Hyperbaric oxygen-associated seizure leading to stroke

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Abstract

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Oxygen toxicity seizures are a well-known complication of hyperbaric oxygen treatment (HBOT). Until now, there have not been any reported cases of an acute ischaemic event (stroke) as the result of a HBOT-associated oxygen toxicity seizure. We report an event in which a seizure and stroke occurred together and consider that the stroke may have been caused by seizure-induced demand ischaemia. This challenges the generally held view that oxygen toxicity seizures in the clinical hyperbaric setting are benign. A discussion of the literature on the subject of seizure-induced brain injury is included. Risk factors for cerebrovascular disease should be taken into consideration in determining treatment pressures for HBOT, as reducing pressure reduces seizure risk.

Introduction

Oxygen toxicity seizures are a well-known complication of hyperbaric oxygen treatment (HBOT).[1] These seizures are generally regarded as benign. Until now, there have not been any reported cases of acute ischaemic events (stroke) as the result of an HBOT-induced oxygen toxicity seizure. Herein, we report the possibility of such an event, challenging the generally held view that oxygen toxicity seizures in the clinical hyperbaric setting are benign and raising questions as to the current acceptable risk threshold for HBOT in patients with multiple risk factors for cerebrovascular accident (CVA). Reducing treatment pressure for at risk individuals may be advisable.[2]

Case report

An 80-year-old male with a past medical history of a CVA without residual deficit, mild chronic obstructive pulmonary disease (COPD), coronary artery disease, stage IV chronic kidney disease and peripheral vascular disease underwent HBOT for a non-healing arterial-insufficiency ulcer of the right second toe. Although he had significant proximal vascular disease, revascularization was felt to be an unacceptable risk given his advanced renal disease, particularly because surgery might not rectify the flow to the affected toe, secondary to his small vessel occlusive disease. HBOT was chosen for treatment in an attempt to save the patient's leg while avoiding the surgery which would likely lead to permanent dialysis.

The patient underwent his first HBOT (90 minutes at 243 kPa, with air breaks) in a monoplace chamber without incident. He presented the next day for a second treatment, which he tolerated well until the time of ascent (depressurization). At the start of the ascent, the patient appropriately acknowledged the nurse informing him of that. Nursing staff noted at the very end of the depressurization that he had altered mentation and did not respond to them. The patient could not be taken off oxygen, being in a monoplace chamber pressurized with oxygen.

On opening the chamber door, the supervising physician noted expressive and likely receptive aphasia, inability to follow commands in his left upper extremity, spastic, clumsy movements of the right hand and rhythmic lip smacking movements. Within one to two minutes, the patient began to have what appeared to be a tonic-clonic seizure lasting approximately 90 seconds. He was noted to be incontinent of urine during this event. His blood sugar was measured to be 4.94 $mmol \cdot L^{-1}$ and there was no ectopy seen on his cardiac monitor. Following cessation of the seizure, the patient seemed to be post-ictal. He was taken directly to the emergency department and the stroke team was activated.

In the emergency department, neurological examination showed somnolence but with response to loud voices, mumbling and garbled speech, intact vestibulo-ocular reflex and an inability to follow commands. Physical examination was otherwise unremarkable. The patient's head CT showed age-indeterminate lacunar infarcts, global parenchymal volume loss, sequelae of mild to moderate small vessel

ischaemic disease but no evidence of haemorrhage, gas or mass effect. His electrocardiogram (ECG) revealed normal sinus rhythm with 1st degree atrio-ventricular block. The patient returned to his baseline function and mental status during this examination time. He was admitted to the hospital for observation and further work-up.

Five hours after this event, he underwent a brain MRI which showed acute to sub-acute infarcts of his right putamen and right frontoparietal cortex. The diffusion weighted, ADC, and T2 weighted sequences indicate that the ischaemia had to have occurred on that day or, less likely, in the several days prior to the event. MR angiography was not indicated as this pattern of ischaemia is not suggestive of a single large artery distribution. There was no reason to do angiography. Carotid Doppler ultrasound revealed mild (1–49%) stenosis of his right carotid artery and moderate (50–69%) stenosis of his left carotid artery.

Chest X-ray showed only postoperative changes in the right lung base and low lung volumes with mild bibasilar atelectasis. There was no evidence of pneumothorax, blebs or other COPD findings. Echocardiography demonstrated no evidence of shunting across the inter-atrial septum. There was aortic valve sclerosis and mitral calcification but no sign of thrombus or other potential source of emboli. Electroencephalography (EEG) was consistent with the presence of moderate diffuse cerebral dysfunction; there were no epileptiform discharges or seizures recorded. The patient was believed to have suffered a seizure as a result of CNS oxygen toxicity, a known complication of HBOT. This seizure was thought to have provoked his stroke and therefore further HBOT was deemed to comprise more risk than benefit to him and his treatment was discontinued.

Discussion

Seizures during HBOT are a well-known complication of such therapy and occur with a 0.03% incidence.[1] Incidence increases with treatment pressure, and may be almost non-existent at 202 kPa (2.0 ATA) or lower.[2] These seizures "*may occur suddenly without warning or they may be preceded by an aura or sequence of premonitory sensations*".[1] Oxygen toxicity seizures generally present with tonic-clonic convulsions; however, they may also start as focal seizures.[1,3] In this case, the patient had both lip twitching and tonic-clonic seizure, both of which are characteristic signs of oxygen toxicity.[1] The pathophysiology of oxygen toxicity seizures is only partially understood, but it is known that cerebral blood flow is increasingly reduced at higher partial pressures of oxygen.[4] This is postulated to be owing to the increased arterial oxygen tension, which causes slight hyperventilation, decreased cerebral blood flow and arterial hypocapnia. However, hyperoxia has also been shown to cause an independent cerebral vasoconstrictive effect.

Regarding the aetiology of this patient's seizure, it is unusual in that the patient did not go on to full-blown tonic-clonic activity until he was out of the chamber. This raises a question about whether the seizure was indeed due to oxygen toxicity and presents an interesting differential diagnosis conundrum. Other possibilities for this event include stroke-induced seizure (perhaps from an embolic event), coincidental seizure from prior infarct or disorder, presyncope (cerebral hypoperfusion) and cerebral gas embolism. Other than prior stroke, the patient had no other seizure history or risk factors. The only MRI evidence of his old stroke was "*scattered foci of T2 hyperintensity throughout the hemispheric white matter, likely sequelae of mild to moderate small vessel ischaemic disease*". These lesions are incidental age-related changes. It is unlikely that such a lesion could have been an epileptogenic focus as such subcortical structures are not thought to be epileptogenic.

EEG failed to reveal an underlying epileptiform pattern. Given the chronology of the event, the hyperoxygen exposure may have triggered a heretofore potential seizure focus from prior ischaemic disease. Thus, the seizure would still be considered an oxygen toxicity event and not a coincidental, first-time seizure secondary to old stroke or a seizure due to coincidental new stroke (discussed as follows).

In this case, the stroke was thought to have been potentiated by the seizure due to the patient's presenting symptoms and the location of the stroke. The patient initially had aphasia and right upper extremity motor symptoms, which would have originated from the posterior inferior left frontal cortex. However, the infarct was found to be located in the right putamen and frontoparietal cortex. The seizure would initially have to have begun in the left frontal cortex before generalizing to the entire brain to present in the way in which it did. The stroke involving the right putamen and frontoparietal cortex would also not have been responsible for the aphasia and right arm issues seen: stroke in these areas would not result in a seizure with initial left hemisphere prodrome. Additionally, the putamen is not a seizure focus.[5] It would be exceedingly unlikely that two distinct (right putamen and right frontal cortex) incidental asymptomatic strokes would happen at the same time. We conclude that this largely asymptomatic stroke was the result of the seizure.

The possibility of this event being due to presyncopal myoclonus seems unlikely. The patient was on a cardiac monitor and no dysrhythmia was noted. Although blood pressure measurements at the time of the event are not available, he had documented hypertension of 179/84 shortly after the event and 144/50 the day prior. No cause or indication exists for transient hypotension. He had what appeared to be oral automatisms of rhythmic lip and mouth movements which are highly suggestive of temporal lobe or complex partial seizures, before proceeding to a generalized tonic-clonic seizure. Hypoperfusion or presyncope can give some shaking movements, as in the case of 'limb-shaking' carotid TIAs, but not complex oral movements or automatisms. Further, this mechanism fails to explain the sub-acute infarcts noted on MRI.

Other possible causes of this seizure and stroke presentation would include cerebral arterial gas embolism (CAGE) and a cardio-embolic stroke. Due to the onset of symptoms during decompression and the history of COPD, air trapping leading to pulmonary barotrauma and subsequently to cerebral arterial gas embolism (CAGE) could be considered as a differential diagnosis. Still, the areas infarcted did not correlate with the early signs prior to tonic-clonic activity and there was no evidence of pulmonary barotrauma (or visible COPD changes for that matter), making this mechanism less likely (although possible, as embolic transient ischaemia could account for signs that would not necessarily correlate with infarct areas). A cardio-embolic stroke is unlikely given no evidence of atrial fibrillation or other arrhythmia, and no right to left shunt in the heart or embolic source on the ECG. Additionally, seizure activity at onset is not common nor is altered mentation or the other signs noted prior to tonic-clonic activity.

It is unclear what the effect was of having the patient removed from the hyperbaric chamber. It is possible that the drop in oxygen partial pressure occurring with the cessation of HBOT combined with ongoing HBOT-induced vasoconstriction and small vessel atherosclerotic disease provided a situation in which demand ischaemia might occur. We posit that the stroke was in fact the result of demand ischaemia in the face of the seizure. First, the initial left-sided symptoms appeared to be due to focal seizure activity which then generalized globally. However, the right-sided stroke findings appear clinically silent. Although the patient had greater left- than right-sided carotid disease, the stroke areas are not proximal carotid strokes, but occurred much farther downstream in locations where the patient's known small vessel ischaemic disease would have come into play.

There have been animal studies which have demonstrated chemical changes and apoptosis in the brain following induced oxygen toxicity seizures, suggestive of non-ischaemic injury.[6–9]

Reversible imaging changes in both functional and anatomic exams during the peri-ictal period have been recognized in human subjects.[10,11] These changes occur both local to the area of maximal EEG signal or remotely. Such changes may persist even weeks after an event. Some may progress to a permanent change. What is not yet understood is the mechanism of these changes and their reversal, although many hypotheses have been suggested.[11]

It is possible that this man had such high metabolic demand during his seizure that, when coupled with his known vascular insufficiency as demonstrated by his peripheral vascular disease and prior stroke, the result was an area of ischaemia. Once the seizure concluded, the metabolic demand returned to baseline and the ischaemic area was again supplied with sufficient oxygen.

Conclusions

Although brain injury secondary to seizure has been described in the literature, ours is the first report of brain injury potentially due to hyperbaric oxygen-induced seizure. Other reports have raised the possibility that hyperbaric oxygen can induce strokes. Hyperbaric oxygen-induced seizures are dose (pressure) related. Reducing treatment pressure can markedly ameliorate, if not eliminate, the risk of an oxygen toxicity seizure. This case serves as a reminder that oxygen toxicity seizures may not always be benign. Cerebrovascular disease may predispose to demand ischaemic insult in the face of oxygen toxicity seizures. Pre-existing cerebral structural lesions may leave one more prone to oxygen-induced focally triggered seizure activity. These risk factors should be taken into consideration when determining treatment pressures for HBOT.

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