Paroxysmal Sympathetic Hyperactivity

Jacqueline Urtecho, MD[1,2]

[1] Department of Neurological Surgery, Thomas Jefferson University, Philadelphia, PA
[2] Department of Neurology, Thomas Jefferson University, Philadelphia, PA

It is not uncommon for physicians who treat patients with traumatic brain injuries to see wide fluctuations in the heart rate, respiratory rate and blood pressure. For decades, these fluctuations were thought to be seizures, caused by pressure on the thalamus. They were originally termed Diencephalic Autonomic Seizures by Dr. Wilder Penfield in 1929. He described episodes of lacrimation, hypertension, diaphoresis and agitation. Dr. Penfield's "seizures" were later shown to have no electrographic correlate. Since that time, many names have been used to describe similar episodes: Dysautonomia, Sympathetic Storming, Brainstem Attacks, Autonomic Dysregulation, Paroxsymal Autonomic Instability with Dystonia and Paroxysmal Sympathetic Hyperactivity to name only a few.

Paroxysmal Sympathetic Hyperactivity (PSH) occurs in acquired brain injury and features simultaneous, paroxysmal transient increases in sympathetic and motor activity.[1] It is most commonly associated with traumatic brain injury. However, it has been documented in many neurologic conditions (Table 1) and an episode can be precipitated by a variety of triggers.[2] (Table 2).

One of the difficulties in recognizing PSH is that many of the symptoms are found in other clinical syndromes. It is a diagnosis of exclusion and the proper workup must be completed before beginning treatment.[3] The clinical features of PSH include tachycardia, tachypnea, hypertension, fever, diaphoresis and dystonic posturing during the episodes. Table 3 highlights many of the conditions which share similar features to PSH.

Table 1. Neurologic Conditions associated with Paroxysmal Sympathetic Hyperactivity

Traumatic Brain Injury
Anoxic Brain Injury
Ischemic Stroke
Intracranial Hemorrhage
Aneurysmal Subarachnoid Hemorrhage
Brain Tumor
Encephalitis

Table 2. Triggers Precipitating PSH Attack

Suctioning
Turning
Bathing
Physical Exam

PSH has been described as occurring in three phases.[4] The first phase occurs immediately after the injury. At this early point in the disease process, there

Table 3.

	Mental Status	T	HR	RR	BP	Pupil Size	Sweating	Agitation	Posturing	CPK
Paroxysmal Sympathetic Hyperactivity	↓	↑	↑	↑	↑	↑	+	+	↑	?
Malignant Hyperthermia	↓	↑	↑	↑	±↑	NA	NA	NA	+>-	↑
NMS	↓	↑	↑	↑	↑/↓	NA	+	NA	+	↑
Increased ICP	↓		↓	↓	↑	±↑	NA	NA	±	NA
Central Fever	±↓	↑	↑	↑	NA	NA	NA	NA	NA	NA
Infection	±↓	↑	↑	↑	↑/↓		±	NA	NA	NA
Nonconvulsive seizures/epilepsy	NA	NA	NA	NA	NA	±↑	NA	±	NA	NA
Narcotic Withdrawal	±↓	NA	↑	↑	NA	↑	+	NA	NA	NA
Autonomic dysreflexia	NA	↑	↑	↑	↑	NA	+	NA	NA	NA

Abbreviations: NMS, neuroleptic malignant syndrome; T, temperature; HR, heart rate; RR, respiratory rate; BP, blood pressure; CPK, creatine phosphokinase; up arrow, increased; down arrow, decreased. Adapted from Blackman et al Archives of Neurology 2004;61:321-328

Table 4. Severity of Clinical Features Assessment Tool

Paroxysmal Sympathetic Hyperactivity – Assessment Measure Clinical Features Scale					
	0	**1**	**2**	**3**	**Score**
Heart Rate	<100	100-119	120-139	≥140	
Respiratory Rate	<18	18-23	24-29	≥30	
Systolic Blood Pressure	<240	140-159	160-179	≥180	
Temperature	<37	37-37.9	38-38.9	≥39	
Sweating	None	Mild	Moderate	Severe	
Posturing during episodes	None	Mild	Moderate	Severe	
				CSF Total	

Severity of Clinical Features	CFS Total
None	0
Mild	1-6
Moderate	7-12
Severe	≥13

Table 5. Diagnosis Likelihood Tool (DLT)

Score 1 point for each feature present	
Clinical features occur simultaneously	
Episodes are paroxysmal in nature	
Sympathetic over-reactivity to normally non-painful stimuli	
Features persist ≥3 consecutive days	
Features persist ≥ 2 weeks post-brain injury	
Features persist despite treatment of alternative differential diagnoses	
Medication administered to decrease sympathetic features	
≥ 2 episodes daily	
Absence of parasympathetic features during episodes	
Absence of other presumed cause of features	
Antecedent acquired brain injury	
DLT total	

	Combined Total Points	
	Clinical Severity Features + Diagnostic Likelihood Tool	
PSH Diagnostic Likelihood	Unlikely < 8	
	Possible 8-16	
	Probable > 17	

(Adapted from Baguley I. et al. Journal of Neurotrauma 2014;31:1515-1520)

are no specific signs that distinguish a patient who will go on to develop PSH from those who don't. Phase two begins after the withdrawal of sedation and or paralytics. It is at this point that patients distinguish themselves and either develop typical PSH features (hypertension, hyperthermia, rigidity etc.) or don't. The PSH episodes are sporadic and intense at times and have variable responses to medical management. The duration of this phase is unpredictable. It can last from weeks to months. The third phase was called PSH "burnt out." The patient no longer exhibits all the clinical features and can be left in a spastic or dystonic position with varying degrees of recovery.

In 2014, the *Journal of Neurotrauma* published a consensus statement aimed at formalizing the nomenclature, including definition and diagnostic criteria. Tables 4 and 5 detail the diagnostic criteria.

PAROXYSMAL SYMPATHETIC HYPERACTIVITY – ASSESSMENT MEASURE

Management of PSH involves both non-pharmacologic and pharmacologic treatment. Non-pharmacologic management includes decreasing external stimuli, limiting visitation, minimizing exams or noxious stimuli, or grouping activities (turning, suctioning, bathing). Pharmacologic management is aimed at dampening sympathetic outflow or activating parasympathetic system. Most commonly used are benzodiazepines, beta-blockers and opiates. Most medical treatment involved depressing the CNS systems and causes increased sedation.[5] (Table 6).

Managing the symptoms is important in preventing secondary brain injury. Patients who are not treated are at risk for cerebral edema, intracranial bleeding from malignant hypertension. There is a risk of ischemia due to decreased cerebral oxygenation and neuronal loss due to prolonged sympathetic activation. There are other non-brain injury risks that occur due to prolonged untreated PSH. These include electrolyte abnormalities, dehydration and kidney injury from excessive diaphoresis. Cardiac injury can occur from repetitive significant tachycardia and muscle wasting. Weight loss and malnutrition can occur from increased metabolic demands.

Lastly, it is critical that physicians discuss PSH with the families, as these episodes can be very upsetting and distressful to witness. Explaining what is happening to the patient and how it is being managed can help alleviate this stress. It is also a way to involve the family in monitoring for triggers and timing of episodes. Developing a bedside chart which details triggers, timing, duration of episodes, medications administered and response to treatment is useful in the long-term management.

Table 6.

	Symptom	Receptor Agonist or Antagonist	Medication	Additional
First Line	Tachycardia	β2-Adrenergic blocker	Propranolol	– Dampens sympathetic activity; decreases serum catecholamines, reduces cardiac workload – Dosing limited by HR and BP – Caution in asthmatics
First Line	Hyperthermia	COX-2 inhibitor	Acetaminophen (Po 650-975mg q6hr) (IV 1gm q6h)	– Dosing max 4gm/daily
First Line	Diaphoresis & hyperthermia	Dopamine agonist	Bromocriptine (2.5-5mg q8hr)	– Acts at the hypothalamic level. – Can increase up to 30-40mg/day
First Line	Tachypnea	GABA-A Antagonist	Diazepam (po 5mg q8 hr and titrate up)	– No max dose – Dosing limited based on sedation
First Line	Pain	Opiate Agonist	Morphine Sulfate Fentanyl Oxycodone	– Start low and titrate to effect – Dosing varies by agent – High abuse potential long term
Second Line	Hyperthermia	Dopamine D2 Antagonist	Chlorpromazine	– Acts along the hypothalamus – Good for recurrent hyperthemia – Should not be used long term – Risk of extra-pyramidal effects & liver failure
Second line	Dystonia	GABA-B agonist	Baclofen	– Low potential for abuse – Long term use requires slow wean to avoid withdrawal/ seizures
Second Line	Dystonia	Post-synaptic muscle relaxant, Inhibits Ca+ release intracellularly	Dantrolene	– Caution if other Ca+ Channel Blockers on board can cause hyperkalemia and – Caution if liver disease
Second Line	Tachycardia	α2 Agonist	Clonidine	– Lowers levels of norepinephrine
Second Line	Tachyacrdia	β1, β2, α1 antagonist	Labetalol	– Dosing limited by HR and BP

Onset time	Trigger	HR	BP	Diaphoresis Y/N	ICP (mmHg)	Dystonia Y/N	Medications given	Duration of episode

REFERENCES

1. Baguley IJ et al. Journal of Neurotauma 2014;31:1515-1520
2. Baguley IJ et al. Semin Neurol 2008;28:716-25
3. Blackman et al Archives of Neurology 2004;61:321-328
4. Baguley IJ et al Journal of Neurosurgical Psychiatry 1999;67:39-43
5. Lemke et al. Crit Care Nurse 2007;27:30-37