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Reversible Brain Death: failure of test or technique?

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Case reports of reversible brain death

- Clarifications
 - Brain death cannot be 'reversible'
 - The issue therefore is 'misdiagnosis'
- The Facts
 - 3 patients satisfied clinical criteria for brain stem death, subsequently regained some reflexes before death
- Explanation and Interpretation
 - What were the causes? Should we be concerned?
- Implications
 - How we should respond
- Conclusions

Reversible brain death after cardiopulmonary arrest and induced hypothermia*

Adam C. Webb, MD; Owen B. Samuels, MD

Objective: To describe a patient with transient reversal of findings of brain death after cardiopulmonary arrest and attempted therapeutic hypothermia.

Design: Case report.

Conclusions: We strongly recommend caution in the determination of brain death after cardiac arrest when induced hypothermia is used. Confirmatory testing should be considered and a minimum observation period after rewarming before brain death testing ensues should be established. (Crit Care Med 2011; 39: 1538–1542)

Can J Anesth/J Can Anesth (2010) 57:927–935
DOI 10.1007/s12630-010-9359-4

CASE REPORTS/CASE SERIES

Conclusion *For both patients, several unrecognized confounding factors for NDD were present. These cases illustrate the difficulties encountered by experienced clinicians in determining brain death using clinical criteria alone, and they suggest that more routine use of ancillary brain blood flow analyses should be recommended.*

Should ancillary brain blood flow analyses play a larger role in the neurological determination of death?

Les analyses secondaires du débit sanguin cérébral devraient-elles jouer un rôle plus important dans le diagnostic neurologique?

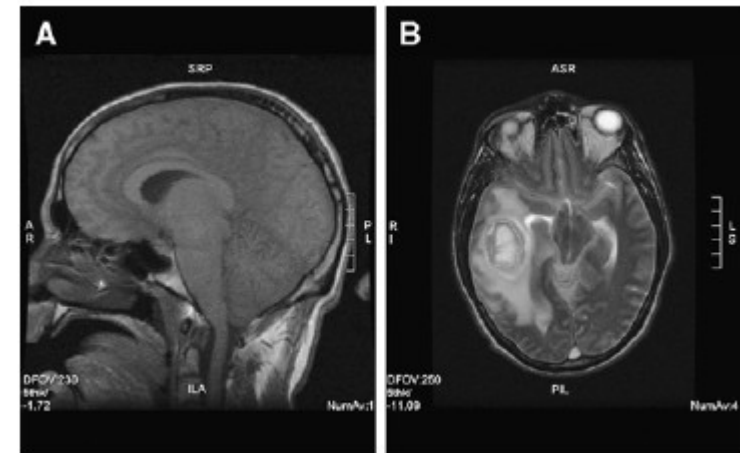
Derek J. Roberts, MD • Kate A. M. MacCulloch, MD •
Eric J. Versnick, MD • Richard L. Hall, MD

Abstract

Purpose *We present two patients who regained spontaneous respiration following clinical neurological determination of death (NDD) while ancillary radiological imaging demonstrated brain blood flow.*

Partial recovery of brain stem reflexes after BSD testing			
Clinical details	Case 1	Case 2	Case 3
Ref	CCM 2011;39:1538	CJA 2010;57:927	
Gender	M	M	
Age	55	26	
Main cerebral insult	Severe asthma. Resp & cardiac arrest in ED. 20 mins CPR.	Mastoiditis, Temporal lobe abscess, E Coli	
Investigations	CT cerebral oedema	CT scan MRI: some blood flow	
Hypothermia	< 35°C from 46 h to 56 h	None: 36.5°C	
Drugs	Propofol, fentanyl 14 h – 50 h	Dexamethasone, ABs	
Progress	Resps & cough reflex 56 hrs, absent at 72h	GCS = 3. Resps & reflexes absent	
Insult-1 st test interval	72 h	7 h	
Adjunctive tests for BSD diagnosis	EEG flat, but artefact from myoclonic jerking pre-1 st tests	None	
2 nd test	78h	None	
Insult-reflex recovery	98 h	35 h (28 post-BSD)	
Reflexes recovered	Cough, respiration, corneals	Respiration	
Concurrent events	Methylpred 1Gm; optimisation, prep for organ harvesting	Organ resuscitation pre-donation	
Further tests	EEG flat (106 h)	NMR brain blood flow	
Clinical progress	Loss of all reflexes at 145 h	Vent support maintained	
Subsequent adjunctive tests	SSEP P17 & N20 absent NMR: herniation; CBF absent	Repeat MRI - herniation	
Outcome	Ventilation discontinued	Apnoea at 5 days	
Recommendation	Caution in hypothermia	Adjunctive tests of CBF rec	

MRI revealed the temporal lobe abscess with associated uncal and tonsillar herniation, descent and deformation of the brainstem, effacement of the basal cisterns, and generalized cerebral edema (Fig. 2A-B). Surprisingly, however, brain blood flow was present (Fig. 2B-D).



Technetium 99 m-DTPA cerebral radionuclide angiogram

Organ resuscitation, as described above (see Case 1), was initiated.¹⁰ Given our experience with the first case (including family request after discussion) and in accordance with Canadian Forum guidelines,⁵ a cerebral radionuclide angiogram was performed as radiological confirmation of brain death and, surprisingly, intracranial arterial flow was visualized (Fig. 5).

Authors' conclusions

CCM 2011;39:1538

- Cautious approach when determining brain death after cardiac arrest when hypothermia is used
- A period of observation after rewarming to normothermia should be observed
- (New guidelines recommending) a single set of BS & apnoea tests may be insufficient

CJA 2010;57:927

- 'As the state of brain death can only be guaranteed by the persistent absence of brain blood flow, it leads us to recommend the requirement for validated ancillary radiological studies in the routine declaration of neurological death'.

Agree?

Hypothermia and brain death

- May confound prognostic indicators
- Neuronal protection slow to emerge
- Requirement for sedation
- Delayed clearance of sedatives & metabolites
- Delay in resolution of cerebral oedema
- Recalibration of electrophysiological and metabolic markers of injury

Hypothermia and brain death

American Academy of Neurology predictors of poor outcome following cardiac arrest resuscitation (Neurology 2006; 67: 203-10):

- Absent pupillary or corneal reflexes at Day 3
- Absent or extensor motor responses at Day 3
- Absent N20 responses on SSEPs Days 1 to 3
- Serum neuron-specific enolase (NSE) > 33 ng/ml at Days 1 to 3
- Myoclonus status epilepticus within 24 hours

– *‘If therapeutic hypothermia becomes standard of care, these predictors may need revision’*

Hypothermia and brain stem testing: UK guidance

- Current AoMRC guidance is $>34^{\circ}\text{C}$, but no duration or interval specified

Predictors of neurologic outcome in hypothermia after cardiac arrest

Fugate JE et al. Ann Neurol 2010; 68(6): 907-14

- 192 patients after successful CPR
- 103 hypothermic, 89 normothermic
- **Confirmed** absent brainstem reflexes, absent motor response, myoclonus, and bilateral absence of N20 SSEP at day 3 as adverse prognostic indicators
- **Neurone-specific enolase** >33ng/ml had false-positive rate of 29.3%
- **Sedative agents** confounded clinical exam: 3 survivors had initially absent motor responses

Does hypothermia influence the predictive value of bilateral absent **N20** after cardiac arrest?

Leithner C. Neurology. 2010 Mar 23;74(12):965-9.

- 185 CPR survivors receiving therapeutic hypothermia.
- 112 patients had SSEPs after 24 hrs
 - 36 patients had bilateral absent N20 SSEPs
 - **2 recovered consciousness and survived**

Studies recommending delaying irreversible management decisions in therapeutic hypothermia

- Samaniego EA, Persoon S, Wijman CA. Prognosis after cardiac arrest and hypothermia: a new paradigm. *Curr Neurol Neurosci Rep* 2011; 11(1): 111-9.
- Oddo M, Rossetti AO. Predicting neurological outcome after cardiac arrest. *Curr Opin Crit Care*. 2011 Jun;17(3):254-9
- Blondin NA, Greer DM. Neurologic prognosis in cardiac arrest patients treated with therapeutic hypothermia. *Neurologist*. 2011 Sep;17(5):241-8.

Cerebral blood flow

The presence of cerebral blood flow does not indicate a live brain

Intensive Care Med (2007) 33:2129–2135
DOI 10.1007/s00134-007-0789-6

ORIGINAL

Christophe Quesnel
Jean-Pierre Fulgencio
Christophe Adrie
Béatrice Marro
Laurent Payen
Nadège Lambert
Sonia El Metaoua
Francis Bonnet

Limitations of computed tomographic angiography in the diagnosis of brain death

PRACTICAL PEARL

False Positive CT Angiography in Brain Death

David M. Greer · Dorothea Strozyk ·
Lee H. Schwamm



neurocritical
care
society Neurocrit Care (2009) 11:261–271
DOI 10.1007/s12028-009-9243-7

ORIGINAL ARTICLE

Diagnosing Brain Death by CT Perfusion and Multislice CT Angiography

Dolores Escudero · Jesús Otero · Lara Marqués · Diego Parra ·

Radionuclide angiography as a confirmatory test for brain death: a review of 229 studies in 219 patients.

METHODS: Flowers WM, Patel BR. South Med J 1997;90(11): 1091-6.

Retrospective review of 229 RA procedures done in 219 patients.

RESULTS: *required replotting as below*

206 patients had interpretable studies + clinical criteria for brain death

10 patients did not meet the clinical criteria

10 patients had repeated studies

CONCLUSIONS: Radionuclide angiography is a sensitive confirmatory test of brain death. The study does not evaluate the posterior fossa circulation, and an occasional patient may have residual brain stem function. The examination is most reliable when the patient is in a deep coma, has no brain stem reflexes, and has failed an apnoea test.

	Brain stem reflexes absent	Brain stem reflexes present	T	Predictive value of CBF
CBF absent	191	12	203	PPV = 0.94 if CBF absent
CBF present	5	5	10	NPV = 0.5 if CBF present
Total	196	17	213	Overall correct classification = 196/213 = 0.92
	Sensitivity = 0.97	Specificity = 0.29		

Brain blood flow in the neurological determination of death: Canadian expert report.

Shemie SD et al & Canadian CCS. Can J Neurol Sci 2008;35(2): 140-5

- Ancillary testing to demonstrate absent brain blood flow:
 - Radionuclide angiography or CT angiography
 - 4-vessel angiography
 - Magnetic resonance angiography
 - Xenon CT
- Acknowledging the existing limitations in this field, further research validating current or evolving techniques of brain blood flow imaging are recommended

Summary: 'Reversible' Brain Death: failure of test or technique?

Mainly technique failure

- Hypothermia and sedative agents
- Optimisation likely improved brain stem perfusion in all three cases
- Very short interval between insult and testing in cases 2 & 3

Partly test failure

- Test reliability depends on test conditions
- Adjunctive tests have failure rates

Conclusions

- **Distinguish diagnosis of death from consequences** of diagnosing death: fiduciary duty is to patient, then family, then society
- **Hypothermia** reversal: needs review
- **Apply 'donor optimisation' techniques** before brain stem testing to ensure optimal environment for accurate testing
- **Timing of tests**: hasty decisions may well be bad ones.
 - Need for repeat testing unknown
 - Pre-testing optimisation process would 'buy time'
- **Adjunctive tests**:
 - All have a failure rate
 - Cortical blood flow could be preserved despite irretrievable destruction of the brain stem
 - Introducing adjunctive tests renders insecure all previous clinical diagnoses of BSD