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Paroxysmal Sympathetic Hyperactivity in Acquired Brain Injury: A Case Series

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ABSTRACT

Background and Aim: Paroxysmal sympathetic hyperactivity (PSH) is a clinical syndrome characterized by paroxysmal and transient episodes of fever, tachypnea, tachycardia, hypertension, diaphoresis, and dystonia following non-noxious stimuli. It is a rare clinical condition and is seen in patients with acquired brain injury (trauma, meningitis, encephalitis, and stroke). Paroxysmal sympathetic hyperactivity-assessment measure (PSH-AM) is a clinical tool for diagnosing PSH. This study aims to describe the clinical characteristics and the outcomes of PSH.

Case Presentation: Of the 412 patients admitted to the neurosurgery intensive care unit at PSGIMSR, Coimbatore, India, 11 (2.6%) patients were diagnosed to have PSH according to the PSH-AM scale. Trauma (72%) was the leading cause of the development of PSH. All patients (100%) had developed at least two PSH episodes per day that persisted for at least 3 consecutive days. Tachycardia and tachypnea were the most common symptoms noted in all PSH patients. The Glasgow Outcome Score (GOS) was less than 3 in 72% of PSH cases at the time of discharge, indicating a poor outcome.

Conclusion: Traumatic brain injury remained the leading cause of PSH. The duration of hospitalization increased in patients with PSH. Along with the prompt treatment of the primary disease, appropriate medications to overcome sympathetic hyperactivity ensure better recovery for these patients. Patients with PSH had relatively poor GOS at the time of discharge.

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Highlights

• Paroxysmal sympathetic hyperactivity (PSH) is a rare clinical condition observed in patients with acquired brain injury.

• These patients present signs and symptoms of sympathetic hyperactivity following non-noxious stimuli.

• Since there is no investigation available to detect paroxysmal sympathetic hyperactivity, the diagnosis is obtained by proper clinical examination and grading of its cardinal features.

• Combination of treatments to ensure early recovery includes medications to overcome sympathetic hyperactivity, early tracheostomy, and implementation of enteral feeding.

Plain Language Summary

Paroxysmal sympathetic hyperactivity (PSH) is characterized by multiple short episodes of abnormal posturing with an increase in the heart rate, blood pressure, respiratory rate, temperature, and sweating. PSH is rarely observed in clinical practice. It occurs in patients with head injury, brain infection, and stroke when the deeper parts of the brain are affected by the disease. Even though computed tomography (CT) scans and magnetic resonance imaging (MRI) of the brain are helpful to locate the damaged parts of the brain, the diagnosis of PSH can be confirmed via thorough clinical examinations only.

Management of PSH includes medical or surgical treatment of the primary disease with other medications to overcome the symptoms produced by it. Duration of hospital stay increased by at least 15 days in patients with PSH when compared to brain injury cases without PSH. The outcome of patients with PSH is also very poor. It is the responsibility of the treating doctor to make the patients' bystanders understand the severity, mortality, morbidity, and economic burden associated with PSH.

1. Background and Importance

In 1954, Penfield and Jasper first reported a series of cases with episodic sympathetic hyperactivity which led to hyperthermia, hypertension, tachycardia, tachypnea, diaphoresis, and dystonia following non-noxious stimuli in the survivors of severe traumatic brain injury [1-3]. Subsequently, this condition gained more attention because of the increased mortality and morbidity, need for prolonged intensive care, and interference with rehabilitation [4]. Different sets of diagnostic criteria were proposed and more than 25 nomenclatures were given, including autonomic dysfunction syndrome, sympathetic storming, hypothalamic midbrain deregulation syndrome, acute midbrain syndrome, and diencephalic epilepsy [4]. In 2014, Baguley et al. proposed the term paroxysmal sympathetic hyperactivity (PSH) to identify the condition characterized by simultaneous, paroxysmal, and transient increases in sympathetic activities [1, 5]. It is an under-recognized condition with a diagnostic pitfall, especially in ICU because of the high prevalence of concomitant diseases that mimic PSH.

Potential mechanisms of paroxysmal sympathetic hyperactivity

The simple disconnection theory and the excitatory-inhibitory ratio model can explain the potential mechanisms for the development of PSH [6, 7].

1) Simple Disconnection Theory: Diffuse or focal brain injury leads to disconnection of cortical inhibitory centers (insula and cingulate gyrus) from the hypothalamus, thalamus, and brain stem which is responsible for the loss of supraspinal control of sympathetic tone leading to autonomic hyperactivity.

2) Excitatory-Inhibitory Ratio Model: Excitatory-inhibitory ratio model explains the development of PSH in 2 stages. Various cortical centers, hypothalamus, and thalamus modulate the activity of the periaqueductal gray matter located within the brain stem. In turn, the periaqueductal gray matter provides the inhibitory

Table 1. Clinical chart for PSH diagnosis

	Symptoms of PSH	Grade 0	Grade 1	Grade 2	Grade 3
Clinical severity scale	Heart rate	<100	100–119	120–139	≥140
	Respiratory rate	<18	18–23	24–29	≥30
	Systolic blood pressure	<140	140–159	160–179	≥180
	Temperature	<37	37–37.9	38–38.9	≥40
	Sweating	Nil	Mild	Moderate	Severe
	Posturing	Nil	Mild	Moderate	Severe

	Cardinal Features of PSH	1 Score If Positive
Diagnosis Likelihood Score	Antecedent of acquired brain injury	1
	Persists for more than 2 weeks of brain injury	1
	Episodes of paroxysm	1
	Hyperactivity to non-noxious stimuli	1
	>2 episodes/day	1
	>3 consecutive days	1
	Symptoms occurs simultaneously	1
	Relieves with medications given to reduce sympathetic activity	1
	No parasympathetic features during the episode	1
	Other presumed causes ruled out	1
	Persists despite of differential diagnosis	1

PSH-AM	Diagnostic possibility of PSH	Score (out of 29)
PSH Assessment Measures=Diagnosis Likelihood Score+Clinical Severity Score	PSH unlikely	<8
	PSH possible	8-16
	PSH probable	≥17

Abbreviations: PSH: Paroxysmal sympathetic hyperactivity

drive to spinal reflex arcs, thereby maintaining the balance between excitatory and inhibitory interneurons. If there is a breach in these excitatory-inhibitory circuits, the disconnection of descending inhibition produces maladaptive dendritic arborization and the spinal circuit excitation triggers the motor response and sympathetic output following non-noxious stimuli.

Diagnosis

Since there is no radiological investigation available to detect PSH, the diagnosis is attained by proper clinical examination and grading of the cardinal features [2, 8]. The paroxysmal sympathetic hyperactivity-assessment measure (PSH-AM) is the scale adopted by many centers to confirm PSH [2, 9]. It is calculated by using two constructs, namely the clinical severity scale which measures the intensity of the cardinal features of PSH,

Table 2. Diagnosis likelihood score observed for PSH

No.	Clinical Parameters Obtained From PSH Patients	1	2	3	4	5	6	7	8	9	10	11
1	Antecedent of acquired brain injury	1	1	1	1	1	1	1	1	1	1	1
2	Persists for more than 2 weeks of brain injury	1	0	0	0	1	1	1	1	1	1	1
3	Episodes of paroxysm	1	0	1	1	1	0	1	1	1	1	1
4	Hyperactivity to non-noxious stimuli	1	1	1	1	1	1	1	1	1	1	1
5	>2 episodes/day	1	1	1	1	1	1	1	1	1	1	1
6	>3 consecutive days	1	1	1	1	1	1	1	1	1	1	1
7	Symptoms occurs simultaneously	0	1	1	1	1	0	0	1	0	0	0
8	Relieves with medications given to reduce sympathetic activity	1	1	1	1	1	1	1	1	1	0	1
9	No parasympathetic features during the episode	0	0	1	0	0	0	0	1	0	1	1
10	Other presumed causes ruled out	0	1	1	1	0	1	1	1	1	1	0
11	Persists despite of treating differential diagnosis	0	0	1	1	0	0	0	1	0	0	0
	Total	7	7	10	9	8	7	8	11	8	8	8

and the diagnosis likelihood tool which is based on the presence of specific features estimating the possibility of PSH [3, 9]. This scoring system (Table 1) helps to diagnose the disease and to grade its severity [8, 10].

Treatment

Management strategies include medical treatment or surgical intervention for primary disease along with a combination of drugs to overcome sympathetic hyperactivity. Opioids, beta-blockers, gabapentin, bromocriptine, benzodiazepines, and central α-agonists are the widely used medications to alleviate sympathetic responses [11, 12]. Hypertension and tachycardia respond well to beta-blockers, propofol, and benzodiazepines. Opioids are used to control tachypnea. Diaphoresis responds well to beta blockers. Meanwhile, bromocriptine and acetaminophen reduce hyperthermic episodes. Dystonic postures can be treated with baclofen and gabapentin [11-13]. Supportive measures, including early tracheostomy, gentle suctioning and sponging, increasing the calorie intake, maintaining hydration, and early

Table 3. Clinical severity score observed for PSH

No.	Cardinal Features of PSH	1	2	3	4	5	6	7	8	9	10	11
1	Heart rate	2	2	3	2	2	2	2	3	2	2	2
2	Respiratory rate	2	2	2	1	2	2	2	2	2	3	3
3	Systolic blood pressure	3	1	3	2	1	3	2	1	2	2	0
4	Temperature	3	3	3	2	3	0	2	2	2	1	2
5	Sweating	2	3	0	2	0	2	2	2	2	2	2
6	Posturing	0	0	1	3	1	2	0	2	0	0	0
	Total	12	11	12	12	9	11	10	12	10	10	9

Table 4. Clinical and radiological findings observed in patients

Score No.	Age (y)	Gender	Etiology	Location of Brain Injury	Comorbidities	Admission GCS/Pupil Size	Procedure Done	Length of Hospital Stay	PSH Scoring	Need for Tracheostomy	Glasgow Outcome Score at Discharge	Associated Injuries
1	38	Male	Trauma	Diffuse axonal injury, injury in basal ganglia and corpus callosum	CKD on dialysis	E2Vetm5, PERL	--	26	7+12	Yes	3	--
2	30	Male	Meningoencephalitis	TB meningoencephalitis, diffuse cerebral edema,	--	E2V2M5 PERL	Rt VP Shunt	18	7+11	No	5	--
3	55	Female	Stroke	Lt ICA infarct	DM, SHT, hypertriglyceridemia	E1VetM2 Anisocoria	Lt FTP decompression	20	10+12	Yes	1	--
4	60	Male	Trauma	Diffuse axonal injury, IVH	DM	E1VetM2, PERL	--	22	9+12	Yes	1	Lt pneumothorax
5	24	Female	Trauma	Rt FTP acute SDH with contusion in basal ganglia	--	E2VetM5 ANISOCORIA	Rt FTP decompression	30	8+9	Yes	4	--
6	40	Male	Trauma	Diffuse axonal injury, injuries in midbrain and diencephalon	SHT	E1VetM3, PERL	--	43	7+11	Yes	3	Rt clavicle # mild hemothorax
7	32	Female	Trauma	Diffuse axonal injury, injury in corona radiata	--	E2VetM5, PERL	--	25	8+10	Yes	4	Pelvis # with Rt femur #
8	54	Male	Trauma	B/l basi-frontal contusion, injury in diencephalon	DM,CAD on antiplatelet	E1VetM3	B/l frontal decompression	48	11+12	Yes	1	Grade 4 spleen injury
9	18	Male	Trauma	Rt FTP acute SDH with midbrain contusion	--	E1VetM3, PERL	--	70	8+10	Yes	2	--
10	25	Male	Trauma	Lt FTP acute SDH with caudate nucleus injury	--	E2VetM5, ANISOCORIA	Lt FTP decompression	37	8+10	Yes	3	C3 lateral mass # without instability
11	55	Male	Stroke	Spontaneous ICH involving pons and medulla	DM, SHT	E1VetM2	--	42	8+9	Yes	1	--

Abbreviations: TB: Tuberculosis; Lt: Left; ICA: Internal carotid artery; IVH: Intraventricular hemorrhage; Rt: Right; FTP: Frontotemporoparietal; SDH: Subdural hematoma; B/l: bilateral; ICH: Intracerebral hemorrhage; CKD: Chronic kidney disease; DM: Diabetes mellitus; SHT: Systemic hypertension; CAD: Coronary artery disease

implementation of enteral feeding ensure early recovery [13, 14].

2. Case Presentation

This was a retrospective analysis study on the data of patients admitted to the neurosurgery ICU at PSG Institute of Medical Sciences and Research, Coimbatore, India, from October 2020 to February 2022. The patients admitted with acquired brain injury (trauma, stroke, and meningoencephalitis) who stayed in the ICU for more than 7 days with a poor Glasgow Coma Scale (GCS<10) were considered a standard and reliable factor to be included in the study. PSH-AM scale was the scoring system adopted in the study to diagnose PSH. The patients admitted with metabolic encephalopathy and acquired brain injury who had less than one week of staying in the ICU and a GCS score of more than 10 were excluded from the study.

3. Discussion

Of the 412 patients admitted to the neurosurgery ICU with acquired brain injury, 11 patients (2.6%) were diagnosed with PSH. Findings of all 11 patients are provided in Table 2, Table 3, and Table 4. In this study, trauma (72%) was the leading cause of the development of PSH. A minority of the patients with stroke (18%) and meningoencephalitis (9%) also developed PSH. Individuals with ages less than 40 years (63%) were more vulnerable to developing PSH. All patients (100%) developed PSH after 1 or 2 weeks of acquired brain injury. About 72% of patients had features of PSH for more than 2 weeks and 80% of patients developed episodes of PSH as paroxysms. As discussed in the potential mechanisms of PSH, most of the patients in the study had pathology in any of the following regions, including the epithalamus, thalamus, subthalamus, hypothalamus, brainstem, or corpus callosum. Patients with comorbidities, such as diabetes, hypertension, and coronary artery disease had poor outcomes. Patients with associated injuries in the chest, abdomen, spine, or long bone had a high chance to develop PSH with poor outcomes. All patients (100%) had developed at least two PSH episodes per day even with mild stimuli, such as positioning, suctioning, and sponging that persisted for at least 3 consecutive days. Tachycardia and tachypnoea were the most common symptoms noted in all patients. Dystonic posturing was the least persistent feature noted in less than 45% of patients and about 80% to 90% of patients presented with hypertension, hyperthermia, and diaphoresis. About 45% of patients developed 2 or more symptoms simultaneously which responded well to the medications used to reduce sympathetic activity. Decompressive craniectomy or ventriculoperitoneal shunt (depending upon the primary pathology) was required for 45% of the patients who were diagnosed with PSH, and 91% of the patients needed a tracheostomy to wean off from the mechanical ventilation. The hospitalization period increased by at least 14 days in all PSH patients compared with other brain injury cases without PSH. The functional outcome of PSH patients was assessed by the Glasgow Outcome Score (GOS) which was less than 3 in 72% of PSH patients at the time of discharge. It was on the poorer side compared with non-PSH patients.

4. Conclusion

PSH is a condition characterized by hyperthermia, hypertension, tachycardia, tachypnea, diaphoresis, and dystonia following non-noxious stimuli in acquired brain injury. The PSH-AM is a method adopted by many centers to confirm PSH. Management strategies, including the treatment of primary disease with a combination of medications to overcome sympathetic hyperactivity and early tracheostomy in ventilator-dependent patients, helped in achieving better recovery for the affected patients. It is the responsibility of the treating doctor to make the bystander understand the severity of PSH and the morbidity associated with it.

Ethical Considerations

Compliance with ethical guidelines

Written informed consent was obtained from all patients. The Institutional Ethics Committee approval was obtained and this study complies with ethical guidelines.

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Authors' contributions

Conception, design, data collection, data Analysis and Interpretation: Jayaprakash Duraisamy; Drafting the manuscript, critically revising, reviewing the final version of the manuscript and final version approval: All authors.

Conflict of interest

The authors declare that they have no conflict of interest to disclose.

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