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Case Report

Brainstem Death Diagnosis Revisited: Lessons from a Case Report

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Abstract

A young male patient was diagnosed as being brain-stem dead following a traumatic brain injury. Despite strict adherence to current guidelines, as the patient approached organ retrieval, the diagnosis was reversed following the observation of spontaneous ventilation by family members. The patient is now discharged from intensive care and following commands. The case lead to a national interim safety alert prior to review by an expert committee. The committee have now updated the relevant guidelines in light of changes in clinical practice making significant adjustments to the process of diagnosing brain stem death in certain traumatised patients. As always, adoption of contemporary guidelines is essential in order to maintain trust in the organ donation programme and the diagnosis of death in brain injured individuals.

Key words: death in brain injured; traumatic brain injury

Introduction

The diagnosis of death using neurological criteria (DNC) is a well-practiced undertaking performed with confidence by the intensive care community within the United Kingdom. Such confidence is clearly of fundamental importance to both patient care, public confidence and to the national organ donation programme. Making the diagnosis of DNC is not always a straightforward process in poly-traumatised casualties as discussed below. Despite these challenges, and pre-existing case reports of the reversal of the diagnosis, [1,2,3], the diagnosis still attracts both public and professional confidence. The current UK guidelines have proven to be largely reliable since their iteration by the Acadamy of Medical Royal Colleges in 2008.[4] Clinical practice in the management of such patients has however evolved in the intervening period and this case illustrates how important guidelines can potentially lead to patient harm if they do not maintain currency against contemporary clinical practice.

Case presentation

A previously healthy young teenage male was struck by a delivery van at approximately 30 mph whilst crossing a road as a pedestrian. He suffered a significant blunt head injury and a small pneumothorax. His on-scene neurology was documented as being Glasgow Coma Score of E1, V1, M3 with a fixed right pupil and a sluggishly reactive left pupil by the pre-hospital medical team. The patient was subsequently intubated, received bilateral thoracostomies, administered 350 ml of hypertonic saline and had a pelvic binder placed. The patient was normotensive with a sinus tachycardia averaging around 130 bpm. On arrival in our Emergency Department one hour following injury, the primary survey revealed a fixed right pupil and a “sluggish” left pupil, hypertension with non-invasive systolic pressures ranging from 160 to 190 mmHg and a heart rate now ranging between 70 to 100 bpm. A further 200 ml of hypertonic saline was administered and a propofol infusion was commenced with bolus doses of Rocuronium administered. The CT traumagram was performed, the initial CT brain demonstrating bilateral intraparenchymal contusions with subarachnoid blood and pneumocephalus. (Fig 1). Bony injuries included multiple calvarial and skull base fractures and a single rib fracture.

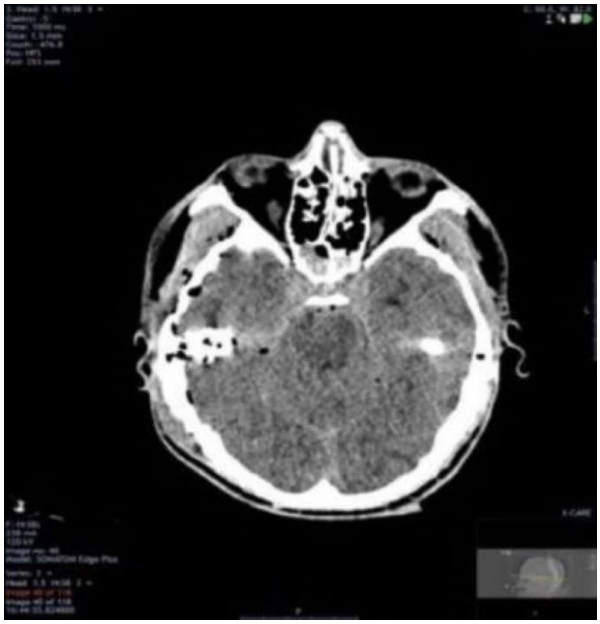

Figure 1

Three hours following injury, the patient was taken to theatre for a right sided decompressive craniectomy and insertion of an intracranial pressure (ICP) measuring bolt. The surgical team noted a pale swollen and non-pulsatile brain at the beginning of the procedure and removed a small haematoma. A total of 375 mg of Thiopentone was administered intra-operatively with a pulsatile brain observed at the end of the procedure. On arrival to ICU post-operativelyapproximately 9 hours after injury, the patient's pupils were both fixed and measured at 4 mm using a pupillometer (NPi-200 Pupillometer, Prospect Diagnostics Ltd, UK). Intracranial pressure was in single figure. Sedation was maintained with a Propofol 1% (25 ml/hr) and Alfentanil infusion (0.5 mg/ml at 10 ml/hr). A midazolam infusion (2 mg/ml at 5 ml/hr) was started the following morning. Despite deep sedation, ICP gradually increased to 25 mmHg resulting in a further CT brain. The patient's second CT brain demonstrating a left extra-axial haematoma and a degree of herniation of brain tissue through the craniectomy defect (Fig 2) Therefore, a further craniotomy was undertaken later on this second day. At surgery, it became apparent that base of skull bleeding was responsible following loss of tamponade after the craniectomy. A swollen herniating brain was noted. During this procedure an EVD was inserted. On return to ICU, the intracranial pressure was noted to be 21 mmHg. CT scan was repeated the next day following left-sided craniotomy and evacuation of extradural haematoma.(Figure 3). As care continued into the third 24-hour period of ICU care, the pupils remained unreactive and there had been no motor response to stimulation, cough or spontaneous breathing activity. After 30 hours of administration, the midazolam infusion was stopped in advance of brain stem death testing. Additionally, having been confirmed as being SARS-CoV-2 negative, the patient was moved from a purple ICU area to a green ICU area under the care of a different medical team. The receiving team noted that the patient was a candidate for brain stem death testing though observed with interest that CT imaging demonstrated space around the brain stem and also noted that the patient's pupils, while not responding to light, were not dilated. Following this move to a new medical team, supportive care was continued without change for a further 24 hours to facilitate becoming familiar with the patient. On day 4 of ICU care, the patient's neurology had not changed. Desmopressin was administered to manage polyuria (paired osmolarities did not support the diagnosis of diabetes insipidus) and a significant vasopressor requirement had developed. In the absence of any evidence of a source of sepsis, it was assumed that this vasopressor requirement was a manifestation of evolving brain stem death pathophysiology. The remaining sedative agents were stopped at midday. On day 5 of the patient's ICU stay, the nursing team confirmed that the patient's neurological examination was consistent with that of brain-stem death. The medical team did not question this further and were therefore unaware that the patient's pupils were documented as having both enlarged from 3 to 4 mm at 8 am.With the assistance of a specialist nurse in organ donation (SN-OD), clinical brain stem death testing was agreed and planned for midday, 24 hours after stopping Propofol and Alfentanil and 48 hours after stopping Midazolam. Brain-stem death testing was undertaken in accordance with the Academy of Medical Royal Colleges code of practice and using the ICS/FICM endorsed documentation [Annex A, A1]. The patient's biochemistry, temperature and bedside monitoring values were all comfortably within the defined ranges for testing. Hepatic and renal function werenormal. The bedside nurse, nurse-in-charge and SN-OD attended the first set of tests. The ICS/FICM endorsed form for the diagnosis of death using neurological criteria was used and testing was completed as directed including 2 apnoea tests. The patient unequivocally met in full the criteria for BSD. The pre and post $PaCO_2$ values were 6.54 kPa and 10.5 kPa followed by 7.89 kPa and 11.5 kPa for each test. After explaining this to the family, the second set of testing (including a repeat of the apnoea test) was undertaken 30 minutes later with the next of kin also at the bedside to witness the tests. The results matched the first set of tests. While the next of kin debated the prospect of organ donation, the local coroner was informed of the patient's death and permission for organ donation sought should this be the wishes of the family. After a period of debate, the patient's extensive family agreed to organ donation. One gram of Methylprednisolone was administered 00:30 following an earlier request from the SNOD. All other care remained the same. An hour or so later, the vasopressor requirement quickly dissipated in conjunction with a further significant diuresis. Between 02:00 and 03:00, family members became increasingly concerned that the patient was making spontaneous breathing efforts. Nursing staff initially reassured the family that this was not uncommon and represented some combination of a hyper-dynamic cardiovascular system, water in the breathing circuit or reverse triggering of the ventilator. Family concerns persisted and the matterwas referred to the doctor covering the unit.

Following examination of the patient, the on-call doctor relayed the families concerns to the on-call consultant. The consultant concerned requested that the doctor again reassure the family and explain the phenomenon of "reverse triggering" of the ventilator. Subsequently, the on-call doctor re-contacted the covering consultant explaining that they were of the opinion that the patient was indeed spontaneously breathing and that additionally a pupillometer was now demonstrating reactive pupils. The on-call consultant attended the patient's bed space and confirmed these findings.

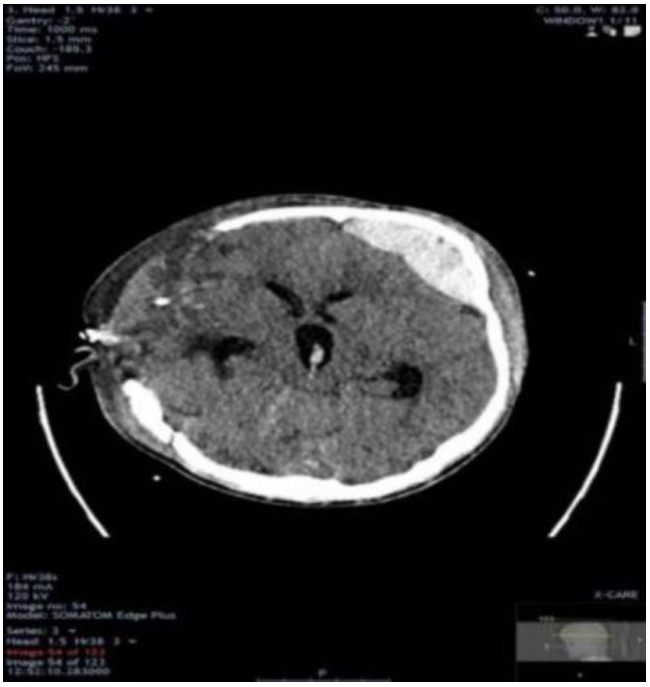

Figure 2

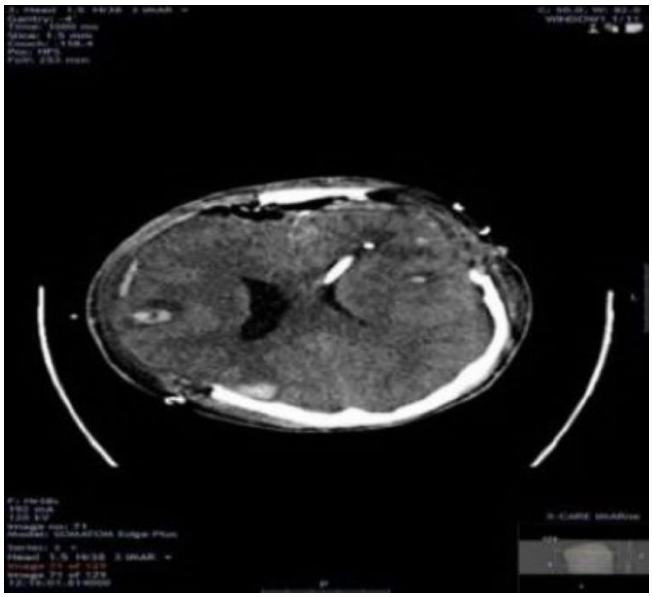

Figure 3

Outcome and follow up

A family meeting was quickly organised in which the consultant concerned explained that a mistake had been made, apologised for this and confirmed that the patient was for full active management, for resuscitation and the organ donation process abandoned. During this meeting, the medical staff also explained that the reversal of this diagnosis would be investigated and referred to national subject matter experts. An MRI brain perfusion scan undertaken 48 hours after the reversal of the diagnosis of DNC revealed a globally perfused brain stem. A "duty of candour" letter was forwarded to the family and we agreed that our intensive care unit will keep the family informed regarding the outcome of the external review of the case that we will instigate. The patient at the time of examination had a Glasgow Coma Score of 11T, was following commands, interacting positively with medical staff and has undergone a reconstructive cranioplasty. The case was immediately referred to the national clinical leads for deceased organ donation and authors of the current guidelines. Reflecting on the case internally, we have identified fixed mental models and interruptions in continuity of care as areas of concern in this patient's care pathway. We have also agreed that two intensive care consultants must agree that the pre-conditions for testing are met and that in the context of decompressive craniectomy, testing must be preceded by 4 vessel cerebral angiography. The

role of the midazolam infusion was also considered but discounted as being causative due to the adequate time for clearance to have occurred (half-life of approximately 1.8 hours). An interim safety alert was issued and an expert committee convened at the direction of the Intensive Care Society to examine the case and make appropriate recommendations. This committee have now concluded that decompressive craniectomy be added as a red flag condition for clinicians working in neurosurgical centres. [5],[6] Red flag conditions detail circumstances in which the diagnosis of DNC has had to be reversed, as mentioned above, and so require increased diagnostic caution and consideration of ancillary investigation. They include allowing a minimum prescribed amount of time after loss of brain-stem reflexes or a hypoxic brain injury before testing (6 and 24 hours respectively), the presence of neuromuscular disorders, the use of prolonged Fentanyl infusions and the presence of cerebral abscess resulting in vasogenic oedema. It is notable that in the three published cases referenced above which have resulted in the identification red flag conditions, all three patients still quickly succumbed to their illness or injury unlike our patient who is making a remarkable recovery. Consensus guidance on ancillary testing is expected to be published in due course.

After an extensive period of rehabilitation, the patient has now been discharged home having made an excellent recovery. They are independent in all activities of daily living, physically active and enjoying playing football in particular.

Discussion

Globally, conceptual and practical approaches to achieving the diagnosis of DNC vary in several ways.[7] The concept of whole brain death rather than brainstem death predominates in Europe and the USA and direction around number of tests required and who is able to undertake testing also varies both between and within countries.

In the UK, human death may be determined by the irreversible loss of the capacity to breathe combined with irreversible loss of the capacity for consciousness.[8] Irreversible cessation of brainstem function produces this clinical state and equates with the death of the individual based on neurological grounds. Where ever it is undertaken, the diagnosis of DNC is a nuanced process aided by firm national guidelines and clear pre-conditions. Clinical acumen is still required however in a number of areas. Clinicians must determine cause or effect when biochemistry deviates from defined pre-conditions, be able to recognise a variety of patient movements as being compatible with DNC and similarly interpret apparent patient interaction with the ventilator. Spontaneous or reflex abnormal movements[9] are common may take a variety of forms including, undulating toe movement,[10] the triple flexion response, the eye opening response and more famously the “Lazarus sign” amongst others.[11] Low frequency respiratory-like movements and reflex triggering of the ventilator, as initially thought to be the case with this patient, are also described following brain-stem death.[12] Reverse triggering of the ventilator is the reflex entrainment of air following every mechanical breath. It is identified by separating the patient from the ventilator as undertaken in this case. Our testing described here would have comfortably met the current guidelines used in the USA leading to the same diagnosis.[13] The same would be true had the guidelines recommended by the World Brain Death Project [14] (a recent attempt to reach international consensus on DNC) been adopted. As discussed above, the current UK guideline does pre-date both the RESCUEicp[15] and DECRA[16] trials following which decompressive craniectomies are now much more readily undertaken. Decompressive craniectomy makes traditional “coning” of the brainstem through the foramen magnum unlikely and may therefore represent a challenge to the existing paradigm of brain-stem death following trauma. The significant recovery of this patient highlights the particular importance of this latest addition to the list of red flag conditions when undertaking brain stem death testing.

Learning points / take home message:

1. Decompressive craniectomy is to be considered as a red flag condition and so requires particularly careful consideration when undertaking brain-stem death testing.
2. Detailed recommendations regarding imaging are available in the UK National guidelines.
3. In this case, next of kin presence during brain-stem death testing facilitated confidence that the testing was done correctly despite subsequent reversal of the diagnosis.

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