REVIEW ARTICLE

DECLARATION OF BRAIN DEATH: A DIAGNOSTIC DILEMMA: NUCLEAR MEDICINE PERSPECTIVE.

Maseeh uz Zaman, Riffat Hussain, Zaffar Sajjad, Mansoor Naqvi, Khalil Khan, Gufran Khan

Department of Radiology, Aga Khan University Hospital, Karachi, Pakistan.

PJR July - September 2008; 18(3): 87-91

Introduction

The widespread use of mechanical ventilators that prevent respiratory arrest can maintain vital functions artificially after the brain has ceased to function. There has been a general consensus among medical community and members of clergy, and laypeople that a person is dead when his or her brain is dead. But in some part of world including some Islamic countries, cessation of cardiac function is considered the usual criterion for declaration of death.[1] This is despite the acceptance of brain death by majority of Islamic jurists in their meeting held in Jordan, in 1986.[2] This is responsible for continued futile treatment, consequently slowing down and hindering the procurement of vital organs for transplantation.

Criteria for Brain Death

There is clear difference between severe brain damage and brain death.[3] Furthermore, misdiagnosis of brain death is possible if a locked-in syndrome (damage of base of pons),[4] hypothermia[5] or drug intoxication[6] is present. The physician must understand this difference, because brain death means that life support is useless, and brain death is s the principal requisite for organ donation.

Term irreversible coma or *coma de'spasse'* was introduced by Mollaret and Goulon[7] in 1959, in comatose patients who had lost consciousness, brain stem reflexes, and respiration and whose electroencephalograms (EEG) were flat. Mohandas and Chou[8] in 1971 described damage to brain stem as a critical component of severe brain damage. This was endorsed by Conference of Medical Royal Colleges in UK[9] in 1976 as brain death was defined as complete, irreversible loss of brain stem functions.

Correspondence : Dr. Maseeh uz Zaman
Department of Radiology,
Aga Khan University Hospital,
Stadium Road, P.O Box 3500, Karachi, 74800
Pakistan. Tel. No. 4930051- Ext 2020
E-mail: maseeh.uzzaman@aku.edu

Protocols for Determination of Brain Death

The guidelines published by American Academy of Neurology in 1995 addressed the tools of clinical examination and validity of confirmatory test and provided a practical description of apnea testing.[10] However, clinical neurological examination remains the standard for the determination of brain death in most of the countries around the globe. But it is very important that clinical examination must be performed with precision by a person who knows legal, ethical and medical aspect of brain death.[11] The paradigm must also include ascertainment of irreversibility, the resolution of any misleading clinical neurological signs, recognition of confounding factors, interpretation of findings on neuroimgaing , and the performance of any confirmatory laboratory test that are deemed necessary.

Confirmatory Tests for Brain Death

The most controversial issue related to determination of death is the occurrence of clinical signs that suggest some retention of brain function.[12,13] Spontaneous body (motor) movements may be observed during apnea testing, while body is being prepared for transport, at the time of surgical retrieval of organs, or in synchrony with respiration produced by mechanical ventilator.[14] These body movements are generated by spinal cord and evidence of brain death in such cases requires documentation by confirmatory tests.

Confirmatory tests for determination of brain death include cerebral angiography, EEG, Brainstem Auditory Evoke Response (BAER) and Somatosensory Evoke Potential (SSEP), transcranial doppler ultrasound and radionuclide brain perfusion imaging. In United States, bed side tests seem to be preferred by the physicians, optional in adults but recommended in children <1 year by American Academy of Pediatrics Task Force on Brain Death in Children.[15] While in Sweden and some other countries only cerebral angiography is required by law.

a. Cerebral Angiography: It's an invasive procedure and performed in catheterization laboratory. It is performed with an injection in the aortic arch (under high pressure) to visualize anterior and posterior circulation. Arrest of flow at the petrosal segment of carotid artery in anterior circulation and at foramen magnum in posterior circulation with no intracerebral filling is considered the diagnostic feature of brain death.[16] (Fig. 1). Furthermore, contrast material from angiography can damage organs that might be harvested.[17]

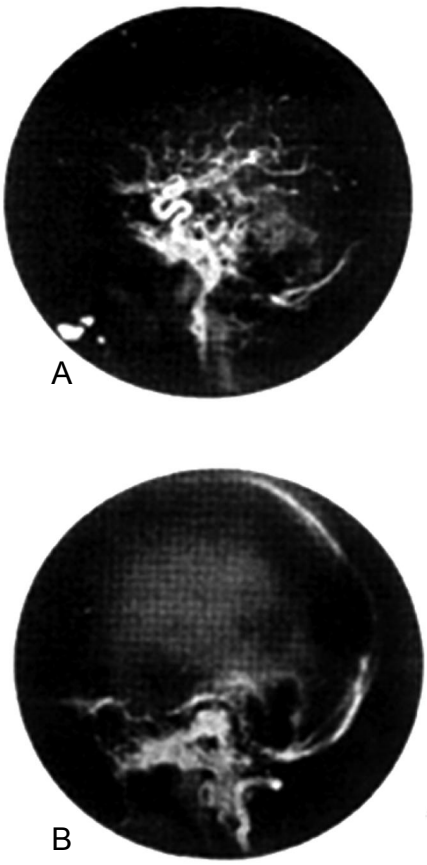

Figure 1: Conventional Cerebral angiography (A) Normal study (B) No flow in brain death.

b. Electroencephalogram (EEG): Most commonly used confirmatory test because of its easy availability and can be conducted at bed side. It should be performed with at least 8 scalp electrodes with an inter-electrode distance of at least 10 cm and recording should be obtained for at least 30 minutes. An absent electrical activity at level higher than 2 μV (instrument set a sensitivity of 2μV/mm) is the diagnostic criterion of brain death[18] (Fig. 2). However, EEG alone is not an ideal confirmatory test because it may be isoelectric while brainstem is still functioning.

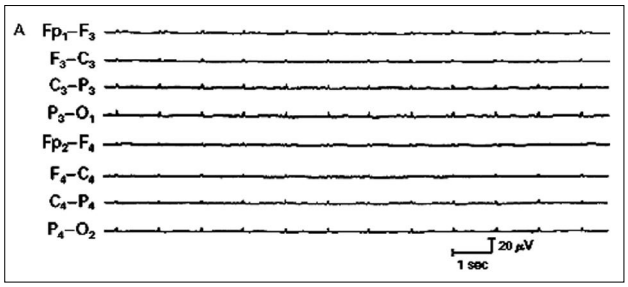

Figure 2: Isoelectric EEG in a patient with brain death.

c. Brainstem Auditory Evoke Response (BAER) and Somatosensory Evoke Potential (SSEP): These tests assess brainstem electrical activity while EEG measures hemispheric activity. Loss of activity is an indicator of loss of brain stem function (Fig. 3). These are less sensitive to metabolic or toxic suppression; however, they sample only a small component of brain function in restricted sensory pathways.[19]

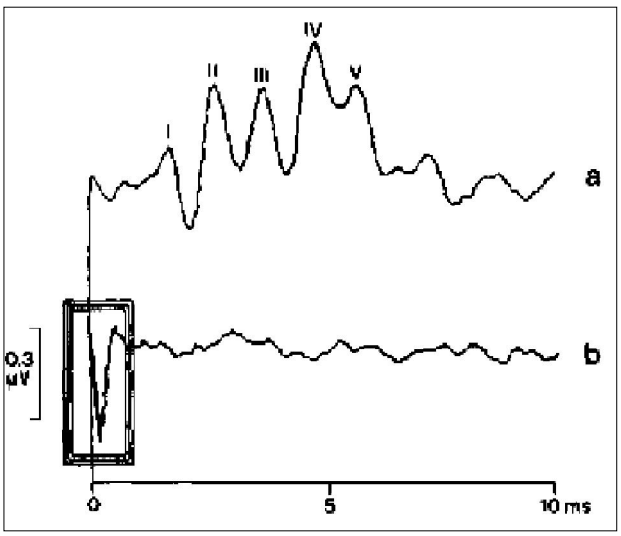

Figure 3: Brainstem Auditory Evoke Response (BAER) in (a) normal adult and (b) brain death.

d. Transcranial Doppler Ultrasonography: Performed with a portable 2 –Hz doppler probe which should be placed at the temporal bone above the zygomatic arch (middle cerebral arteries) or vertebrobasilar arteries through the suboccipital trasncranial window.[20] Criteria of brain death are absence of diastolic or reverberating flow and small systolic peaks in early systole. But absence of a signal may be artifactual if a bone window interferes with isonation.

e. Radionuclide Brain Perfusion Scan: This is useful because of its specificity and availability and because it can be performed at patient's bedside by using a bedside gamma camera. Furthermore, injected contrast does not damage the organs which might be harvested.

Two types of radiopharmaceuticals are used for brain flow studies; (1) Non-diffusible tracer like Tc-99m Diethylene Triamine Pentacetic Acid (Tc-99m DTPA), and (2) Diffusible, lipophilic like Tc-99m –hexamethylepropylene amine oxime (HMPAO) or ethyl cysteinate dimer (Tc-99m ECD). Although diffusible tracers like HMPAO and ECD are increasing popularity, there is no clear evidence that they are more accurate than non-diffusible agent like Tc-99m DTPA.[21]

These tracers are injected intravenously as a bolus (Tc-99m DTPA 15-20 mCi, Tc-99m HMPAO and ECD 10-30 mCi) and dynamic (flow) images (1-3 second per frame) are acquired for 1 minute under a digital gamma camera (preferably dual or triple heads) with low energy and high resolution (LEHR) collimator in anterior and posterior projection (with multi-detectors system). This is followed by acquisition of anterior, posterior and lateral planar images (immediately after dynamic study for Tc-99m DTPA but after 20 min for HMPAO and ECD) and also SPECT images (Single Photon Emission Computerized Tomography) in case of HMPAO or ECD. In most of cases, dynamic (flow) and planar images are sufficient and SPECT images are rarely required, although SPECT allows better visualization of perfusion to posterior fossa and brain stem structures.

In normal individual flow images shows blush due to both middle and anterior cerebral arteries with appearance of circle of Willis as well. In addition, blush over scalp is also seen due to patent external carotid arteries. Planar images show appearance of tracer in superior sagittal and transverse sinuses (Tc-99m DTPA) while HMPAO and ECD shows uptake over both hemispheres.

In brain death, no flow is seen in middle, anterior and posterior cerebral arteries resulting in "Hollow Skull Sign"[22] (Fig. 4 and 5). This cessation of internal carotid artery flow at siphon is due to increased intracranial pressure, and not to intraluminal obstruction (Brain Tamponade)[23] However, some flow to scalp is present due to patent external carotid arteries and should not be mistaken for brain flow.

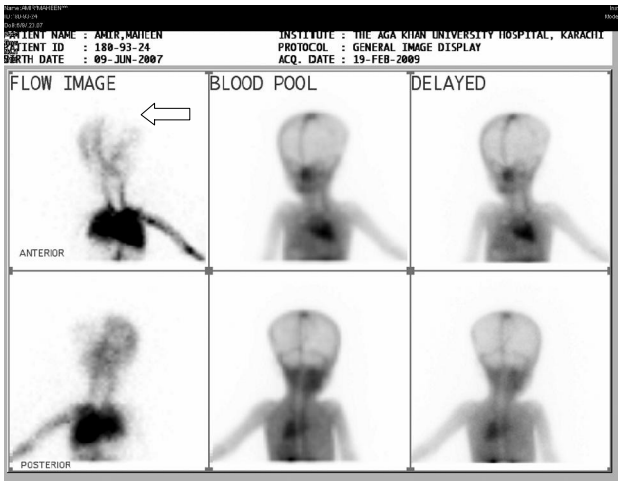

Figure 4: Planar dynamic and static Tc-99m DTPA scan in a patient with suspected brain death showing intact flow in carotids bilaterally, markedly reduced arterial blush over left hemisphere (arrow) due to an extensive infarct. Normal blush is seen over right hemisphere with normal activity in sagittal and transverse venous sinuses.

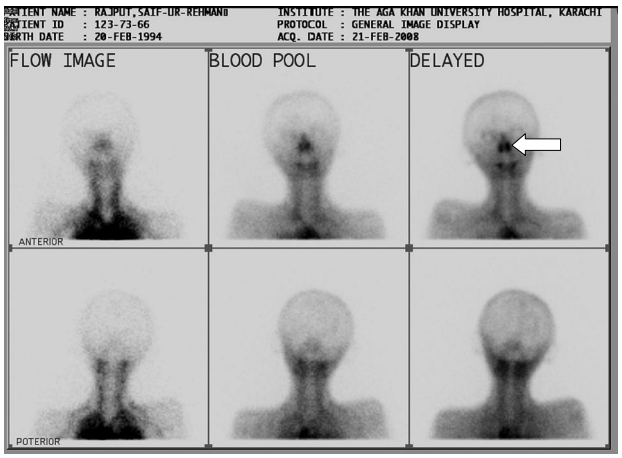

Figure 5: Planar dynamic and static Tc-99m DTPA scan in a patient with brain death showing intact flow in carotids bilaterally with no intracranial arterial or venous flow and no tracer in venous sinuses (Hollow Skull Sign). There is also evidence of increased blood pool activity over nasal region, i.e. Hot Nose Sign (arrow).

Planar and SPECT images are characterized by absence of activity in superior sagittal sinus (Tc-99m DTPA) and brain substance (ECD and HMPAO). However, low level of superior sagittal activity with no intracerebral flow on dynamic images is not uncommon. One possible explanation for this phenomenon is filling of intracranial venous sinuses through emissary veins via the external carotid circulation, despite "non-filling" of cerebral arteries.[24] Secondly, the increased scintigraphic activity in the region of the sagittal sinus may not be tracer activity within the sinus itself, but rather the activity within the circulation of the vascular network of the dura and falx.[25] For ECD and HMPAO, no tracer uptake might be due to improper preparation or instability of radiopharmaceutical, therefore, these images should always be read with flow images.[21]

Another finding that may be seen in brain death is enhanced blood pool activity in the nasal region and this is called "Hot Nose Sign"[26] (Fig. 5). It is due to increased in collateral blood flow from the external carotid artery through the facial and opthalamic arteries. It is seen in 52% of patients with brain death[27] and can also be present whenever diminished blood flow in one or both internal carotid arteries results in increased external carotid flow.[28]

Conclusion

Declaration of brain death for comatose patient is neither easy nor straightforward. But delay in its declaration result in continued futile mechanical support and hindrance in procurement of vital organs for donation. Various bed side clinical neurophysiological examination, electrophysiological tests and imaging options like contrast angiography, and transcranial doppler ultrasound are recommended by various authorities to confirm brain death. However, these tests are time consuming and needs expertise. But radionuclide brain perfusion studies are simple, sensitive, specific and reliable tool to confirm brain death with a high level of confidence.

References

1. S Al-Shammri, M Al-Feeli. Confirmation of Brain Death Using Brain Radionuclide Perfusion imaging technique. Med Princ Pract 2004; **13:**267-72.

2. Darr As, Al KhitmayAB. Bioethics for clinicians. 21. Islamic Bioethics. CMAJ 2001;**164:**60-3.

3. Wijdicks EF. Determining brain death in adults. Neurology 1995;**45:**1003-11.

4. Patterson JR, Grabois M. Locked-in syndrome: a review of 139 cases. Stroke 1986; **17:**758-64.

5. Danzl DF, Pozos RS. Accidental hypothermia. N Engl J Med 1994; **331:**1756-60.

6. Goldfrank LR, Flomenbaum NE, Lewin NA, Weisman RS, Howland MA, Hoffman Rs, eds. Goldfrank's toxicologic emergencises. 6th ed. Stanmford , Conn.: Appleton and Lange, 1998.

7. Mollaret P, Goulton M. Le coma depasse (memoire prelimnarie). Rev Neurol (Paris) 1959;**101:**3-5.

8. Mohandas A, Chou SN. Brain death: a a clinical and pathological study. J Neurosurg 1971;**35:** 211-8.

9. Diagnosis of Brain Death: statement issued by honorary secretary the Conference of Medical Royal Colleges and their Faculties inn United Kingdom on 11 October 1976. BMJ 1976;**2:** 1187-8.

10. The Quality Standards Subcommittee of the American Academy of Neurology. Practice parameters for determining brain death in adults (summary statement). Neurology 1995;**45:**1012-4.

11. Van Norman GA. A matter of life and death: what every anesthesiologist should know about the medical, legal, and ethical aspects of declaring brain death. Anesthesiology 1999;**91:**275-87.

12. Ropper AH. Unusual spontaneous movements in brain-dead patients. Neurology 1984;**34:**1089-92.

13. Saposnik G, Bueri JA, Maurino J, Saizar R, Garretto NS. Spontaneous and reflex movements in brain death. Neurology 2000;**54:**221-3

14. Marti-Fabregas J, Lopez-Navidad A, Caballero F, Otermin P. Decerebrate-like posturing with mechanical ventilation in brain death. Neurology 2000;**54:**224-7.

15. American Academy of Pediatrics Task Force on Brain Death in Children. Report of special task force: guidelines for the determination of brain death in children. Pediatrics 1987;**80:**298-300

16. Bradac GB, Simon RS. Angiography in brain death. Neuroradiology 1974;**7:**25-8.

17. Reid RH, Gulenchyn KY, Ballinger JR: Clinical use of technetium-99m HM-PAO for determination of brain death. J Nucl Med 1989; **30:**1621–6.

18. American Electroencephalographic Society. Guideline three: minimum technical standards for EEG recording in suspected cerebral death. J Clin Neurophysiol 1994;**11:**10-3.

19. Young GB, Ropper AH, Bolton CF: Coma and Impaired Consciousness: A Clinical Perspective. New York, McGraw-Hill, 1998, pp 69–71.

20. Petty GW, Mohr JP, Pedley TA, et al. The role of transcranial Doppler in confirming brain death: sensitivity, specificity, and suggestions for performance and interpretation. Neurology 1990; **40:** 300-3.

21. Kevin JD, Kirk AF, Victor HG, Guiliano M, James SN, Bary S. Society of nuclear medicine procedure guideline for brain death scintigraphy. J Nucl Med. 2003;**44:**846–51.

22. Abdel-Dayem HM, Bahar RH, Sigurdsson GH, Sadek S, Olivecrona H, Ali AM. The hollow skull: a sign of brain death in Tc-99m HM-PAO brain scintigraphy. Clin Nucl Med 1989 Dec;**14**(12): 912-6.

23. Vante K, Nakstad P, Lundar T. Digital subtraction angiography (DSA) in the evaluation of brain death. Neuroradiology 1985; **27:**155-7.

24. Hazratji SM, Singh BM, Strobos EJ. Angiography in brain death. NY State J Med 1981; **81:**82-3.

25. Vatne K, Nakstad P, Lanciar T. Digital subtraction angiography (DSA) in the evaluation of brain death. Neuroradiology 1985; **27:**155-7.

26. Amy HH. The Hot Nose Sign. Radiology 2005; **235:**216-7.

27. Mrhac L, Zakko S, Parikh Y. Brain death: the evaluation of semiquantitative parameters and other signs in HMPAO scintigraphy. Nucl Med Commun 1995; **16:**1016–20.

28. Mishkin FS, Dyken ML. Increased early radionuclide activity in the nasopharyngeal area in patients with internal carotid artery obstruction: “hot nose.” Radiology 1970; **96:**77–80.