

Prolonged duration of apnea test during brain death examination in a case of intraparenchymal hemorrhage

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Abstract

Objective: Apnea test is required as part of the brain death examination. The duration of the apnea test is variable but typically requires 8–10 min. Prolonged apnea tests have been reported in the setting of hypothermia. Here, we describe a case of prolonged duration of apnea test secondary to a phenomenon called cardiac ventilation.

Methods: The patient presented in coma with brainstem areflexia after having an intracerebral hemorrhage resulting in subfalcine, central, uncus, and tonsillar herniations. Confounding variables were excluded. Brain death testing was performed, and she was found to have brainstem areflexia. Pre-requisites for apnea test were then met.

Results: Apnea testing, however, was prolonged at 110 min. When reconnected to ventilator, it was noted that she had small (30–35 cc) tidal volumes at a rate of her heart rate without respiratory effort. Ancillary testing with four-vessel cerebral angiogram confirmed cerebral circulatory arrest.

Conclusions: To our knowledge, this is the longest reported case of apnea testing during brain death testing. Variables known to cause a delay in the rise of carbon dioxide (PaCO₂) levels were excluded. We suspect the hyperdynamic cardiac state caused cardiac ventilations resulting in slow increase in carbon dioxide levels.

Keywords

Apnea test, brain death, pitfalls, ancillary tests, death by neurological criteria

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Introduction

Medical standards for the determination of death by neurological criteria were first published by the American Academy of Neurology (AAN) in 1995.¹ They have since been updated.² The determination of death by neurologic criteria requires the pre-requisites of a mechanism causing irreversible injury, exclusion of confounding medical complications, and establishing coma with brainstem areflexia including apnea testing. Before initiating apnea testing, all patients must meet pre-requisite baseline characteristics including a body temperature >36°C, a systolic blood pressure >90 mmHg, the absence of hypoxia and acidosis, and a euvolemic state.² Typically, the apnea test requires 8–10 min of apnea to reach the goal carbon dioxide (PaCO₂) level.¹

We present a patient with a large right basal ganglia hemorrhage and brainstem areflexia with a prolonged apnea test. We suspect the etiology for the prolonged duration to be due to the phenomenon known as cardiac ventilation.

Case report

A 50-year-old female with body mass index (BMI) of 36 kg/m² and untreated hypertension presented to an outside facility with left arm numbness and weakness and new-onset seizure. She was treated with levetiracetam. Computed tomography (CT) of the head along with CT angiography (CTA) was obtained which showed a right basal ganglia hemorrhage measuring about 3 cc (Figure 1). Her blood pressure was initially 157/100 mmHg and controlled with nicardipine infusion. Subsequent blood pressure was 132/70 mmHg. Her international normalized ratio (INR) was 1.0. She was not taking anticoagulants or antithrombotics. While in the emergency department, her neurological examination rapidly worsened.

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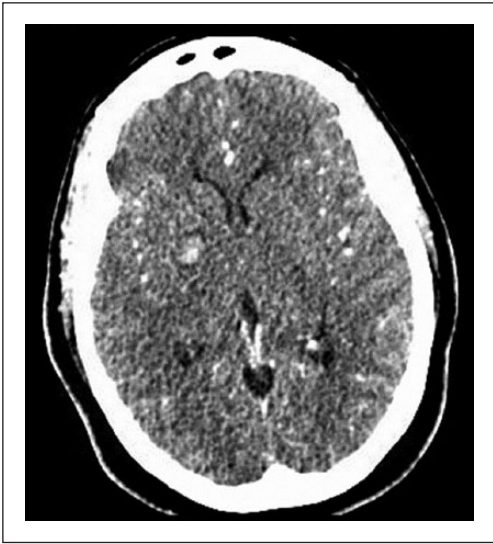


Figure 1. Computed tomography angiography (CTA) of the head. A small (~3 cc) right putaminal intracerebral hemorrhage is noted. CT spot sign is negative.

She was intubated for airway protection and was transferred to the neurosciences intensive care unit (NSICU).

On arrival to the NSICU, she was on a nicardipine infusion for blood pressure control. Her blood pressure was well controlled initially in the 130/90s range but acutely fell to 80/50s. The infusion was immediately stopped. Patient was bolused with normal saline and started on norepinephrine infusion. She subsequently became unresponsive to central or peripheral noxious stimulation. She had absent brainstem reflexes except for over breathing the respirator. She was hyperventilated and given 100 g of mannitol. Train-of-four was then performed and showed four twitches. Repeat CT of the head showed hematoma expansion to 47 cc with intraventricular extension (Figures 2 and 3). There was now effacement of the basilar cisterns as well as uncus, central, and tonsillar herniations (Figures 2 and 3).

Over the course of the next day, she stopped breathing over the ventilator. Confounding variables on the neurological examination were excluded (Table 1). Brain death testing ensued. She was found to have brainstem areflexia. Prior to apnea testing, her core temperature was 36.1°C, systolic blood pressure was 141 mmHg, and PaCO₂ was 39.6 mmHg. After pre-oxygenation, her PaO₂ was 83 mmHg. With continued pre-oxygenation, the PaO₂ increased to 279 mmHg (Table 2). She was subsequently disconnected from the ventilator with 5–6 liters per minute of oxygen delivered via red rubber catheter to the carina. During testing, there were no cardiopulmonary complications. Her systolic blood pressure remained 140 mmHg without any vasopressors. Her oxygen saturation remained 96.2%–99.3%. There were no cardiac arrhythmias or respiratory movements. However, the duration of the apnea testing was 110 min before PaCO₂ reached the required level of >60 mmHg and serial blood gas analysis was obtained during this entire 110 min (Table 2).

At the end of the apnea testing, she was reconnected to the ventilator. It was then noticed that she had tidal volumes of 30–35 cc with a “respiratory rate of 44” which corresponded to her heart rate on telemetry (Figure 3). Given the unusual duration of apnea testing, ancillary testing was subsequently completed. Four-vessel cerebral angiography confirmed cerebral circulatory arrest (Figure 4). Autopsy was declined.

This case report was approved by the institutional review board.

Discussion

Our case report documents, to our knowledge, the longest duration of apnea testing in the literature. It also highlights a pitfall that can occur during apnea testing resulting in a slow rise in PaCO₂. It is important for the clinician to recognize cardiac ventilations as a source of prolonged apnea testing. If the patient is stable during the apnea testing, the testing should continue.

Apnea testing is a requirement as part of the brain death testing.² The duration of necessary apnea time to reach a blood level of PaCO₂ of 60 mmHg or an increase of PaCO₂ of 20 mmHg above patient’s baseline is variable and depends on factors such as baseline PaCO₂, flow delivery of oxygen, and body temperature.³ Many brain death protocols accept a period of apnea time of 8–10 min before checking PaCO₂.³ It is expected that average rate of PaCO₂ increase is 3.7 ± 2.3 mmHg/min.⁴ In actual practice, the rate of CO₂ rise displays high inter- and intra-personal variability and often is difficult to predict.⁵ The duration of the apnea test can be prolonged. One case report discussed an apnea test of 71 min.⁶ This case report failed to provide an explanation for the prolonged testing.⁶ However, our case report does illustrate that the apnea test can continue if patient remains hemodynamically stable (i.e. systolic blood pressure >90 mmHg, oxygen saturation >85%, and no cardiac arrhythmias or respiratory movements).⁷ These hemodynamic changes may occur from the hypoxemia and/or respiratory acidosis that may occur during apnea.⁷ Previous studies have described clinical factors affecting the increment rise of PCO₂ during the apnea test.³ Hypothermia, defined as a core temperature below 35°C, will decrease the production of PaCO₂ compared to normothermia/hyperthermia.³ Additionally, CO₂ elevation and elimination may be skewed by the oxygen flow via a catheter placed in the endotracheal tube.⁸ Modification of the apnea testing have been proposed. Benzel et al.⁹ modified their protocol by initially reducing mechanical ventilation settings to allow for a higher initial PCO₂ a baseline prior to apnea. This was shown to reduce the amount of time required to reach the desired goal of 60 mmHg.⁹ This method, however, is not endorsed by the AAN guidelines.^{1,2}

Certain pitfalls such as hypoxia/hemodynamic instability before or/and during the test, CO₂ retention, and false ventilator registering of the breaths lead to inconclusive apnea tests.¹⁰ In our case, there was initial transient hypoxia during

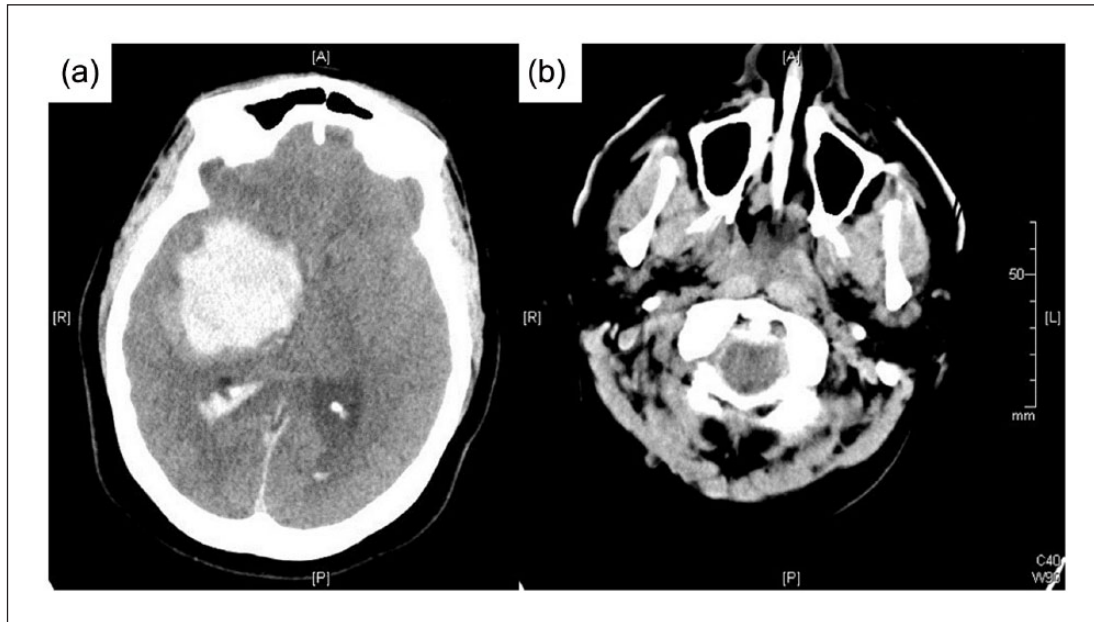


Figure 2. Noncontrast computed tomography (CT) of the head. (a) The right putaminal intracerebral hemorrhage has expanded to 47 cc. There is also intraventricular hemorrhage in the occipital horns of the lateral ventricles, right to left midline shift, and perihematomal edema. (b) The foramen magnum shows tonsillar herniation and effacement of the cervico-medullary junction.

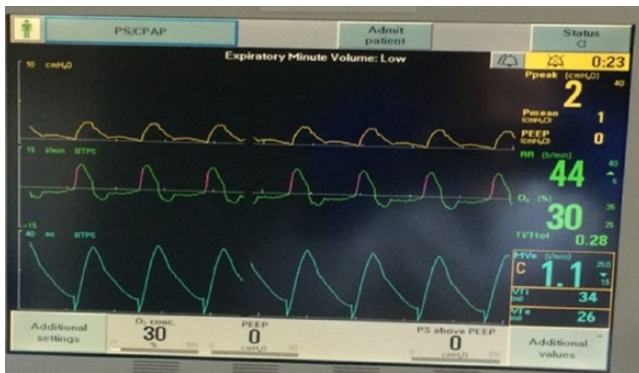


Figure 3. Ventilator image. After apnea test, patient was reconnected to ventilator. Prior to setting controlled ventilation with PEEP 0 and pressure support 0, it was noted that her heart rate (44 bpm) was causing small tidal volumes of 30–35 cc creating minute ventilation of 1.1 L, which we hypothesize as the cause for the slow rise of CO_2 during the apnea test.

arterial blood gas (ABG) sampling due to inadvertent opening of the port in the 14–16 Fr BARD X-ray opaque suction catheter placed just above the carina used for apneic oxygenation. Oxygen flow rate initially was 5 L/m but increased to 6 L/m after there was an episode of hypoxia. The PaO_2 had decreased from 83 to 57.4 mmHg during the first 10 min. Pulse oximetry at this time was 79.3% for <15 s with rapid improvement to 94% with increased O_2 delivery via the catheter. No further hypoxic episodes occurred. The apnea test continued. During the testing, other factors like hypothermia, low baseline PaCO_2 , hypotension, and CO_2 washout were excluded.

Table 1. Baseline variables prior to brain death testing.

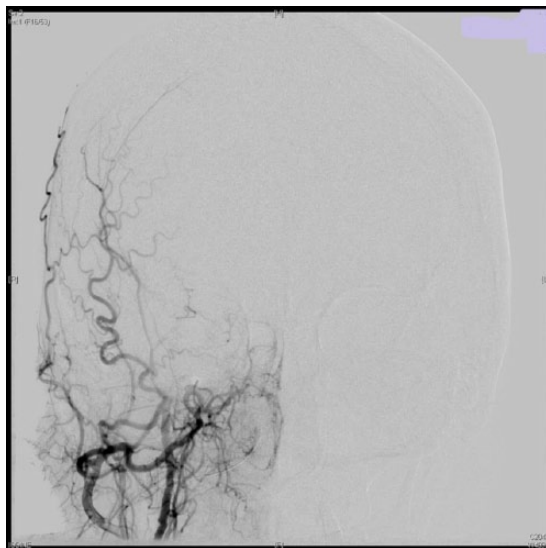
Lab	Value
Sodium	149 mmol/L
Ammonia	24 $\mu\text{mol/L}$
Bicarbonate	24.7 mmol/L
Glucose	153 mg/dL
BUN	9 mg/dL
Creatinine	0.69 mg/dL
Temperature	36.1 °C
Urine toxicology	Negative
Sedation	None
Results of train of four	4 twitches
PaO_2	83 mmHg
PaCO_2	39.6 mmHg
pH	7.413

BUN: blood urea nitrogen.

We suspect the etiology for the prolonged apnea testing to be cardiac ventilation as termed by Benzel et al.⁴ Cardiac ventilation occurs from the hyperdynamic cardiac state that is created during apnea which can cause a delayed rise of PCO_2 during the apnea test.⁴ It is hypothesized that the hyperdynamic cardiac state causes robust cardiac pulsations resulting in compression and relaxation of nearby alveolar units. Our patient had no history of chronic obstructive pulmonary disease (COPD), smoking, or any factor causing compromised lung compliance. Her cardiac ventilations were enough to prevent the normal expected rise in PaCO_2 during apnea. Furthermore, our patient did not have autopsy or organ donation completed which could allow for other

Table 2. Arterial blood gas (ABG) results during apnea test.

Time	PCO ₂ (mmHg)	PO ₂	%O ₂
13.41	39.6	83	96.2
13.51	34.2	57.4	79.3
14.02	49.1	76.6	94
14.05	50.0	114	97.9
14.12	50.7	102	97
14.21	47.5	112	97.7
14.22	50.9	117	98
14.33	49.7	134	99
14.47	54.8	276	99.7
14.48	52.7	264	99.9
14.57	53.5	279	99.9
14.58	53.3	275	99.4
15.31	62.1	253	99.3

**Figure 4.** Cerebral angiography. Right carotid injection showing filling of the extracranial carotid artery but not the intracranial carotid artery which is consistent with cerebral circulatory arrest.

anatomical changes in the cardiopulmonary system as an explanation for the observed prolonged apnea time.

If certain parts of the neurological examination or apnea test cannot be reliably performed, or their validity is drawn into question, such as in our patient with the prolonged apnea test, ancillary testing should be completed to support the clinical diagnosis of brain death.¹⁰ Officially recommended tests demonstrating cerebral circulatory arrest are four-vessel conventional angiography, transcranial Doppler (TCD), Tc99HMPAO SPECT scan, and electroencephalography (EEG).¹ In cases where PCO₂ is not uniform over time within a given patient, performing a modified apnea test with PCO₂ diffusion has been suggested.¹¹ Given the prolonged duration of the apnea test in our patient, we pursued four-vessel cerebral angiography to confirm cerebral circulatory arrest.

In summary, cardiac ventilations should be recognized as a factor in slow rise in PCO₂ during apnea testing. Our case highlights this pitfall in brain death testing.

Acknowledgements

All authors contributed equally to the writing of the case and formatting the images. This case report was approved by the Institutional Review Board.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval to report this case was obtained from the University Of Missouri Institutional Review Board (IRB No. 2005806).

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Informed consent

Obtained written informed consent from patient's mom (patient's legal guardian) as the patient was deceased.

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