Paroxysmal Sympathetic Hyperactivity (Sympathetic Storm) in a Patient with Permanent Vegetative State

Emily R. Levy

Ursula McVeigh, MD

Allan M. Ramsay, MD

1University of California San Francisco School of Medicine, San Francisco, CA 94122

2Fletcher Allen Health Care

Palliative Care Service

University of Vermont Department of Family Medicine

Burlington 05405.

Correspondence: Allan Ramsay, MD

215 SM2
111 Colchester Ave
Burlington, VT 05401
Allan.Ramsay@vtmednet.org
Introduction

Profound complications of neurological disease and injury are a common reason for palliative care consultation [1]. The focus of the consultation is often family psychosocial support and helping establish a plan of care based on the patient’s values rather than pain or symptom management. Vegetative state is defined by the Multi-Society Task Force on PVS as a "clinical condition of complete unawareness of the self and the environment, accompanied by sleep wake cycles, with either complete or partial preservation of hypothalamic and brain-stem autonomic functions” [2]. A permanent vegetative state (PVS) is one which has lasted beyond three months following non-traumatic injury (hypoxic/ischemic) or beyond twelve months following traumatic brain injury [2]. Traumatic brain injury is the most common cause of the vegetative state; of vegetative states related to non-traumatic brain injury, hypoxic/ischemic injury is a major cause [2, 3, 9]. Life expectancy in patients with PVS is 3-5 years [2]. Death usually occurs as a consequence of infection or withdrawal of life supporting therapy. It is estimated that there are approximately 15,000 people living with PVS in the United States [4].

An uncommon but well recognized complication of profound brain injury is paroxysmal sympathetic hyperactivity (PSH), formerly called “sympathetic storming”. This exaggerated stress response may occur in 15% to 33% of comatose patients with severe traumatic brain injury (TBI) in the acute phase of recovery [5, 6, 10]. PSH is most likely to occur in the immediate period (7 days) after an injury, with much fewer cases continuing on into rehabilitation [7]. The exact cause of this increase in sympathetic
activity is unknown. There is some evidence that paroxysmal sympathetic hyperactivity is an excessive responsiveness to afferent stimuli in patients with severe brain injury. There have been many names applied to paroxysmal sympathetic hyperactivity including sympathetic storm, dysautonomia, autonomic dysfunction syndrome, and initially, diencephalic seizures, when this syndrome was thought to be a form of midbrain or thalamic seizure activity [8, 9].

Paroxysmal sympathetic hyperactivity has been reported in conditions other than TBI. These include hypoxic injury, brain tumors, hydrocephalus, and subarachnoid hemorrhage [9]. PSH is primarily a clinical diagnosis of exclusion and it is likely this condition often goes unrecognized. Some have defined it as a clinical condition in a patient with diffuse brain injury requiring paroxysmal increases in a combination of, or five out of the seven, following criteria: temperature, heart rate, blood pressure, respiratory rate, diaphoresis, extensor posturing, and/or dystonia in the absence of other potential causes for these clinical signs [10, 11]. A recent review by Perkes identified two distinct types of dysautonomia which have previously been grouped under this syndrome, sympathetic hyperactivity and mixed autonomic hyperactivity [9]. We report the case of a patient on our Palliative Care consultation service in a permanent vegetative state who developed paroxysmal sympathetic hyperactivity eight months after his initial anoxic brain injury.
Case Report

A 27-year-old man with a history of bipolar disorder and intravenous drug abuse was found unresponsive one morning by his wife. The patient was reportedly in his usual state of health until one day prior to this admission. When EMS arrived the patient had pinpoint pupils and was unresponsive to verbal or painful stimuli. The patient was initially admitted to the intensive care unit for presumed Methadone overdose; his course was complicated by rhabdomyolysis, renal failure, aspiration pneumonia, and an NSTEMI. After his initial extubation, the patient had two generalized tonic clonic seizures thought to be secondary to alcohol withdrawal and required re-intubation for respiratory distress secondary to altered mental status and pneumonia. At that time, an MRI revealed posterior reversible encephalopathy syndrome (PRES) which was thought to be related to substance withdrawal, rhabdomyolysis, and acute kidney injury. The patient was medically sedated during this second intubation; however he could track, squeeze hands in response, and intermittently follow commands when alert.

On hospital day 19, the patient was sent for a follow-up MRI to assess the state of his PRES. During the MRI, the patient developed cardiac arrest with pulseless electrical activity. CPR was performed for 13 minutes and included chest compressions, epinephrine, and atropine, until cardiac function was restored. The patient returned to the unit where he then had a generalized tonic-clonic seizure, controlled with lorazepam. Over the next few days the patient was found to have intact brainstem reflexes only, with no purposeful movement or response. Clinical examination indicated he had experienced significant hypoxic/ischemic brain injury during the cardiac arrest. The patient would
blink to loud auditory stimuli, had a positive occulocephalic ("doll’s eyes") reflex, a corneal reflex, and a gag reflex. The patient had flexor withdrawal to painful stimuli, spontaneous respirations and circadian rhythm sleep/wake cycles intact. He had no responses to verbal stimulation despite weaning of his sedation. An EEG and somatosensory evoked potential test (SSEP) were each completed twice over the next two weeks, both times demonstrating no cortical response and diffuse flattening suggestive of poor prognosis. The patient was diagnosed with a vegetative state secondary to diffuse anoxic brain injury.

After multiple family meetings with Neurology, Ethics, and Palliative Care, the patient’s family opted to continue life-prolonging therapies and to pursue placement in a long-term care facility. Tracheostomy and gastric feeding tube were placed. The patient’s subsequent ICU course was complicated by pseudomonal pneumonia, lung abscesses, and prolonged ventilator support. After three months he was able to transfer to the general medicine ward where he continued on nutritional support therapy. An EEG and SSEP were repeated at six months and showed no improvement, still demonstrating no cortical responses on somatostimulatory testing and diffuse EEG flattening.

The patient remained in the hospital in a vegetative state for the next eight months; he is now considered in a permanent vegetative state based on accepted neurologic criteria. His neurological exam has remained constant with intact brainstem reflexes but no purposeful responses. He has developed mild contractures but otherwise his overall exam is unchanged. During this period a fentanyl patch was prescribed for treatment of
pain because of the limited understanding of a patient’s pain experience while in a vegetative state.

On hospital day 256, the patient underwent his usual routine of having a weekly bath with no noted complications. After return to his room, he had an episode of profound tachypnea (respiratory rate 40-50), tachycardia (heart rate in the 140s), diffuse skin erythema, tonic neck posturing, and progressively worsening hyperhidrosis; this episode resolved after 30 minutes. The patient then had two more similar episodes over the course of the day, separated by 3-5 hours with each episode lasting 30 minutes to one hour. The patient was afebrile throughout the day, although his extremities were cool to touch. The patient was given lorazepam and sublingual morphine with each episode, although administration of these medications was not clearly correlated with resolution of the events.

The patient was evaluated for any signs of an infection which could trigger this excessive sympathetic activity. He had a normal complete blood count and chest x-ray. Subsequent lab studies excluded hypothyroidism, hypercortisolism, or pheochromocytoma. Our clinical diagnosis was paroxysmal sympathetic hyperactivity (PSH). A clonidine 0.1mg transdermal patch was added to his medical regimen. Following initiation of the clonidine patch, the episodes resolved and have not reoccurred.
Discussion

Paroxysmal sympathetic hyperactivity (PSH) is a relatively common complication of traumatic brain injury; however it has not been previously reported as a late complication of a stable patient in a permanent vegetative state. The majority of reports of paroxysmal sympathetic hyperactivity in patients with anoxic brain injury have occurred during the initial weeks after the CNS event. The PSH response can be elicited by a specific trigger (fever, position change, suctioning). Our patient was in a permanent vegetative state for more than eight months before his paroxysmal sympathetic hyperactivity began.

Considering the number of patients living in permanent vegetative states in the United States, it is relevant to alert the palliative care and hospice community to this possible late stage complication of brain injury, as well as to briefly explore the therapies recognized to treat this condition.

The clinical presentation of this syndrome can be varied. In our patient paroxysmal sympathetic hyperactivity presented with tachypnea, tachycardia, diffuse skin erythema, profound diaphoresis, and neck posturing which worsened over the course of the episodes. This presentation met the clinical definition of PSH which includes sympathetic over-activity with additional motor features [9]. The motor features of PSH may include decerebrate or decorticate posturing, spasticity, hypertonia and/or dystonia, teeth grinding, and agitation. In the past twenty years, at least eight different sets of clinical criteria have been proposed for paroxysmal sympathetic hyperactivity, thus this is a disease for which precise clinical definition is still evolving [9, 10]. Physicians and
other health care providers should have an index of suspicion when the clinical picture suggests sympathetic over-activity so that appropriate therapy can be implemented.

Although it was formerly questioned whether patients in vegetative states could experience discomfort of any sort, studies using PET imaging have illustrated that there is residual perception in vegetative state patients [12]. PET scans of patients in vegetative states undergoing noxious stimuli showed similar reactions to controls in regions of the primary somatosensory cortex. This processing is thought to be incomplete because the PVS patients failed to show reactions in the secondary somatosensory cortex and frontal cortex. Based on this evidence, it is reasonable to assume that patients in a vegetative state with PSH would be experiencing discomfort at some somatosensory level. There is an additional debate whether patients with PVS experience nociceptive or neuropathic pain because of the cortical atrophy associated with the progression of the disease and lack of awareness. Regardless of these intellectual questions, the clinical picture of paroxysmal sympathetic hyperactivity is so dramatic it demands immediate therapy and resolution, not only for the possibility of neurologically perceived discomfort but also for family/caregiver distress in witnessing these episodes.

In addition to immediate treatment, clinicians must also evaluate whether this syndrome is an unrestrained sympathetic response to a noxious stimuli, similar to patients with spinal cord injuries who experience extreme sympathetic output in response to autonomic triggers like bladder fullness, infection, or increased intracranial pressure. Clinicians
must thoroughly evaluate for any new noxious stimuli or infections, and for other triggers of sympathetic activity like thyroid dysregulation or adrenal pathology.

Several treatment and palliation algorithms have been developed using multi-study reviews of PSH. Since PSH is a syndrome of overactive sympathetic tone, it is logical that effective treatment begins by attempting to reduce or block the sympathetic nervous system. Suggested medications include bromocriptine, clonidine, dantrolene, lorazepam, morphine sulfate, and non-selective beta blockers such as propranolol. These may be used individually or in combination [13]. The current literature provides little consensus for how to choose an initial therapy. Targeting the individual patient’s clinical picture is assumed to be the best approach. Our patient was already being treated with scheduled metoprolol for hypertension and lorazepam for muscle contraction, neither of which seemed to prevent his paroxysmal sympathetic hyperactivity. Based on the peripheral mechanisms of action of metoprolol and lorazepam, we choose to start a clonidine patch which would centrally target sympathetic output as an additional therapy. Clonidine offers the benefit of centrally inhibiting the sympathetic nervous system and providing the ease of transdermal administration.

In summary, we have presented the case of a patient in a permanent vegetative state who developed paroxysmal sympathetic hyperactivity more than eight months after his initial hypoxic/ischemic brain injury. In this case of PSH, palliation of symptoms was aimed at controlling tachycardia, tachypnea, diaphoresis, and posturing. Opiates and benzodiazepines are unlikely to control all the clinical signs of PSH and, for our patient,
were ineffective in preventing further events. The episodes ceased when transdermal clonidine was initiated. Considering the number of patients living in vegetative states, many of whom are in long term care facilities, it is important that palliative care services recognize this symptom complex and understand the initial treatment options.

References


