and nausea. This was interpreted as worsening coronary artery disease.
versus orthostatic hypotension with abdominal distress. The third day she again experienced dizziness upon standing as well as chest pain and shortness of breath that resolved. This was interpreted as chest pain, likely of cardiac origin versus gastroesophageal reflux disease. The fourth day she suffered a severe posterior headache with confusion, slow speech, left upper extremity weakness, and chest pain. The differential diagnosis included CVA, sepsis, MI, and pericarditis, but none of these diagnoses alone explained all the symptoms. A head CT was obtained which showed old lacunar infarcts. The left upper extremity weakness continued on the fifth day and she developed new left lower extremity weakness. Her headache continued, and her affect was flat. MRI of the brain showed right frontal ischemic changes. Her headache was thought to be a migraine. That evening she had worsening dyspnea, weakness, confusion, a new heart murmur, and pulmonary edema. The morning of the sixth day she complained of chest pain and dyspnea. She then developed lethargy, hypotension, chest pain, new EKG ischemic changes, and elevation of Troponin-I to 1.7ng/ml. She was diagnosed with myocardial infarction and CVA. An echocardiogram showed air in the right ventricle with no intra-cardiac shunt, but possible intrapulmonary shunt. A repeat CT of the head showed evidence of air in the brain. That afternoon a TTE was done, which showed no air in the right ventricle. On the sixth evening the diagnosis of CAGE was made, and she was referred for HBO$_2$ therapy.

DISCUSSION

Our results agree with published literature showing that patients experience iatrogenic CAGE from many different procedures performed in different fields of medicine. When these procedures introduce gas into the arterial system, it travels to the cerebral arteries to cause CAGE. All CAGE patients have neurological signs and symptoms. Patients suffering venous gas embolism often do not have neurological symptoms and are not treated with HBO$_2$. However, the patients with venous gas embolism in our study exhibited signs and symptoms of CAGE and therefore were treated with HBO$_2$. Gas may egress from venous to the arterial circulation from imperfect filtering by the lungs or due to a right to left cardiac shunt, such as a patent foramen ovale, present in 15-20% of the normal population. Depending on where gas is introduced into the circulation, CAGE patients may also have cardiac or pulmonary signs and symptoms. Figure 1 illustrates the venous and arterial entry of gas bubbles into the circulation at various points and signs and symptoms associated with gas entry at each location.

Pulmonary signs or symptoms may occur when gas is introduced into the venous circulation. Gas introduced into the venous system flows through the right heart and then to the lungs. The lungs serve as a good but imperfect filter for the gas bubbles. This has been shown by studies on dogs (18-21), sheep (22), and swine (23). Gas in the microcirculation of the lungs causes tissue damage, and the patient experiences shortness of breath, pulmonary edema and/or ARDS. Prior human studies (24-26) have shown radiographic changes to the lungs from venous gas introduction. Bubbles that pass through the lungs emerge on the arterial side of the circulation, and enter the left heart and subsequently the coronary arteries, brain and other sites.
Cardiac signs and symptoms may occur when gas is introduced into the venous system or into the arterial circulation proximal to the coronary arteries. As noted above, gas introduced into the central venous system may pass through the imperfect filtering system of the lungs and arrive in the left heart, to be distributed to the coronary arteries as well as the cerebral and systemic arteries. Gas introduced directly into the pulmonary vein or left heart is already in the arterial system and is also distributed to the coronary as well as the cerebral and systemic arteries. Gas introduced into the arterial system distal to the takeoff of the coronary vessels has access to the cerebral and systemic arteries but not the coronary arteries.

Ours is the only clinical series delineating the signs and symptoms of patients experiencing iatrogenic CAGE based on the gas entry point. Our study demonstrated that patients with arterial introduction of gas had no pulmonary symptoms or radiographic signs of pulmonary edema or ARDS. This is consistent with our hypothesis, since gas introduced directly into the arterial system makes it to the brain without passing through the lungs. Our results are also consistent with expectations that patients with venous entry of gas or arterial introduction proximal to the takeoff of the coronary arteries were more likely to have acute EKG changes, (50% vs. 30%). Ischemic EKG changes were only demonstrated in patients with gas entry proximal to the coronary arteries. However, lethal cardiac arrhythmias mediated by autonomic activity do occur from gas entry into the cerebral circulation (27).

Imaging studies of the brain were performed on our patients to try to confirm the diagnosis of CAGE. Approximately one fourth of the studies detected gas. Less than one half showed either gas or secondary evidence of CAGE. This is consistent with prior reports that MRI and CT scanning of the brain do not necessarily demonstrate cerebral air embolism or the pathologic changes associated with the embolism (13, 28, 29). If the CT scan is not obtained within a few hours, the gas is absorbed and often not demonstrable (29). Diagnostic tests may confirm but do not rule out CAGE and may cause unnecessary treatment delays.

It has been reported that a short time between the insult and HBO₂ is associated with better outcome. In our study, patients had the same complete recovery rate whether they were treated in less than 6 hours or greater than 6 hours after CAGE. This finding may be due to
variation in time to treatment and earlier diagnosis and referral of more severely injured patients. For example, two patients with unusually long treatment delays (greater than 24 hours) were in the complete recovery group, which skewed the mean. We would need a larger or more uniform group of patients to assess the effect of delay to treatment controlling for severity of injury. Intuitively, shorter treatment delays will best serve the patient (30).

HBO2 is accepted treatment for CAGE, and the majority of our patients improved during and immediately after HBO2 therapy. Two patients in whom treatment was initiated at 28 and 30 hours after CAGE both had complete recovery. Benefit of HBO2 therapy initiated greater than 12-24 hours after injury has been reported previously (31-34). Some of our patients continued to improve neurologically in the ensuing months after HBO2 therapy, and no patient who improved with HBO2 deteriorated subsequently.

There is little literature reporting similar patients with which to compare the mortality of 26% in this series. Murphy’s series of 16 patients had 13% mortality but does not contain sufficient information to compare initial severity of injury (3). All patients in our study died who had a GCS of 3 at the time of initiation of HBO2 therapy. Many case reports provide information that the patient presented in coma, leaving the GCS score indeterminate and, therefore, not comparable to our data. However, there is a report of a patient who sustained an iatrogenic CAGE during liver transplant, (bubbles were present in the inferior vena cava) with a GCS of 3 after discontinuation of anesthesia and sedation, who survived after HBO2 therapy (35).

There are limitations of our study. First, it was not a clinical trial of treatment of iatrogenic CAGE, there are no controls, and all patients were treated with HBO2. Second, iatrogenic CAGE is uncommon, so the numbers of patients for study is small. The number of patients was insufficient to determine whether the trend is real that patients with venous gas entry have a better neurological recovery than patients with arterial gas entry. Third, the study was retrospective; so some data was not available for some patients. For instance, it was not possible due to incomplete echocardiography data to comment on the number of patients that had pre-existing anatomic right to left cardiac shunt (e.g. patent foramen ovale) in our venous gas embolism patients. Nor was it possible to comment on the number of patients showing radiographic resolution of pulmonary edema during HBO2 treatment, even though many patients showed clinical improvement in pulmonary function. We also were not able to provide detailed neurological outcome because formal testing was not available for review.

CONCLUSION

The diagnosis of iatrogenic CAGE is primarily clinical and diagnostic imaging of patients with suspected iatrogenic CAGE is of limited utility. The clinical findings of this study are useful for recognizing the signs and symptoms of iatrogenic CAGE based on suspected point of entry of gas. Patients with introduction of venous gas have pulmonary signs or symptoms, such as shortness of breath, pulmonary edema or ARDS, whereas patients with arterial introduction of gas are unlikely to have pulmonary signs or symptoms. This knowledge should result in more frequent and earlier detection and treatment of this rare but serious neurological disorder.
ACKNOWLEDGEMENTS

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REFERENCES

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