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Diagnosing death using neurological criteria in isolated brainstem lesions.

A case report to highlight the issues involved

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Key Words: brain death, brainstem death, ancillary tests, blood flow, organ donation and transplantation. Intensive care

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Abstract

The neurological determination of death in patients with isolated brainstem lesions or by disruption of the posterior cerebral circulation is uncommon and many intensivists may never see such a case in their career. It is also the only major difference between the ‘‘whole brain’’ and ‘‘brain stem’’ formulations for the neurological determination of death. We present a case of a patient with infarction of the structures supplied by the posterior cerebral circulation in whom death was diagnosed using neurological criteria, to illustrate the issues involved. We also suggest that international consensus may be achieved if ancillary tests, such as CTangiography, are made mandatory in this situation to demonstrate loss of blood flow in the anterior cerebral circulation as well the posterior circulation.

Keywords

Brain death, brainstem death, ancillary tests, cerebral blood flow, organ donation and transplantation, intensive care

Introduction

The neurological determination of death (NDD) has been undertaken for close to half a century. In the past, much debate centred around whether the “whole brain” (irreversible loss of all functions of the brain including the brain stem) or the “brainstem” formulations (irreversible loss of functions of the brain stem) was the correct approach to making the diagnosis[1]. In clinical practice both formulations adopt a three-staged approach to the NDD: first, establishing a known cause for the condition; second, excluding confounders and reversible causes for the coma and apnoea, and; third, confirming the absence of all brainstem reflexes, including the capacity to breathe[2]. Continuing to highlight differences between the whole brain and brainstem approaches to NDD is unnecessary since it is now generally accepted that while the two formulations may be semantically different, they are clinically synonymous[3], particularly in jurisdictions like the United Kingdom (UK) and parts of the United States (USA), where ancillary tests are not compulsory to make the diagnosis. However, differences still exist when the coma and apnoea are caused by an isolated brain stem lesion or by a disruption the posterior cerebral circulation. We report such a case to increase awareness of these differences and their possible resolution

Case Report

A 66-year old woman was involved in a high-speed motor vehicle collision and suffered multiple injuries. She was hypotensive at the scene and her Glasgow Coma Score was 6 (E1 V2 M3), She was given intravenous fluid, and underwent a rapid sequence intubation at the scene and then transferred to the regional major trauma centre. There were no episodes of hypoxaemia recorded throughout her resuscitation, and only a single brief episode of hypotension (86/58 mmHg). A whole-body CT scan on admission demonstrated mild global cerebral atrophy but no acute intracranial haemorrhage, collections, mass lesion or acute infarct (Figure 1). The left atlanto-occipital joint was subluxed and there was haemorrhage around the odontoid peg extending tom the foramen magnum, suggesting ligamentous disruption. There was a small left sided haemothorax, fractured right ribs, multiple pulmonary contusions in the right upper lobe,

hepatic and splenic lacerations, and a forearm fracture. There was active bleeding from a truncated mesenteric arterial branch of the distal superior mesenteric artery, and a pneumoperitoneum suggesting perforation of the ascending colon. She underwent continued resuscitation before undergoing an emergency laparotomy and damage limitation surgery during which the bleeding was controlled, and a limited bowel resection performed. Postoperatively, the patient was transferred to the ICU with a laparostomy. On admission to ICU she had reactive pupils, and was kept sedated with propofol 200 mg/hr and alfentanil 1mg/hr. After six hours of rewarming and further stabilisation she returned to theatre for fixation of the forearm fracture and to close the laparostomy. It was planned to undertake an MRI of the cervical spine postoperatively but, at the end of the procedure, the patient's pupils were noted to be fixed and dilated to 7 mm bilaterally. An MRI confirmed cranio-cervical soft tissue and ligamentous disruption. This resulted in traumatic injury to both vertebral arteries and restricted diffusion involving the entire posterior circulation territory bilaterally. There was cerebellar swelling, brainstem compression and coning at the foramen magnum. There were no abnormalities demonstrated in the supratentorial structures supplied by the anterior circulation, suggesting that perfusion was not compromised at this time (Figure 2). MR angiography was limited to a study of the vertebro-basilar system and demonstrated loss of flow in both vertebral arteries and consequent bilateral infarction of all structures supplied by the posterior cerebral circulation. These findings were discussed with the neurosurgeons who felt that there was no surgical option.

The patient returned to ICU and the sedation stopped. It was presumed that the patient had already progressed to brain death and a further 24-h period of continued cardiorespiratory support and stabilisation was planned to exclude the possibility of any confounding factors before undertaking neurological testing. Death was confirmed using neurological criteria 26 hours after stopping all sedation and after the loss of brainstem reflexes was first noted. Two full sets of bed side tests were undertaken including two apnoea tests in accordance with UK criteria[4]. The PaCO2 at the end of the first and second apnoea test was 7.4 kPa and 9.8 kPa, respectively. The potential for organ donation was discussed with her family who confirmed that this would respect

the patient's expressed wishes. Her corneas, kidneys and liver were recovered and transplanted successfully.

An autopsy confirmed thrombotic occlusion of both vertebral arteries and of the basilar artery secondary to ligamentous disruption. Histological examination of cross sections of the cord was normal. Microscopic examination showed patchy acute selective ischaemic neuronal necrosis throughout the brain stem, in both occipital lobes, both basal ganglia particularly the putamen, the cingulate gyri of the corpus callosum and the thalami.

Discussion

An isolated brain stem lesion, or one limited to structures supplied by the posterior cerebral circulation, is an unusual diagnosis as a cause for the NDD, accounting for only 1.9% of all causes in a recent observational study[5]. Data from the potential donor audit (PDA), which records details of every death in each ICU and emergency department, suggest that many intensivists in the UK will never make the diagnosis in these circumstances[6]. The absolute number of patients tested, as well as the proportion of those suspected of meeting the criteria who were actually tested, have both increased slightly over the past 7 years (Table 1) [6]. In 2016 – 2017, death was diagnosed using neurological criteria in 1502 patients[7]. Since each patient is tested twice, UK intensivists undertook a total of 3044 sets of clinical tests. There were 2246 consultants registered with the Faculty of Intensive Care Medicine (FICM) in 2015 (personal communication FICM) meaning that few consultants working outside neuroscience ICUs will diagnose death using neurological criteria more than once a year. The estimated annual number of patients with isolated brain stem lesions being tested in the UK suggests that this will be a rare diagnosis even for intensivists working in a neuroscience ICU (Table 1).

The diagnosis of death in this patient was undertaken in accordance with the latest guidance published by the Academy of Medical Royal Colleges in 2008[4]. This no longer uses the term ''brain stem death'' but, instead, the irreversible loss of brainstem reflexes. In effect it moves towards the NDD being based on the confirmation of irreversible loss of function rather than on an unhelpful anatomical basis that attempts to differentiate between brainstem and whole brain death.

The guidance also does not require ancillary tests routinely to support the diagnosis; specifically, there is no requirement to demonstrate the complete absence of cerebral blood flow. Our patient had a clearly demonstrated cause for irreversible loss of consciousness and apnoea, no confounding or reversible factors, and absent brainstem reflexes. She therefore clearly met all the criteria for the NDD. Caution is, however, advised when diagnosing death using neurological criteria in patients with isolated brain stem or posterior cerebral circulation lesions, and such patients are recognised as a “Red Flag” group in the Faculty of Intensive Care Medicine / Intensive Care Society endorsed forms for making the NDD[8]. To ensure irreversibility, it is prudent to allow more time between loss of the last brainstem reflex and undertaking the clinical testing, as currently occurs in patients with hypoxic brain injury. Hydrocephalus must be actively sought as it may contribute to the coma and apnoea and, if active management is considered appropriate, ventricular drainage should be undertaken before assuming irreversibilty. Finally, time should be allowed for any active therapies to exert an effect, for example steroids prescribed when the primary lesion is a brain stem or posterior fossa tumour, the use of antivirals in suspected brain stem encephalitis, or decompressive craniectomy to reduce pressure in the posterior fossa.

The continued presence of supra-tentorial blood flow in this case may cause concern, but it should be remembered that some preservation of supratentorial blood flow and filling of the cortical branches of the middle cerebral artery is not only seen in isolated brainstem lesions but also in 15%–16% of all patients diagnosed using the NDD irrespective of the underlying cause[9,10]. The increasing availability of investigations that study not only brain structure but also cerebral blood flow, means that, as in this patient, the presence of some blood flow will have been demonstrated primarily to establish the underlying diagnosis, rather than during the performance of an ancillary test to confirm the NDD. Interestingly, a recent observational study identified four cases with posterior fossa lesions who met the criteria for the NDD but retained supratentorial blood flow on an initial CT angiography; this flow was absent on repeat CT angiography in all patients[5]. Furthermore, some investigators question the relevance of persistent perfusion, arguing that opacification of larger supratentorial vessels results from stasis filling, since the loss of flow starts at capillary level[11]. This argument is supported by further work from the same authors

demonstrating non-viable brain on CT perfusion scan despite the presence of flow on CT angiography[12].

Diagnosing death using neurotological criteria in isolated brain stem or posterior circulation lesion remains the main outstanding issue in the “Transatlantic Divide” for the NDD[1], and one of continued debate. In effect, the patient presented in this report could be declared dead in the UK but not in parts of the USA, a situation that can undermine confidence in the NDD within the medical profession and the general public, and one that we believe requires resolution. In 2008, the US President’s Council on Bioethics published an influential but highly disputed and controversial white paper on controversies in the determination of death[13]. Primary brainstem lesions were excluded from the group considered to have ‘‘total brain failure’’ because the condition of the brainstem was not by itself considered to be a reliable indicator of the condition of the higher brain centres. Primary brainstem lesions were excluded from the group considered to have ‘‘total brain failure’’ because the condition of the brainstem was not, by itself, considered to be a reliable indicator of the condition of higher brain centres. The council went further by suggesting that the acceptance of death of the brainstem, rather than of the entire brain, as a sufficient criterion for declaring a patient dead is conceptually suspect and clinically dangerous[13]. Yet, in 98% of cases, the NDD identifies the infratentorial manifestations (brainstem) of a supratentorial (whole brain) diagnosis such as subarachnoid or intraparenchymal haemorrhage, head injury, tumours or hypoxic brain injury. In these circumstances US guidance recommends ancillary tests need only be undertaken where a clinical diagnosis cannot be made[14]. That guidance also recognises the wide variability in the type of test used, and an absence of evidence to determine whether newer ancillary tests accurately confirm the cessation of function of the entire brain[14].

The outstanding question is how to confirm death using neurological criteria to satisfy both the whole death and brainstem death formulations in the presence of an isolated brain stem lesion. It is reassuring that supratentorial cerebral blood flow is lost with time in patients with isolate brain stem lesions[5], and that our patient showed on-going ischaemic necrosis both infratentorially and supratentorial at post mortem examination. Some may therefore argue that

ancillary tests are unnecessary even in this scenario. There are no reported cases of reversible “brainstem” death or “whole brain” death determined using established criteria. However, it seems unlikely that international consensus will be achieved unless death using neurological criteria is not declared in patients with isolated brain stem lesions until absence of cerebral blood flow has been confirmed. Apart from providing further reassurance to all concerned, the time between loss of brainstem reflexes and loss of cerebral blood flow will allow further confirmation of irreversibility.

In summary “brainstem death” is most commonly the infratentorial manifestation of a catastrophic supratentorial, “whole brain”, cerebral pathology. Only an estimated 30 cases per annum in the UK are caused by an isolated brainstem lesion, and many intensivists will not diagnose death in these circumstances in their career. If international consensus is to be achieved, we suggest that anatomical terminology such as “whole brain death” and “brain stem death is abandoned and replaced by terminology such as NDD or the “determination of death using neurological criteria” (DDNC). The three sequential, but interdependent, steps should remain the basis for confirming the clinical diagnosis, and ancillary tests need only be used in cases where confounding factors cannot be excluded. It is accepted that individual jurisdictions may require ancillary testing more widely, and this should be respected. However, all jurisdictions should consider introducing a mandatory requirement to demonstrate the absence of cerebral perfusion before declaring death using neurological criteria in patients with isolated brain stem lesions or posterior cerebral circulation lesions.

Consent

Consent to publication was kindly given by the patient’s relatives.

Declaration of conflicting interests

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Figure 1: CT head scan on admission demonstrating no acute intracranial haemorrhage, collections, mass lesion or acute infarct, and unremarkable CSF spaces and ventricles.

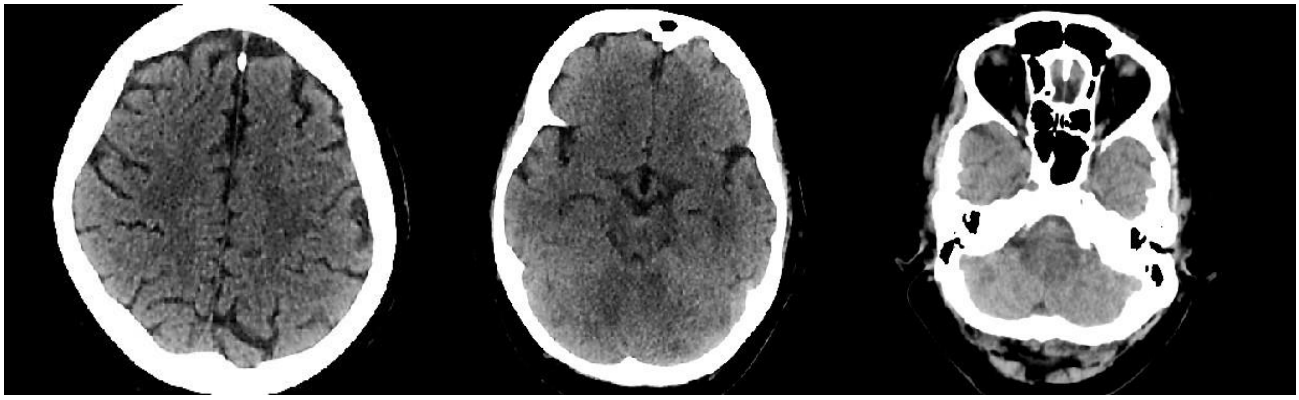

Figure 2: MRI scan after second operative procedure showing restricted diffusion involving the entire posterior circulation territory bilaterally. The cerebellum was swollen, the brainstem compressed and there was effacement of the CSF space at the foramen magnum

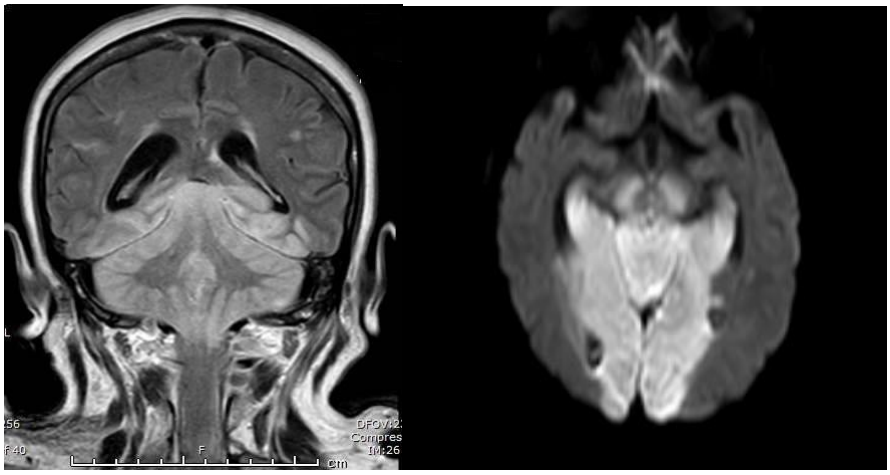

Table 1. Data from the potential donor audit on the number of patients meeting the criteria for testing for DNC and the proportion actually tested between 2010 and 2017 and the estimated number of patients with an isolated brainstem / posterior circulation lesion based on Varedas and colleagues[4].

	2010 - 11	2011 -12	2012 - 13	2013 -14	2014 -15	2015 - 16	2016 - 17
Patients meeting criteria to test for DNC (n)	1672	1659	1631	1787	1733	1742	1775
Patients actually tested (n)	1205	1232	1268	1422	1444	1472	1522
Patients not tested (n)	467	427	363	365	289	270	253
Proportion of patients meeting criteria who were tested %	72.1	74.3	77.7	79.6	83.3	84.5	85.7
Patients tested and DND not confirmed (n, %)	20 (1.7)	14 (1.1)	26 (2.0)	29 (2.0)	22 (1.5)	19+ (1.3)	20 (1.3)
Estimated no. with isolated brainstem lesion (Varelas 2017)	24	25	25	28	28	29	30