Isolated medulla oblongata function after severe traumatic brain injury

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Abstract
The objective was to report the first pathologically confirmed case of partly functionally preserved medulla oblongata in a patient with catastrophic traumatic brain injury.

A patient is described with epidural haematoma with normal breathing and blood pressure and a retained coughing reflex brought on only by catheter suctioning of the carina. Multiple contusions in the thalami and pons were found but the medulla oblongata was spared at necropsy.

In conclusion, medulla oblongata function may persist despite rostrocaudal deterioration. This comatose state (“medulla man”) closely mimics brain death.

Keywords: brain death; head injury; apnoea test; outcome

Any neurological catastrophe may result in brain death and its transition is typically determined by clinical neurological examination alone.1 In many countries of the world, confirmatory tests are optional in adults but remain obligatory in children and the newborn.2 Therefore, clinical examination should be unequivocal and precise. It should include testing of respiratory drive after maximal stimulation of the respiratory centres with hypercarbia using apnoeic oxygenation techniques. Only a few cases have been described in which spontaneous breathing occurs during apnoea testing.3

We report on a patient with an isolated, barely detectable, cough response and spontaneous breathing of several days’ duration until withdrawal of support. This comatose state closely mimics brain death.

Case description
This patient was extracted from a car after a motor vehicle accident. During transport to the hospital he remained unconscious, possibly had an apnoeic episode, developed bradycardia, and was intubated. On arrival, Glasgow coma sum score was 3, the left pupil was dilated (diameter of 8 mm), fixed to light, the right pupil was normal size (diameter of 4 mm) with a normal light response, but oculocephalic reflexes were absent. Brain CT documented a large left epidural supratentorial haematoma in addition to subarachnoid blood in the basal cisterns and fourth ventricle and intraparenchymal haemorrhage in both cerebellar peduncles and pons. Laboratory tests including serum alcohol concentration and urinary toxicology screen were unremarkable. He was taken to surgery as an emergency for left craniotomy and removal of epidural haematoma.

POSTOPERATIVE COURSE
After evacuation of the epidural haematoma he remained comatose. Repeat brain CT showed a new large epidural haematoma in the posterior fossa with a stellate haematoma in the pons and newly imaged contusions in both thalami. Neurological examination by one of the attending physicians showed lack of consciousness, virtually absent brain stem reflexes (with specific attention to vertical eye movement and blinking), and no motor response to pain. A cough response was momentarily noted by one of the attending nurses but no recognisable response was seen with movement of the endotracheal tube. A brief episode of hypotension with a systolic blood pressure of 80 mm Hg was noted.

Phenylephrine was administered to ensure adequate perfusion. No diabetes insipidus was seen. An apnoea test was performed. Within minutes after disconnection a spontaneous regular respiratory effort with tidal volumes between 300–500 ml was recorded at a Pco2 of 34 mm Hg. Re-examination of the patient (by EFMW) showed absent brain stem reflexes but a notable discrepancy between upper and lower tracheal stimulation and response. Up and down movement of the endotracheal tube produced no response. Deep catheter suctioning of the carina or mainstem bronchus elicited a reproducible, but faint, cough response. This clinical condition persisted for 48 hours. Two additional apnoea tests with roughly 12 hour intervals produced similar results. The family decided to withdraw support and the patient was placed on a T piece with 4 l oxygen. For an additional 8 hours the patient had normal respiratory drive but was intermittently tachypnoeic with rates varying from 20–30/minute. Oxygenation measured by pulse oxymetry remained normal. Blood pressures stabilised at 90–100 mm Hg systolic pressure without the...
use of pharmacological support. Respiratory arrest within minutes occurred after extubation after withdrawal of support.

NEUROPATHOLOGY

At necropsy, there were multiple closed skull fractures involving the bilateral parieto-occipital sutures, the occipital bone, the petrous portion of the temporal bones, and the roof of the right orbit. Superficial contusions were noted in the ventral surfaces of the frontal lobes; the anterior, ventral, and lateral aspects of the temporal lobes; splenium; and the ventral surfaces of the cerebellar hemispheres.

The lesions central to the clinical presentation of this case were found in the rostral and middle brain stem constituting deep contusive lesions (figure).

Most rostrally, haemorrhages were found in the hypothalami and paramedian thalami, bilaterally and in the left lateral thalamus and internal capsule. In the midbrain, smaller haemorrhages were dispersed across the cross sections, whereas at the upper and midpontine levels, they coalesced to form a large central confluent area measuring $3 \times 3$ cm at its maximal dimension. There was a limited rupture into the fourth ventricle. In the lower pons, small haemorrhages were largely limited to the midline area.

Also present were haemorrhages in the interior of the dorsal vermis, the white matter and dentate nuclei of both cerebellar hemispheres, separate from the mild cortical lesions described previously in the ventral surface of the cerebellum.

The medulla showed only a mild extrinsic compression of its posterolateral aspects at its middle level by a mild tonsillar herniation but showed no intrinsic lesions save for minimal perivascular haemorrhages along the fourth ventricular surface.

Additionally, there was herniation of the left lateral hemispheric brain tissue through the large craniotomy defect, up to 1.5 cm in height, accompanied by evidence of recent venous-type infarction, most notable at the marginal zones of the herniated tissue which had been compressed against the bony edge of the craniotomy defect. There were no residual epidural or subdural haemorrhages in this area.

However, there was a large $(16 \times 9 \times 2)$ cm fresh epidural haemorrhage making a mild indentation of both the occipital and posterior, particularly lateral temporal, aspects of the cerebrum.

There was mild shift of the cerebral midline structures from left to right. A mild bowing of the paramedian cerebral cortex above the corpus callosum was seen and limited bilateral uncal herniation without any significant mesial temporal lobe herniation, or rostral or caudal compression of the midbrain or upper pons. Histological examination showed no well developed areas of axonal disruption except in the vicinity of contusion or postoperative areas (APP and neurofilament immunostains). Eosinophilic degeneration among scattered neocortical and hippocampal neurons was seen.

Discussion

Our case is unique because we document the presence of retained coughing with a vigorous stimulus, normal breathing drive and oxygenation, and normal blood pressure despite the loss of other brainstem reflexes. Typically, medullary destruction loss is a final event in rostrocaudal herniation syndromes; however,
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A few cases of spontaneous breathing during the apnoea test in patients who have fulfilled all other clinical criteria of brain death have been published. Notably, Ropper et al reported four patients with sparing of only the medulla oblongata “indicated by normal respirations” and these patients “survived for several days to 3 weeks with stable unsupported blood pressures.” Details on cough responses and necropsy confirmation of sparing of the medulla oblongata were not described. Only one instance of breathing efforts while fulfilling other criteria for brain death was found in our series of 145 apnoea procedures but apnoea, in both cases, was documented hours later. Other cases of breathing during the apnoea test have been explained by spinal reflex activity resulting in intercostal retraction and shoulder movements but with minimal ineffective air movement.

Partial retained function of the medulla oblongata precludes the diagnosis of brain death. The traumatic brain lesions in our case illustration are characteristic of a severe impact in which primary brainstem lesions are more commonly found. In fact, a recent MR imaging study documented 64% brainstem lesions of 61 consecutive patients with traumatic brain injury and a fatal outcome in patients with bilateral pontine lesions. Although not particularly of primary relevance to our case, we think that the brainstem lesions are primary because the confluent distribution in the midbrain is different from the typical secondary linear type of haemorrhage which occurs along the midline perforators in the midbrain. No evidence of anterior-posterior elongation of the midbrain caused by lateral compression of the mesial temporal lobe herniation was found. In addition, the admission CT demonstrated rostral brainstem haemorrhages.

Our patient example not only reinforces the need for apnoea testing but also careful evaluation of cough reflexes. Failure to examine cough responses with bronchial suctioning or deferral of a formal apnoea test (for example, in patients with neurogenic pulmonary oedema) may lead to incorrect diagnosis of brain death. The presence of an intact or partly damaged medulla oblongata may result in normal regulation of cardiovascular, respiratory, and autonomic function and may stabilise the patient rather than lead to the usual expected demise of haemodynamic systems and cardiac arrest.

Three categories of pitfalls in the diagnosis of brain death have been identified by Pallis and Harley. These are failure to meet preconditions and exclusions, difficulty with interpretation of signs, and failure to elicit them appropriately. In our case, these pitfalls were clearly apparent during evaluation in the intensive care unit. In addition to these pitfalls, the presence of a locked in syndrome needed to be excluded through absence of responsiveness, vertical eye movements, and blinks on command. The declaration of brain death requires academic precision and failure to do so may lead to a false diagnosis of brain death. Clues to retained brain stem function are normal blood pressure and faint coughing during suctioning while pontomesencephalic reflexes are absent.

We speculate that this patient may represent some of the recently reported cases of “chronic brain death.” In his provocative review, Shewmon collected patients from the literature who apparently fulfilled the clinical criteria of brain death but had a prolonged somatic survival. Intensive care was continued because family members were strongly motivated by religious reasons, failed to accept the hopelessness of this state, or support was prolonged to have a pregnancy come to term. The tendency of these cases to “survive” with simple support systems casts doubt on the somatic disintegration after brain death. However, we suspect that in some of these accumulated patients, cough reflexes and breathing drive were not specifically mentioned as absent or remained untested. Failure to recognise persistent medulla function may not only lead to misdiagnosis of brain death, but may also incorrectly imply that the brain and brain stem are not critical organs for function of physiological systems.