BMC Neurology

Case report

Confounding factors in diagnosing brain death: a case report

Jeffrey M Burns * and Ivan S Login

Address: Department of Neurology, University of Virginia Health Sciences Center, Box 800394, Charlottesville, VA 22908, USA

E-mail: Jeffrey M Burns* - jburns@virginia.edu; Ivan S Login - isl@hscmail.mcc.virginia.edu

*Corresponding author

Published: 26 June 2002

BMC Neurology 2002, **2**:5

Received: 23 April 2002

Accepted: 26 June 2002

This article is available from: http://www.biomedcentral.com/1471-2377/2/5

Abstract

Background: Brain death is strictly defined medically and legally. This diagnosis depends on three cardinal neurological features: coma, absent brainstem reflexes, and apnea. The diagnosis can only be made, however, in the absence of intoxication, hypothermia, or certain medical illnesses.

Case presentation: A patient with severe hypoxic-ischemic brain injury met the three cardinal neurological features of brain death but concurrent profound hypothyroidism precluded the diagnosis. Our clinical and ethical decisions were further challenged by another facet of this complex case. Although her brain damage indicated a hopeless prognosis, we could not discontinue care based on futility because the only known surrogate was mentally retarded and unable to participate in medical planning.

Conclusion: The presence of certain medical conditions prohibits a diagnosis of brain death, which is a medicolegal diagnosis of death, not a prediction or forecast of future outcome. While prognostication is important in deciding to withdraw care, it is not a component in diagnosing brain death.

Background

Brain death is strictly defined medically and legally [1–5]. We encountered a patient who met the three cardinal neurological features of brain death but the diagnosis was not possible due to the confounding presence of an underlying medical illness. Further, the only known surrogate was unable to participate in medical decisions and withdrawal of care was therefore not immediately possible. We present this case to teach two critical lessons in patient care: first, the need for rigorous understanding of the means by which brain death is diagnosed and second, the important distinction between a grave prognosis versus brain death.

Case presentation

A 62-year-old white female collapsed at home after a period of shortness of breath and "foaming at the mouth." Her brother, who has Down's syndrome, witnessed these events. A basic life support team began cardiopulmonary resuscitation approximately 15 minutes later, noting absent pulse and respirations. An advanced cardiac life support team arrived 30 minutes after her collapse. Evaluation at that time confirmed absent respirations and pulse with asystole on electrocardiogram. Atropine was administered followed by epinephrine. The patient's pulse was restored about 35 minutes after her collapse. She was intubated and transferred to the emergency department.

There, she had pulmonary edema, inferior Q waves, primary atrioventricular block and a right bundle branch block with right ventricular strain. Abnormal lab values included white blood cell count, 15.7; hematocrit, 25.8; prothrombin time, 22.3; INR, 2.0; PTT, 84.0; CO2, 10; BUN, 41; creatinine, 1.7; and glucose, 594.

She had a history of hypothyroidism, chronic renal insufficiency, hypertension, coronary artery disease, non-insulin dependent diabetes mellitus, and psoriatic arthritis. Her daily medications included aspirin, levothryoxine, lisinopril, glipizide, simvastatin, omeprazole, lasix, amlodipine, prednisone, paroxetine, digoxin, and metoprolol.

A neurological consultation four hours after admission revealed an intubated woman who did not respond to noxious stimuli. The pupillary, corneal, oculocephalic, gag and cough reflexes were absent. Caloric testing was not performed at this time. Her temperature was 33.1°C.

Her profound hypothermia and history of hypothyroidism led us to initiate investigating thyroid functions. Treatment included re-warming and control of hyperglycemia.

Seven hours after admission, a head CT demonstrated loss of the gray/white junction, diffuse low density, loss of sulci, and obliterated cisterns suggesting diffuse, severe hypoxic injury.

An apnea test conducted 10 hours after admission did not induce breathing during the 10-minute evaluation. Concurrently, she had absent pupillary, corneal, gag, cough, oculocephalic and caloric responses. There was no response to deep pain stimulation. At this time she met the three clinical neurological requirements to diagnose death by neurological criteria, however, we learned that her TSH was strikingly elevated at 67.38 uIU/mL (normal 0.4 – 6.00), indicating profound hypothyroidism. Free T4 was low at 0.4 ng/dl (normal 0.8 – 1.8). T3 uptake was normal (34%). Her last prior TSH level was 2.18 uIU/mL 10 weeks earlier.

From an ethical perspective, we felt justified in offering the opinion that even if death by neurological criteria was inappropriate because of hypothyroidism, treatment could be withdrawn based on her dismal prognosis and the support of a surrogate decision-maker. Unfortunately, the only known relative was mentally retarded and incapable of participating in the decision to terminate care for futility.

Given the profound hypothyroidism confounding a diagnosis of brain death, a technetium radionuclide perfusion study was obtained and revealed absent intracranial blood flow compatible with brain death. Almost simultaneously, remote relatives were contacted who agreed support should be terminated. This was done and the patient expired.

Conclusions

This interesting case taught us two clinical lessons. First, the importance of recognizing that certain medical illnesses, like severe hypothyroidism, prevent diagnosing death by neurological criteria, even when the three cardinal neurological features exist. Second, a hopeless prognosis may still allow for withdrawal of care but only when a surrogate can participate in clinical decisions and agree with the proposal.

Brain death is defined as the irreversible cessation of function of the entire brain with three specific criteria: 1) coma, 2) absent brainstem reflexes and 3) apnea. In addition to these clinical criteria, there are important prerequisites: 1) no drug intoxication or poisoning, 2) core temperature greater than 32 degrees Celsius, 3) clinical or neuroimaging evidence of acute central nervous system catastrophe and 4) absence of confounding medical conditions such as severe electrolyte, acid-base, or endocrine disturbances [5].

Our patient had a severe hypoxic-ischemic injury supported by the abnormal head CT. While she satisfied the cardinal neurological aspects for diagnosing brain death, the laboratory evidence indicated the presence of a confounding medical illness, thus precluding satisfaction of the necessary brain death prerequisites. Her profound hypothyroidism had a major impact on our clinical and ethical decisions.

The role hypothyroidism played in her clinical state may be debatable. We considered whether the elevated TSH might have simply "leaked" from an ischemic pituitary gland but TSH levels are not usually increased in brain dead patients [6]. Additionally, the patient was awake prior to her collapse and not overtly impaired until after her cardiac arrest suggesting against a substantial contribution from hypothyroidism. With the severe structural brain damage from her hypoxic-ischemic event, we recognized she had little chance of meaningful recovery [7]. Her poor prognosis, therefore, was seemingly unrelated to hypothyroidism. However, life-threatening hypothyroidism can manifest as hypothermia and depressed neurological function, in essence exaggerating neurological impairment. We, therefore, felt unable to meet the strict exclusionary aspects to diagnose death by neurological criteria.

Our reluctance to declare brain death due to hypothyroidism led us to assess cerebral perfusion with a Techne-

tium radionuclide scan. Confirmatory tests are optional in most countries, including the United States [8,9]. In the United Kingdom, the concept of brainstem death precludes examination of the cortex and subcortex with EEG and other ancillary tests [10]. Confirmatory testing is most commonly needed when specific neurological evaluations cannot be performed, (e.g., orbital trauma may frustrate attempts to evaluate pupillary function or hypotension may preclude an adequate apnea test). Generally accepted confirmatory tests include electroencephalography (EEG) or a conventional angiogram [5], although standardized guidelines have not been published. In the intensive care unit it is often difficult to perform an EEG of sufficient sensitivity due to the presence of artifact, while the invasive nature of an angiogram can be limiting. Alternatively, the American Academy of Neurology has accepted the use of Doppler ultrasound after a comprehensive review of its utility indicated it was 94% sensitive and 100% specific in the diagnosis of brain death [11]. Less evidence exists to support the use of other miscellaneous tests including brain perfusion studies, such as the one we utilized, although the sensitivity of the technetium radionuclide scans has been reported to be 94% with a specificity of 100% [12].

The family's decision to withdraw care removed the burden of applying the results of the perfusion scan. We think, however, that lacking family input, the absent cerebral blood flow would have persuaded us to diagnose brain death.

This clinical interaction demonstrates some of the medical and ethical challenges in the diagnosis of brain death. Brain death is synonymous with death and not a prognostication of future outcome. While a patient's prognosis plays an important role in decisions about withdrawal of care, prognosis does not play a role in the medico-legal realm of declaring brain death. In the setting of a poor prognosis, a capable surrogate can support a plan to terminate care for futility even when the brain death diagnosis is thwarted. Clinicians should not allow a dismal prognosis to introduce bias into declaring brain death but should strictly adhere to the clear medicolegal criteria.

Competing interests
None declared.

Authors' contributions
JMB drafted the manuscript. ISL revised the manuscript and conceived the project.

Acknowledgements
The authors appreciate valuable input from Dr. Myla D. Goldman.

References
1. **Ad hoc committee of the Harvard medical school to examine the definition of brain death. A definition of irreversible coma.** *JAMA* 1968, **205:**337-340
2. Molinari GF: **Review of clinical criteria of brain death.** *Ann NY Acad Sci* 1978, **315:**62-69
3. **Guidelines for the determination of death: report of the medical consultants on the diagnosis of death to the president's commission for the study of ethical problems in medicine and biomedical and behavioral research.** *JAMA* 1981, **246:**2184-2186
4. **Report of the quality standards subcommittee of the American Academy of Neurology. Practice parameter for the determination of brain death in adults (summary statement).** *Neurology* 1995, **45:**1012-1014
5. Wijdicks EFM: **Determining Brain Death in Adults.** *Neurology* 1995, **45:**1003-1011
6. Howlett TA, Keogh AM, Perry L, Touzel R, Rees LH: **Anterior and posterior pituitary function in brain-stem-dead donors: a possible role for hormonal replacement therapy.** *Transplantation* 1989, **47:**828-834
7. Levy DE, Caronna JJ, Singer BH, Lapinski RH, Frydman H, Plum F: **Predicting outcome from hypoxic-ischemic coma.** *JAMA* 1985, **253:**1420-1426
8. Wijdicks EFM: **Brain death worldwide: accepted fact but no global consensus in diagnostic criteria.** *Neurology* 2002, **58:**20-25
9. Swash M, Beresford R: **Brain death: still unresolved issues worldwide.** *Neurology* 2002, **58:**9-10
10. Pallis C: **ABC of brain stem death.** *BMJ* 1983, **286:**284-287
11. American Academy of Neurology Therapeutics and Technology Assessment Subcommittee: **Assessment: transcranial doppler.** *Neurology* 1990, **40:**680-681
12. Laurin NR, Driedger AA, Hurwitz GA, Mattar AG, Powe JE, Chamberlain MJ, Zabel PL, Pavlosky WF: **Cerebral perfusion imaging with technetium-99 m HM-PAO in brain death and severe central nervous system injury.** *J Nucl Med* 1989, **30:**1627-1635

Pre-publication history
The pre-publication history for this paper can be accessed here:

http://www.biomedcentral.com/1471-2377/2/5/prepub