

Sympathetic hyperactivity syndrome following cerebral fat embolization

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ABSTRACT

To date, there have been no reports of paroxysmal sympathetic hyperactivity syndrome (PSHS) associated with cerebral fat embolization. We describe the case of a young male who developed acute brain injury and acute hypoxemic respiratory failure secondary to significant fat embolization following a traumatic femur injury. Our patient demonstrated episodes of significant hypertension, tachycardia, fever and extensor posturing. Extensive evaluation lead to the diagnosis and appropriate treatment for PSHS. Ultimately, the patient went on to have a good neurologic recovery after a prolonged hospitalization. We will discuss PSHS diagnostic criteria, pathophysiology and treatment options. This diagnosis should be considered in all brain-injured patients with paroxysms of autonomic instability and abnormal movements.

Key words: acute brain injury, myoclonic encephalopathy, fat embolism, autonomic nervous system diseases, adult respiratory distress syndrome, wound, injuries

Introduction

We report a case of a young male with a femur fracture following a motor vehicle collision who develops cerebral fat embolization. As a consequence of his brain injury he develops a constellation of signs/symptoms consistent with Paroxysmal Sympathetic Hyperactivity Syndrome (PSHS). This clinical presentation is one of sympathetic autonomic dysfunction. Four of the 6 following criteria (tachycardia, fever, hypertension, tachypnea, diaphoresis or extensor posturing) are necessary for diagnosis. Awareness of this syndrome will lead to a timely diagnosis and appropriate therapy.

Case report

A 21 year-old male was involved in a

high-speed motor vehicle collision. His past medical history was significant for methamphetamine abuse. Injuries were limited to a mid-shaft femur fracture with an open distal patellar fracture. On the evening of the injury, he underwent irrigation and debridement with antibiotic bead placement for his open fracture along with a proximal tibial traction pin for temporary stabilization. There were no immediate intraoperative complications and the patient was transferred to an orthopedic general care unit after satisfactory anesthetic recovery. Approximately fourteen hours postoperatively, he developed sudden onset of confusion and agitation associated with chest pain, dyspnea, tachycardia, hypoxemia, and hypotension. The rapid response team was called to his bedside. He was subsequently intubated for hypoxemic respiratory failure and transferred to the intensive care unit (ICU) with the presumptive diagnosis of an embolic syndrome (fat vs. thromboembolic).

Physical examination was unremarkable except for his lower extremity injuries and scattered crackles anteriorly on lung auscultation. No petechial rash was identified. A portable chest film showed new bilateral infiltrates. An emergent chest computed tomography (CT) angiogram did not demonstrate any filling defects. Bilateral parenchymal interstitial changes consistent with edema were noted. Transthoracic echocardiogram revealed moderately reduced right ventricular (RV) function with dyssynchronous interventricular septal motion, right ventricular systolic pressure of 44 mm Hg (systemic pressure was 108 mm Hg) and a dilated inferior vena cava (IVC). Left ventricular (LV) ejection fraction was reduced (48%), but no regional wall motion abnormalities were seen. Laboratory data were unremarkable except for mild leukocytosis and anemia. The ratio of partial pressure of oxygen in arterial blood to fraction of inspired oxygen (P/F ratio) was 100. A working diagno-

sis of acute respiratory distress syndrome (ARDS) secondary to fat emboli syndrome was made. A lung-protective ventilation strategy and other supportive measures were employed.

On ICU day 2, femur stabilization with an external fixation device and patellar tendon repair occurred without complication. A chest film demonstrated improving bilateral infiltrates with a corresponding increase in his P/F ratio. During a sedation holiday on ICU day 3, the patient experienced 2 episodes of extensor posturing in all extremities with eye deviation and masseter muscle rigidity. These spells appeared to have resolved with intravenous benzodiazepines and fosphenytoin loading. Head CT was negative for any acute intracranial pathology. Physical exam demonstrated new petechiae over his upper chest and axilla. Despite therapeutic phenytoin levels, the patient continued to have episodes of extensor posturing, tachycardia, tachypnea, profuse sweating and fevers on ICU day 4. Electroencephalogram (EEG) monitoring demonstrated no epileptogenic activity during these spells.

A neurology consultation was requested for these spells and the patient was subsequently diagnosed with PSHS. An

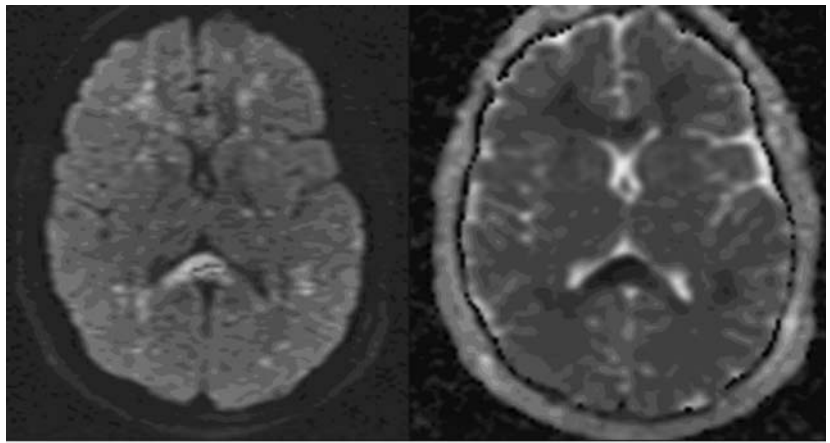


Figure 1: "Starfield" pattern seen in cerebral fat embolization characterized by innumerable foci of restricted diffusion, predominantly within the subcortical and deep white matter, but also involving the thalamus, basal ganglia and corpus callosum.

magnetic resonance imaging (MRI) was obtained and demonstrated changes consistent with cerebral fat embolism with innumerable foci of restricted diffusion within the subcortical and deep white matter involving both infra and supratentorial regions. The imaging was consistent with the "star field pattern" of cerebral fat emboli (figure 1). (1) The treatment of the PSHS included clonidine, gabapentin, morphine, propranolol and lorazepam. Ultimately, the spells decreased in frequency and duration.

On ICU day 15, he was transferred to a general neurology floor. He was obtunded, had intermittent eye opening, and did not follow any commands. He had undergone tracheostomy and percutaneous gastrostomy tube placement. Prior to dismissal from the hospital, the patient became more alert and interactive. This improvement resulted in admission to brain rehabilitation program 51 days post injury. Ultimately, his spells resolved and he was weaned from all neuroleptic medications. After

Table 1. Differential diagnosis of paroxysmal sympathetic hyperactivity syndrome.

	PSHS	Seizures	NMS	MH	Serotonin Syndrome	Sympathomimetic Syndrome
History	Acute brain injury	Acute or remote brain injury, epilepsy syndrome	Neuroleptics – initiation or dose titration	Volatile Anesthetics &/or Succinylcholine	SSRI, serotonin agonists (fentanyl, triptans), amphetamines or cocaine	Amphetamines, MDMA, cocaine
Treatment	Symptomatic	Antiepileptic agents	Cessation of neuroleptics Bromocriptine	Discontinue triggering agents Dantrolene	Benzodiazepines Cyproheptadine	Symptomatic support Benzodiazepines Haloperidol
Clinical Signs	Altered mental status Hyperthermia Autonomic dysfunction Muscle Rigidity	Altered mental status Eye deviation Autonomic dysfunction Muscle Rigidity	Altered mental status Hyperthermia Autonomic dysfunction Muscle Rigidity	Altered mental status Hyperthermia Autonomic dysfunction Muscle Rigidity	Altered mental status Hyperthermia Autonomic dysfunction Muscle Rigidity	Altered mental status Hyperthermia Autonomic dysfunction Muscle Rigidity
Onset	variable	variable	24-72 hours	Immediate to a day	6-24 hours	Immediate to a day
Laboratory/Diagnostic	none	Electroencephalogram	Elevated serum creatine kinase	Elevated serum creatine kinase	none	Tox Screen

NMS, Neuroleptic Malignant Syndrome; MH, Malignant Hyperthermia; MDMA, 3,4-methylenedioxy-N-methylamphetamine/"Ecstasy"; PSH, Paroxysmal sympathetic hyperactivity syndrome; SRI, Serotonin Reuptake inhibitors.

completion of his in-patient rehabilitation the patient was dismissed to his parents' home ninety-three days post initial injury.

One year following injury, the patient continues to live at home and is working at the family business. He is independent in all Activities of Daily Living (ADL's), but continues to have issues with mild cognitive impairment and impulse control.

Discussion

In this case, fat embolization in the setting of a long bone fracture resulted in a significant global central nervous system insult. This insult caused a constellation of signs and symptoms known as PSHS not previously described in the setting of cerebral fat embolization.

Fat embolism syndrome is a well-described event often associated with long bone injuries or surgical techniques requiring bone marrow space pressurization. It is characterized by a classic triad of findings including hypoxia, mental status alteration (confusion to coma) and a petechial rash. The first two criteria are nonspecific, and the third is often considered pathognomic for fat emboli despite it being present only ~20 % of the time.

Paroxysmal sympathetic hyperactivity syndrome was first described over 80 years ago as diencephalic autonomic epilepsy. (2) However, a comprehensive review references thirty-one different terms used to describe this phenomenon. (3) Rabinstein and colleagues proposed criteria and nomenclature that describes this constellation of signs and symptoms as paroxysmal sympathetic hyperactivity syndrome in an attempt to standardize diagnosis and nomenclature. Accordingly, a diagnosis is achieved if 4 of the 6 following criteria are met: tachycardia, fever, hypertension, tachypnea, diaphoresis or extensor posturing. (4) To our knowledge, this

is the first case to describe PSHS as a consequence of cerebral fat emboli. There have been multiple descriptions of PSHS as a result of traumatic brain injury, anoxic brain injury, (3,5,6) intracranial tumors, (2,7-9) and hemorrhage. (10,11)

Pathophysiology

The underlying pathophysiology of PSHS is poorly understood but it is felt to represent dysregulation of the autonomic nervous system. Initially it was believed to be a result of seizures occurring within the diencephalon, however, there has been no EEG evidence to support that belief in patients exhibiting PSHS. (7,8,10,12) Case reports involving PSHS utilizing anti-convulsant therapy were unsuccessful at controlling these spells. (7,12) Certainly seizure activity may cause a similar clinical picture, and Metz et al. were able to treat a patient with an ictal EEG correlate successfully with anti-convulsant therapy. (13) Rather than attribute the paroxysm to seizure activity, Bullard was the first to propose a disconnection type theory in which loss of control from higher cortical and subcortical centers leads to the dysregulated autonomies. (12) Baugely et al. refer to conventional disconnection theories suggesting that one or more separate sympathetic-excitatory centers in the hypothalamus and brainstem actively drive paroxysms once "released" from higher control. (13) Implicated sites of damage have ranged from diencephalon to brainstem and include regions such as the periventricular hypothalamic nucleus, lateral periaqueductal gray substance, lateral parabrachial nucleus, or rostral ventral medulla among others. (6,10,12) More recently Baugely has proposed that these centers themselves are inhibitory. Thus, damage to these structures results in uncontrolled excitatory spinal cord processes and

proposes an excitatory: inhibitory ratio model to explain observations in patients with PSHS following head trauma and with similar central nervous system conditions. (13) Regardless of the precise mechanism, there is a net increase in sympathetic activity with a measurable increase in serum catecholamine levels during paroxysms. (11) However, measuring serum catecholamine levels is not essential to diagnose PSHS.

Treatment

Treatment is supportive and focused on symptomatic relief during catecholamine surges. Multiple medications have been used successfully in the treatment of PSHS. While no single medication has universally been successful, opioids (morphine) and beta blockers (propranolol) seem to be the most efficacious. Other medications cited in the literature include: bromocriptine, benzodiazepines, clonidine, dantrolene, intrathecal baclofen and more recently gabapentin and dexmedetomidine.

Differential Diagnosis

PSHS has clinical features similar to other syndromes that can make diagnosis difficult. Awareness of the subtle differences of these diagnoses will lead to timely and appropriate therapy. Table 1 outlines conditions which can mimic PSHS.

Conclusion

Paroxysmal sympathetic hyperactivity syndrome presents unique challenges to physicians treating brain-injured patients. Unpredictable autonomic discharges can lead to large swings in hemodynamics and abnormal movements. It is important for all physicians caring for brain-injured patients to be aware of PSHS and to familiarize themselves with treatment regimens; as inappropriate diagnosis may lead to unnecessary ineffective interventions and therapies.

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