

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 in our unit. For the diagnosis of vegetative state, he underwent formal and systematic assessment of the three major sensory systems (auditory, visual and somatic) and the motor system.^{2,8} The awareness assessment consisted of ten sessions over a 14-day period, at varying times of the day and lasting approximately 40 minutes. This process was repeated two months later after a multimodal sensory stimulation programme. He showed a generalised startle response to loud noise, occasional slow but inconsistent localisation of sound by turning his head and no response to verbal commands. He had normal pupillary responses, spontaneous eye movements, spontaneous blinking but no consistent tracking and no response to visual threat. There was reflex flexion to pain in the legs but no response to pain in the arms or face. Some grunting noises were made, but not with any consistency or

meaning. His level of awareness was therefore rated at level two on the Rancho Los Amigos Scale, which is a cognitive functioning scale⁷ (Table 1).

In view of the significance of a diagnosis of PVS, a second opinion⁹ 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.⁵ 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.^{1,2,5}

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 uri-



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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 repeat 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 Stenderup, OTR.

Table 2: Dexamethasone Suppression Test

The patient failed to suppress cortisol levels on the low dose dexamethasone suppression test. On the high dose test there was satisfactory cortisol suppression and a fall in ACTH. These results indicated Cushing's syndrome, most likely secondary to a pituitary microadenoma (Cushing's disease).

Low-dose Dexamethasone Suppression Test	Day 1	Day 2	Day 3
Cortisol	365 nmol/L	172 nmol/L	245 nmol/L
High-dose Dexamethasone Suppression Test	Day 1	Day 2	Day 3
Cortisol	385 nmol/L	12 nmol/L	12 nmol/L
ACTH	11 ng/L	< 5 ng/L	< 5 ng/L

nary free cortisol. A low- and high-dose dexamethasone suppression test indicated Cushing's syndrome, probably secondary to a pituitary microadenoma⁹ (Table 2).

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.^{1,2,5} 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.⁶ 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.^{9,10} 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 brain MRI with contrast, followed, if necessary, by inferior petrosal sinus sampling in a specialist centre. This would require general anaesthesia to enable him to lie still. Subsequently, pituitary surgery and/or radiotherapy would be required.

After discussion between the family, the medical and the rehabilitation teams it was felt inappropriate to employ invasive investigations and it was decided instead to use simply symptomatic treatment. It was also agreed not to resuscitate him in the event of cardio-respiratory arrest, or to transfer him to an acute hospital for management of intercurrent illness. However, transfer to an acute hospital for technical help such as PEG tube problems was felt to be appropriate.

Advice was sought from the trust's solicitors as to the need for High Court involvement. This was felt unnecessary as all parties involved were in full agreement with the management plan.

Subsequently the patient was transferred to a long stay community facility to receive ongoing

care, where he remains, having developed no adverse sequelae from his Cushing's syndrome. The treatment plan was agreed with his new clinical team prior to transfer, with regular monitoring of blood pressure and blood sugar. Up to the present time he has not developed diabetes, but if he does so the plan is to treat only symptomatic diabetes, such as dehydration and infection. His parents remain satisfied with the approach we, and his new clinical team, have taken.

Discussion

We have presented the medical and ethical dilemmas encountered in a 16-year-old boy with concurrent PVS and Cushing's syndrome.

Accurate diagnosis of PVS is crucial. A structured, systematic clinical assessment² of awareness is required because errors in diagnosis have occurred.^{3,4} It is important to establish the mechanism of brain injury, aided by neuroimaging; 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.¹¹ 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.⁵

Cushing's syndrome was diagnosed concurrently with the confirmation of PVS, raising additional management issues. Untreated 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 syndrome¹² are effective but the effect is modest because normally treatment is directed towards dealing with the Cushing's.¹³

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 implica-

tions, 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 to 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.

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