A Sixteen-Year-Old in PVS Who Develops Cushing’s Disease: Medical and Ethical Issues

Introduction
We present the medical and ethical concerns we encountered when a young adolescent in permanent vegetative state (PVS) developed Cushing’s disease.

History and Examination
A previously healthy boy of 16 years presented with two tonic clonic seizures due to an arteriovenous malformation (AVM). He underwent embolisation, which was complicated by catastrophic postoperative bleeding resulting in severe brain injury. On transfer to the neurological rehabilitation unit three months later he appeared to have no awareness of himself or his environment. His tracheostomy had been removed just prior to his transfer and he was maintaining normal respiration and circulation. He was fed through a percutaneous endoscopic gastrostomy tube. He exhibited minimal spontaneous movements in his limbs. Tone was generally increased with flexion contractures in upper limbs, extensor posturing in lower limbs and his feet were fixed in equinovarus. He had sleep-wake cycles with non-purposeful roving eye movements, chewing movements and reflex response to noxious stimuli. His Wessex Head Injury Matrix (WHIM) score was 1/7.

Rehabilitation goals
The main aims of his rehabilitation were, firstly, to establish whether there was any evidence of recovery that might result in him improving from a vegetative state to a higher level of awareness, with the attendant possibility of communication; secondly, to establish a clear nursing and postural management plan, including managing issues related to growth. Thirdly, it was important to provide his family with appropriate emotional and psychological support.

Diagnosis of PVS
In order to confirm the diagnosis of PVS, it was necessary to review his treatment and cognitive state. His clinical condition did not improve over the following nine months. His level of awareness was therefore rated at level two on the Rancho Los Amigos Scale, which is a cognitive functioning scale(1) (Table 1).

In view of the significance of a diagnosis of PVS, a second opinion(2) was sought from an experienced clinician from another institution. He independently confirmed our clinical findings.

His medication was reviewed to consider the potential for sedative side-effects. (2) He was on baclofen and carbamazepine. The baclofen was stopped to judge any change in his level of arousal, with no positive effect. The dosage of carbamazepine was extremely low and felt unlikely to be contributory.

A brain CT scan at six months confirmed the presence of widespread ischaemia in both hemispheres (see figure). In summary he was found to have intact primary sensory pathways and primary motor output but no evidence of sustained, reproducible, purposeful or voluntary behavioural responses to normal or noxious visual, auditory or tactile stimuli, no language comprehension or expression. He only had reflex motor responsiveness with no evidence of co-ordinated motor activities. As his neurological status remained unchanged for one year after catastrophic brain injury, the diagnosis of PVS was made.(2,3)

Presentation and diagnosis of Cushing’s Syndrome
At the time the patient was being assessed for PVS one year after his haemorrhage he was found to have hypertension with no obvious cause, unexplained weight gain and rapidly progressive purple striae on his arms, trunk and thighs. He was also noted to be severely osteopenic on an ankle x-ray.

Four 24-hour urine collections showed elevated urinary 5 Responses may be significantly delayed.

Table 1: Rancho Los Amigos Scale Level 2: Generalised Response: Total Assistance

| 1 | Demonstrates generalised reflex response to painful stimuli. |
| 2 | Responds to repeated auditory stimuli with increased or decreased activity. |
| 3 | Responds to repeated external stimuli with generalised physiological changes, gross body movement with or without purposeful vocalisation. |
| 4 | Responses noted above may be same regardless of type and location of stimulation. |
| 5 | Responses may be significantly delayed. |

Original Scale co-authored by Chris Hagen, PhD, Danese Malkmus, MA, Patricia Durham, MA Communication Disorders Service, Rancho Los Amigos Hospital, 1972. Revised 11/15/1974 by Danese Malkmus, MA and Kathryn Stendrup, OTR.
Management of the dual diagnosis

It was now necessary to consider not only the implications of PVS but also Cushing’s syndrome which would very likely shorten his life if left untreated. Moreover, with the diagnosis of PVS the possibility of withdrawal of artificial nutrition and hydration (ANH) was considered.1,2 The situation was further complicated by the fact that the patient was still a child in law, but having reached the age of 16 years, his parents had no legal power to give or withhold consent to treatment.9 Nevertheless it was felt essential to fully involve his parents in the decision-making process. After full reflection and consideration it was decided not to pursue withdrawal of ANH.

Management of Cushing’s syndrome would normally include invasive procedures to localise the source – in this case, most likely a pituitary adenoma, followed by definitive surgery where possible.3,4 Palliative treatment with medical treatment (e.g. aminoglutethimide or ketoconazole) or adrenal resection is an option in otherwise untreatable cases. Medical treatment is associated with significant side-effects. Expert input was provided by a paediatric endocrinologist. Usual management of pituitary adenoma would involve high resolution imaging: however, the diagnosis remains essentially clinical. Observational tools such as the WHIM can be used to assess and monitor cognitive recovery after severe head injury.5

Exclusion of reversible causes such as sedative medication is important. Patients in persistent vegetative state should be observed for twelve months after a traumatic brain injury and six months after other causes before it is judged to be permanent (PVS). When the diagnosis of PVS is being considered, the patient should be examined by at least two doctors, both of whom are experienced in assessing disorders of consciousness.

Cushing’s syndrome was diagnosed concurrently with the confirmation of PVS, raising additional management issues. Un-treated Cushing’s syndrome has a poor prognosis and will very likely shorten the patient’s life due to impaired immunity, increased vulnerability to hypertension and cardiovascular disease, diabetes, propensity to skin breakdown with poor wound healing and pressure sores, osteoporosis, peptic ulceration and gastrointestinal haemorrhage. Symptomatic treatment such as bisphosphonates to ameliorate osteoporosis in Cushing’s syndrome are effective but the effect is modest because normally treatment is directed towards dealing with the Cushing’s.8,9

The combination of PVS and Cushing’s disease is previously unreported. It raises the possibility that unrecognised Cushing’s syndrome may have contributed to the catastrophic intracranial haemorrhage. Diagnosis of PVS has important implications, especially in conjunction with an additional life-threatening diagnosis. With the family’s agreement, we felt intervention to investigate or treat the Cushing’s syndrome was inappropriate beyond employing simple symptomatic measures.

In summary, the approach we took with early involvement of an endocrine specialist in our face-to-face meetings with the family and multi-disciplinary team was very effective in achieving a satisfactory resolution of a very difficult, and distressing situation. This had the significant advantage of obviating recourse to legal proceedings and is an approach we would commend to others confronted with complex issues of dual diagnosis.

References