University of CINCINNATI
Emergency Medicine

ANNALS OF B POD

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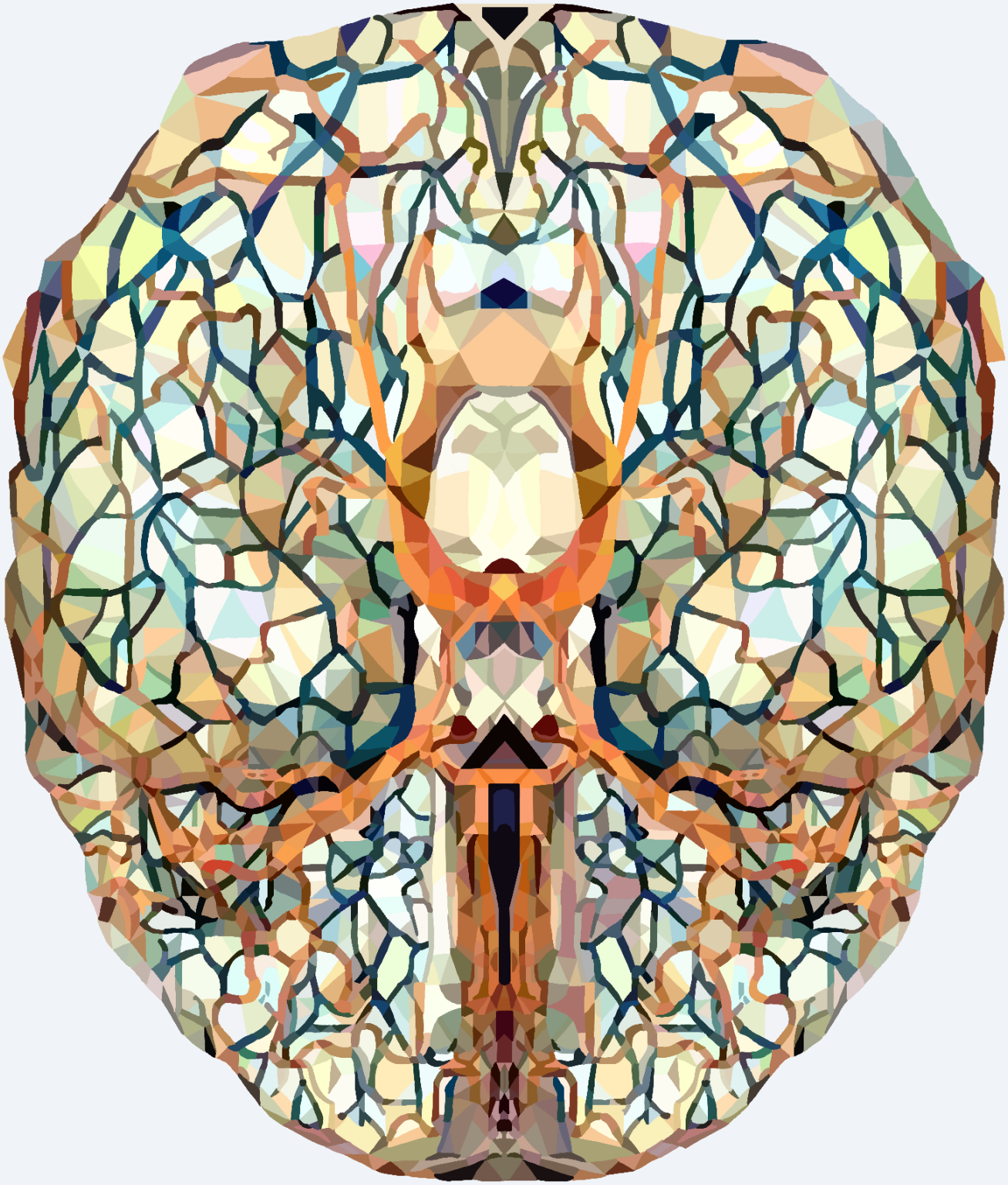
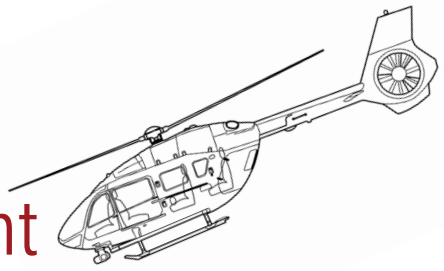
Volume XII Issue II
Winter Issue 2019



ANNALS OF B POD
WINTER 2019

Winter is coming in B pod and in this issue we explore explore several of the interesting presentations our residents encounter on every shift! We dive into the critical care management in the air of a patient decompensating from a massive pulmonary embolism, sodium managment in hyponatremic patients, the diagnosis and management of neurogenic shock, and the rare presentation of a patient with dural venous thrombosis. Join us as our authors present the evidence behind our interventions and prepare you to care for these interesting disease processes.

Air Care Annals: Pulmonary Embolism Management



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History of Present Illness

Air Care was dispatched for an inter-facility transfer of a female in her 80s who initially presented with shortness of breath and was found to have a saddle pulmonary embolism. Prior to Air Care's arrival, the patient developed acute hypoxic respiratory failure requiring endotracheal intubation. Following intubation, the patient experienced two distinct episodes of hypoxia leading to pulseless electrical activity (PEA) arrests. Standard ACLS was performed and atropine was administered during the initial PEA arrest leading to return of spontaneous circulation (ROSC). During the second PEA arrest, epinephrine was administered with immediate ROSC. Following the second arrest, 100mg of tPA was administered.

Past Medical History	Allergies
Depression	Codeine
Hypertension	Penicillin
Obesity	

Vitals

HR 30 RR24 BP 92/50 O2 Sat 82%
Ventilator Mode: Volume Control (Assist Control)
Tidal Volume: 400mL
PEEP: 14
FiO2: 100%

Physical Exam

The patient was an elderly obese female who was intubated and unresponsive. The patient was bradycardic with no murmurs, rubs, or gallops. The patient was unresponsive and comatose with no motor movement to painful stimulus. Her skin and abdominal exams were within normal limits.

Pre-Hospital Course

Given the patient's presentation to a hospital without intensive care capabilities, this patient required critical care transportation to a higher level of care. When the medical crew arrived, the patient remained bradycardic and hypoxic, and shortly thereafter experienced a third PEA arrest. CPR was initiated and 1 mg of epinephrine was administered. Following two minutes of CPR, ROSC was achieved. Post-ROSC, an amp of calcium chloride was administered. The patient's initial ventilator setting of positive end expiratory pressure (PEEP) was decreased to 10 cm H2O to decrease the intrathoracic pressure and improve the patient's preload.

After exchanging the outside hospital ventilator for Air Care's transport ventilator, the patient's respirations became dyssynchronous and she was sedated with ketamine. Although dyssynchronous, the patient did not exhibit bradycardia at that point and had oxygen saturations between 80-88%. Given the patient's critical condition, the medical crew elected to load the patient in the aircraft and continue to optimize ventilator settings throughout transport.

En route, the ventilator was changed from volume control to pressure control with a PEEP of 8. The patient became more synchronous with the ventilator and maintained stable oxygen saturations while having significant improvement in mean arterial pressure from 67mmHg to 96mmHg. Upon arrival to the receiving hospital, the patient remained stable,

though critically ill, and was transported to the hospital's cardiovascular intensive care unit (CVICU).

Hospital Course

One day after arrival to the hospital's CVICU, the patient was extubated to nasal cannula at 3 liters per minute and subsequently maintained an oxygen saturation between 92-95%. Following extubation the patient was neurologically intact. Given that the patient had received tPA, she was not considered a candidate for thrombectomy and was continued on a therapeutic heparin drip. Four hours post-extubation, the patient experienced confusion and difficulty moving her left upper and lower extremities. An emergent CT scan demonstrated a large intraparenchymal hemorrhage. Ultimately the patient's family choose hospice care for the patient.

Discussion

The incidence of pulmonary embolism is approximately 60-70 per 100,000 people with a mortality rate of approximately 30% when left untreated and 8% when treated appropriately.[1] While significant data exists regarding thrombolytics in patients with pulmonary embolism, there is limited research on the medical optimization of these patients prior to therapy. This discussion serves to describe the pathophysiology of hemodynamic decompensation in the setting of pulmonary embolism and optimal medical management of these challenging patients.

Pathophysiology

The pathophysiology of a massive pulmonary embolism is directly related to right ventricular function. For a patient with no previous cardiopulmonary disease, the right ventricle will function normally until approximately 25-30% of the pulmonary vasculature is obstructed by thrombus. Once this threshold is reached, pulmonary arterial pressure begins to rise from the normal value of 8-20 mmHg due to physiologic vasoconstriction of the pulmonary vasculature in response to hypoxia. Patients will then begin to experience signs and symptoms of pulmonary embolism such as dyspnea, tachycardia, and pleuritic chest pain.[2] As clot burden approaches 50-75% of the pulmonary vasculature and pulmonary arterial pressures start to eclipse 40 mmHg, the right ventricle begins to dilate and right ventricular stroke volume decreases

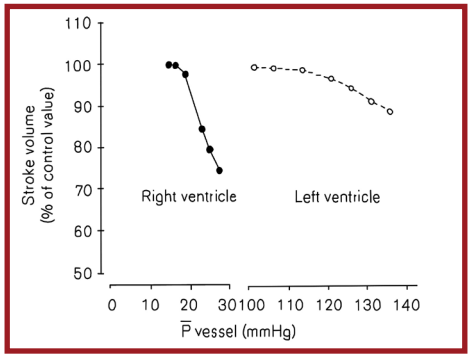

Figure 1: A graph depicting the effect of arterial pressures on right and left ventricular stroke volumes

abruptly. This is because right ventricular stroke volume is more sensitive to afterload when compared to the left ventricle (Fig. 1).[3]

Right ventricular wall stress (pressure x radius) is inversely proportional to right ventricular oxygen uptake. Therefore during acute pulmonary embolism, the right ventricle slowly starts to become ischemic. Right ventricular dilation additionally leads to decreased cardiac output. Cardiac output is reduced due to both decreased stroke volume and septal shift into the left ventricle. Right ventricular septal shift decreases left ventricular distensibility and ultimately left ventricular end-diastolic volume, further lowering the overall cardiac output.[3] All of these changes lead to profound obstructive and cardiogenic shock. This cycle, colloquially known as the "death spiral of pulmonary embolism," can be prevented with prompt diagnosis and optimal hemodynamic management.

Volume Resuscitation

The primary treatment for pulmonary embolism is to reduce clot burden and pulmonary vascular resistance via anticoagulation and/or thrombolysis. Providers can assist the patient who continues to decompensate despite appropriate treatment by optimizing the patient's preload. In the setting of

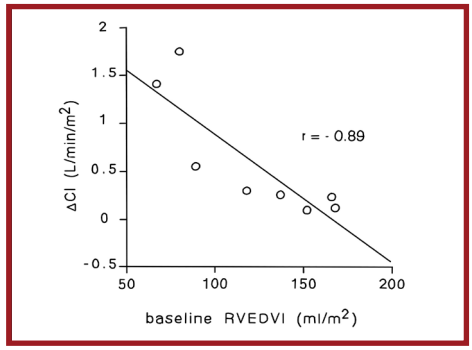

Figure 2: A graph depicting the effect of baseline right ventricular end diastolic volume to change in cardiac index

right ventricular dilation, providers must be judicious in the amount of fluid administered. A prior study done by Mercat et al. (1999) demonstrated that a 500 mL bolus given over 20 minutes had a variable effect on hemodynamics in those with acute massive pulmonary embolism. This variable effect is likely based on the patient's initial right ventricular end-diastolic volume (RVEDV).[5,6,7] Unfortunately, prehospital providers cannot measure RVEDV directly and must instead administer fluid based on hemodynamic response. In patients with dilated right ventricles, cardiac output decreases with additional fluid administration (Fig. 2). If fluid is continuosly administered to the already dilated RV, the septum is shifted further into the left ventricle and accelerates the vicious cycle described previously, resulting in worsening shock. Although volume may provide benefit in those are that are initially hypovolemic, clinicians should only administer small volume boluses and quickly abandon further volume resuscitation and move to pressor support if no measurable response is made to fluid administration.

Avoiding Intubation

Patients with pulmonary embolism develop tachypnea and hypoxia, prompting providers to consider intubation. In the setting of tenuous hemodynamics due to right ventricular failure, intubation can lead to acute decompensation and cardiac arrest. If intubation must be performed, it is important to consider the downstream effects and prevent post-intubation decompensation. When performing rapid sequence intubation, providers must remain vigilant when selecting induction agents. Patients in shock have a very high intrinsic sympathetic tone, and induction agents often cause hypotension when this tone is lost. Once the patient is intubated and receives positive pressure ventilation, he or she will experience an immediate reduction in right ventricular preload due to increased intrathoracic pressure. Providers should be aware of this phenomenon and put ventilated patients on the minimal amount of PEEP that allows adequate oxygenation. Providers also must be aware of the effect of tidal volume and respiratory rate on pulmonary vascular resistance. An appropriate tidal volume must be selected to minimize both the resistance of extra-alveolar vessels and intra-alveolar

Annals Air Care
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Osmotic Demyelination Syndrome

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History of Present Illness

The patient is a male in his late 30s with a past medical history of alcohol abuse and hypertension who presented to the emergency department (ED) with a chief complaint of urinary incontinence and altered mental status. His symptoms started 18 days ago when he first noticed gait problems. He presented to the ED on day seven of symptoms, at which point his gait abnormalities worsened and he had associated seizures. At that time, he had an ataxic broad-based gait and fell backwards while walking. He was hyponatremic with a sodium of 109 and had a witnessed seizure in the ED. He was given hypertonic saline and admitted to the medical intensive care unit (MICU) for further management. His sodium was gradually corrected at a rate of 4-6 mEq per day. On hospital day three he left against medical advice (AMA); his sodium that morning was 126 and he continued to have an ataxic gait but was able to ambulate 30 steps unassisted.

He was seen in another ED 13 days after his initial presentation for ataxia and confusion and was diagnosed with alcohol withdrawal syndrome and discharged with a lorazepam taper. He presented to the ED again on day 18 of symptoms with worsening mental status and was no longer able to ambulate or perform his activities of daily living (ADLs). At this time, the patient's mental status deteriorated to the point that he could answer simple questions but could not provide any additional history.

Past Medical History

Alcoholism, Hypertension

Past Surgical History

None

Medications

Folic Acid, Thiamine, Multivitamin, Metoprolol, Lisinopril-HCTZ, Lorazepam

Allergies

No known

Diagnostic Work-up

5.2	12.1 / 33.9	266		
137	100	14	92	
4.4	28	1.03		

AST 33 /ALT 28
Total bilirubin 0.6
Ammonia 83
Folic acid 24.8
Vitamin B12 1430

UDS: Positive for benzodiazepines

CXR: Normal
Non-contrast CT Head: Normal

Vital Signs

T97.7 HR 62 RR 12 BP 157/104 O2 Sat 100%

Physical Exam

The patient appears well nourished but disheveled. He is alert and oriented to person, place, and time. His speech is delayed but he is able to answer simple questions. Extraocular movements show vertical and horizontal nystagmus with roving eye movements. The remainder of his cranial nerve exam is normal. He has normal strength in bilateral upper and lower extremities, and his sensation to light touch is grossly intact. His reflexes are normal throughout with down going Babinski bilaterally. His finger to nose testing is slow with dysmetria bilaterally but worse on the right. He has slow rapid alternating movements. He is unable to take a step unsupported. He has no asterixis in his upper extremities. The rest of his exam is unremarkable.

Hospital Course

The patient was given intravenous thiamine, folic acid, and a multivitamin for presumed Wernicke's encephalopathy. He was admitted to medicine and started on high dose thiamine replacement. He went on to develop pseudobulbar affect on hospital day one with inappropriate emotional lability, and neurology evaluated the patient. An MRI was performed and was consistent with osmotic demyelination syndrome (ODS; previously referred to as central pontine myelinolysis) and severe cerebral and cerebellar volume loss. A representative image of the patient's MRI is shown below.

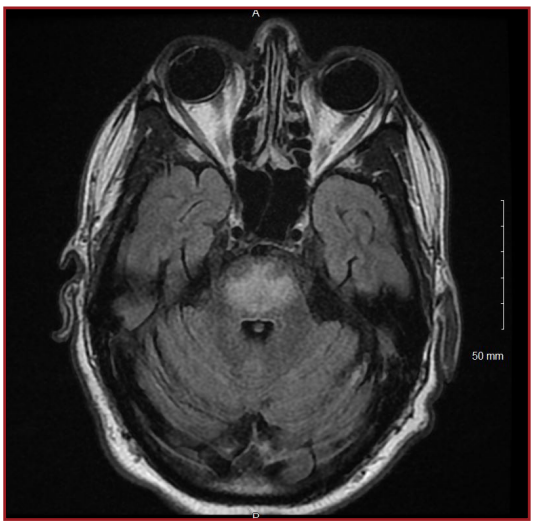

Image 1: Patient's MRI showing cerebellar and cerebral volume loss consistent with ODS

The patient was unlikely to have neurologic benefit from reducing sodium levels to previous state given the amount of time that had elapsed since correction. He received five treatments of plasmapheresis with improvement in his symptoms. He was discharged on hospital day 17 with significant improvement in his dysmetria and gait. He was able to ambulate with minimal assistance and complete ADLs with minimal difficulty.

Discussion

Pathophysiology

Sodium is the primary determinant of serum tonicity. When the concentration of sodium in the serum decreases, water traverses the blood brain barrier and enters brain cells in an attempt to maintain isotonicity with the surrounding environment. This movement of water causes the cells to swell, and this triggers several protective mechanisms which attempt to maintain normal cell volume. Within minutes, the increased intracranial pressure and hydrostatic force pushes interstitial fluid into the cerebrospinal fluid. Cellular edema activates channels within the cell membrane releasing potassium, chloride, taurine, glutamate, aspartate, myo-inositol, and other osmotic solutes into the interstitial space.[1] As these osmotic substances pass into the surrounding interstitial fluid, water follows, allowing brain cells to remain isotonic with their surrounding environment without large increases in intracellular water or cell volume. Substantial intracellular osmolyte depletion and fluid shifts occur within the first 24 hours, and full adaptation is complete within 48 hours.[1]

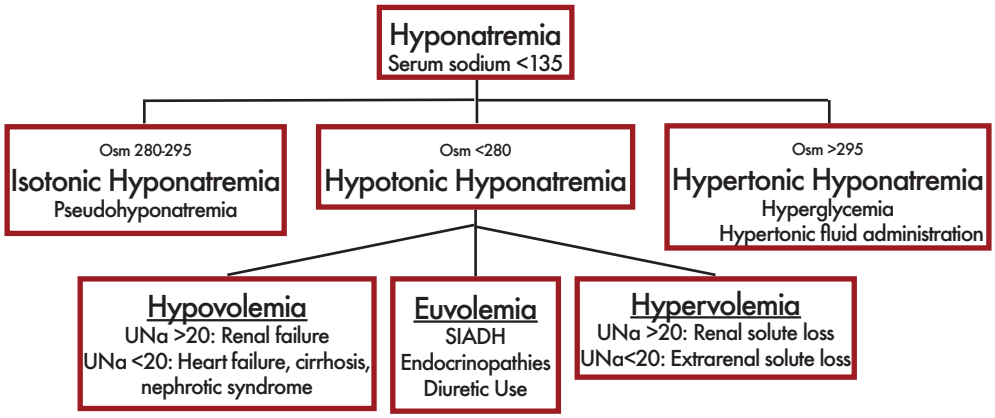

Figure 3: A graph depicting the different classifications and etiologies of hyponatremia based on tonicity and volume

When hyponatremia is corrected, the serum sodium increases and extracellular tonicity begins to rise. Brain cells must once again adapt to a now relatively hypertonic environment. Inorganic ions such as sodium, potassium, and chloride now move back into the depleted cells. Further adaptation relies on the transport and synthesis of organic osmolytes within the cells, however this process takes much longer.[2,3] When replenishment of organic intracellular osmolytes cannot keep up with the rate of rise in serum tonicity, fluid shifts from the intracellular environment into the interstitial fluid in an attempt to maintain isotonicity. The shift of inorganic ions into the cell coupled with the shift of free water out of the cell results in cell shrinkage and intracellular hypertonicity.[2,3] These cause cellular damage and apoptosis. Astrocytes and oligodendrocytes are particularly susceptible to these changes, and death of these cells ensues within 24 hours leading to the development of ODS.[1,4,5] Several studies have demonstrated that the pons is the slowest region of the brain at restoring intracellular organic osmolytes, making this area of the brain most susceptible to demyelination.[6,7]

Clinical Presentation

ODS includes the more common central pontine myelinolysis (CPM), as well as extrapontine myelinolysis (EPM), which occurs in addition to CPM in approximately 10% of cases.[8] Osmotic demyelination syndrome typically presents two to six days following overcorrection or rapid correction of hyponatremia.[1,9,10,11] Patients typically present with a multiphasic history initially with acute decompensation due to significant hyponatremia followed by a brief recovery phase as the patient becomes normonatremic. Patients who develop ODS then further decompensate after this brief recovery period. The initial symptoms of ODS include dysarthria, dysphagia, and pseudobulbar palsy due to involvement of the corticobulbar tracts. Late symptoms include flaccid paralysis that becomes spastic due to involvement of the corticospinal tracts, diplopia, disorientation, confusion, altered mentation, seizures, coma, and locked in syndrome.[1,9,10] Osmotic demyelination can extend into other sites including the cerebellum, lateral geniculate, external capsule, hippocampus, putamen, cerebral cortex, thalamus, and caudate nucleus. EPM can lead to movement disorders including catatonia and parkinsonism, as well as behavioral and psychiatric disorders.[1,9] The prognosis of ODS varies wildly from no residual deficit to profound neurologic deficits and even death due to complications of the disease. In general, the deficits associated with ODS are typically permanent and severe.

ODS is more common in patients with a serum sodium <120, particularly in those who are chronically hyponatremic.[10] Patients with liver disease, especially liver transplant patients, have been shown to be at a significantly increased risk of ODS. One study demonstrated the incidence of CPM in liver transplant patients to be up to 30%.[12] Although this predisposition is not entirely understood, it is believed to be because this patient population frequently has concomitant hyponatremia and malnourishment, making them ill-equipped to replenish the osmolytes necessary to combat fluctuations in serum tonicity.[15]

Due to the wide range of symptoms that may be present in ODS, it can be difficult to distinguish from other disorders. Patients with ODS often present with normal sodium, and if the emergency physician is not aware that the patient has been previously hyponatremic this diagnosis can be missed. In such cases, the diagnosis must be suspected based on physical exam and history, as emergency physicians are unlikely to order a diagnostic MRI without significant clinical suspicion. Some key risk factors that should raise clinical suspicion of ODS are chronic alcohol abuse, chronic malnutrition, liver disease, or liver transplant. Recent history of acute illness from which the patient recovered and then subsequently decompensated again is extremely suspicious for ODS, particularly in a patient with significant risk factors.

Differential and Diagnosis

The differential diagnosis of ODS includes intracranial hemorrhage, acute ischemic stroke, Wernicke's encephalopathy, acute intoxication, and various metabolic derangements. Intracranial hemorrhage and ischemic stroke often present with focal neurologic deficits and acute onset as opposed to the subacute presentation of ODS.

Osmotic Demyelination
continued on page 14

Neurogenic Shock

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History of Present Illness

A male in his 50s with a history of human immunodeficiency virus (HIV), hepatitis C, and hypertension presented to the emergency department (ED) via ambulance following a single motor vehicle collision. The patient was the restrained driver who crashed into a utility pole. Per emergency medical services (EMS), the patient had a decreased level of consciousness at the scene, which improved following administration of 0.5 mg of naloxone. The patient struck his head but it was unknown if he lost consciousness. On arrival to the ED, he complained of numbness throughout his arms, torso, and legs, and stated that he could not move his legs. He also endorsed shortness of breath. He denied headache, neck pain, chest pain, abdominal pain, nausea, and vomiting. He denied any use of anticoagulant agents although he was prescribed aspirin.

Past Medical History

HIV, Hepatitis C, Hypertension,
Diabetes mellitus, Bipolar disorder

Past Surgical History

Abdominal hernia repair

Medications

Aspirin, Atorvastatin, Lisinopril, Metformin,
Quetiapine

Allergies

Sulfa antibiotics

Vital Signs

Temp	HR	BP	RR	SpO2
98.8	94	84/48	14	92% on reservoir mask at 15L

Physical Exam

The patient was awake, alert, and immobilized on a backboard. A small right scalp abrasion was present. A cervical collar was in place with no midline cervical tenderness. All four extremities and the pelvis were non-tender with no obvious deformities. The thoracic and lumbar spines were non-tender without step-offs or deformity. The patient had a GCS of 15. He demonstrated occasional spastic flexion of his upper extremities and could not intentionally move his upper or lower extremities. Sensation to light touch was absent below the level of the nipple. He had no response to painful stimuli in the lower extremities. Rectal tone was absent. Patellar reflexes were absent with reduced muscle tone in all four extremities. Cardiac, pulmonary, and abdominal exams were normal.

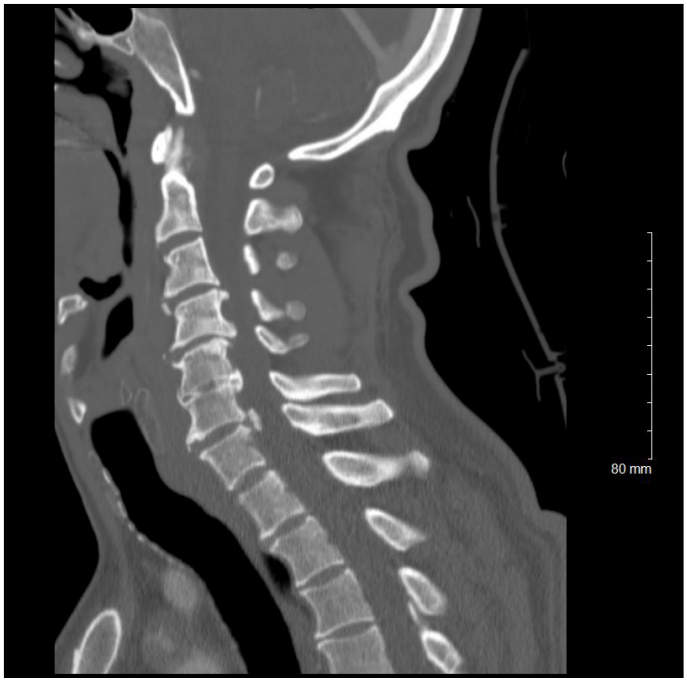

Image 2: Sagittal section of patient's CT depicting widening and offset C4-C5 vertebral bodies. Osteophyte complex with canal stenosis at C4-C7.

CT C-spine: Comminuted mildly displaced fracture of left transverse foramen of C4. Widening and offset of bilateral C4-5 facet joints. Osteophyte complex with severe canal stenosis at C4-5. Moderate to severe canal stenosis at C5-7.

CTA neck: Left > right vertebral artery contour irregularities at C4 concerning for focal dissection.

CT chest: Right hemidiaphragm elevation.

Hospital Course

While in the emergency department, the patient was hypotensive with a systolic blood pressure in the 80s without compensatory tachycardia or evidence of blood loss. A norepinephrine drip was started for treatment of presumed neurogenic shock with improvement of his systolic blood pressure to the 130s without additional fluid resuscitation. The patient was admitted to the neuroscience intensive care unit (NSICU) and underwent C3-T1 fusion with C3-C6 decompression on hospital day 0 (HD0). A 7-day mean arterial pressure (MAP) goal of 85 mmHg was established. This was achieved with a norepinephrine drip, midodrine, and pseudoephedrine until HD3, at which time a phenylephrine drip replaced the norepinephrine until HD8. The patient failed multiple extubation attempts after the procedure and a tracheostomy was eventually placed for prolonged ventilator weaning. His course was further

complicated by Serratia pneumonia and bacteremia on HD2, followed by methicillin-resistant Staphylococcus epidermidis bacteremia on HD20. He completed two full courses of antibiotics for each respective infection. Prior to discharge to a long-term acute care facility, the patient had 4/5 strength in his deltoids and 1/5 strength in his biceps bilaterally with paralysis and loss of sensation distal to the nipple line, consistent with a C6 American Spinal Injury Association (ASIA) A spinal cord injury.

American Spinal Injury Association (ASIA) Scale for Traumatic Spinal Cord Injuries		
Class	Symptoms/Findings	Overall recovery of ambulation
A Complete	No sensory or motor function is preserved in the sacral segments S4-S5.	2.5-10%
B Sensory incomplete	Sensory but not motor function is preserved below the level of injury, including the sacral segments.	33%
C Motor incomplete	Motor function is preserved below the level of injury, and more than half of muscles tested below the level of injury have a muscle grade less than 3	75%, moreso in patients <50yo
D Motor incomplete	Motor function is preserved below the level of injury and at least half of the key muscles below the neurological level have a muscle grade of 3 or more.	100%
E Normal	No motor or sensory deficits, but deficits existed in the past.	

Table 1: American Spinal Injury Association (ASIA) Scale classifications system (14,15)

Shock is defined as the failure of circulation to provide adequate oxygenation to meet cellular demand. To better identify and manage this compromised physiologic state, shock is subcategorized into four overlapping mechanistic models: hypovolemic, cardiogenic, obstructive, and distributive.[1] Neurogenic shock is a subset of distributive shock caused by a spinal cord injury (SCI) with associated loss of sympathetic innervation to the heart and systemic vasculature. With the sympathetic trunks damaged, the uninjured vagus nerve provides unopposed parasympathetic innervation to the heart. Clinically this causes hypotension and bradycardia, which are the hallmark features of neurogenic shock.[2]

It is important to note that neurogenic shock is distinct from spinal shock, which is the loss of sensation, motor function, and reflexes distal to a spinal cord injury that develops within 24 hours of the initial insult. The name derives from the return of some degree of function over time as the "shock" of acute cellular and metabolic derangements dissipates.[2] All further discussions of shock in this article will refer to neurogenic shock.

Although no universal objective parameters exist to formally define neurogenic shock, it is generally defined as a cervical or upper thoracic SCI with associated systolic blood pressure less than 90-100 mmHg and a heart rate less than 60-80 beats/minute. Because the T1 to T5 thoracic paraspinal ganglion provides sympathetic innervation to the heart, it is classically taught that cord injuries distal to this level should not cause neurogenic shock.[3] The incidence of neurogenic shock is indeed greater with higher SCIs. Approximately 25% of patients with cervical injuries and between 5-20% of patients with thoracic injuries develop neurogenic shock.[4] Contrary to classic teaching, lower thoracic and even lumbar SCIs have precipitated cases of neurogenic shock.[2] Bradycardia is not a universal finding early in neurogenic shock, often developing in the first few hours after injury in some animal models and over four days after injury in some humans.[5]

In the clinical arena, neurogenic shock can present with variable vital sign abnormalities on a widely variable timeline, making the diagnosis challenging. While neurogenic shock may seem easy to identify in patients who present with isolated SCIs, the traumatic context inherent to neurogenic shock places the burden on the emergency physician to rule out multiple other etiologies that may be contributing to the patient's inadequate perfusion.[6] Hypovolemia from blood loss, obstructive physiology secondary to cardiac tamponade or tension pneumothorax, and cardiogenic shock from cardiac contusion can all coexist in a patient simultaneously suffering from neurogenic shock. It is therefore critical to keep neurogenic shock in mind, particularly when evaluating and treating hypotensive patients who present after traumatic injuries.[3]

Three patterns of neurological deficits on physical exam comprise 90% of incomplete spinal cord injuries.[7] It is useful to review these patterns, as neurogenic shock is more commonly occurs in patients who present with these physical exam findings. The first is central cord syndrome, which typically is the result of a hyperextension injury. This causes the ligamentum flavum to exert pressure on the central aspect of the spinal cord. The crossing fibers of the pain-mediating spinothalamic tract and the medial descending fibers of the corticospinal tract that mediate motor control of the upper extremities are damaged with this type of injury. This classically results in decreased pain, temperature, and motor function in the upper extremities. Patients may present with abnormal upper extremity movement or arm pain only. The second pattern of deficits is anterior cord syndrome. This frequently occurs following a flexion injury that causes disruption of the anterior spinal artery that supplies the spinothalamic and corticospinal tracts. This results in bilateral loss of motor function and pain sensation below the level of injury but spares light touch sensation. The third and rarest of the incomplete cord injuries is Brown-Sequard syndrome. This is caused by complete hemisection of the cord, and is more likely to be seen in penetrating trauma. This injury causes ipsilateral loss of motor function, light touch sensation, and pain sensation at and below the level of the lesion. This injury also causes contralateral loss of pain sensation slightly below the level of the lesion due to the ascending pain fibers that have already crossed the anterior commissure further down in the cord.[8]

With other sources of shock being managed or ruled out with ultrasound and cross sectional imaging, it is prudent to initiate appropriate treatment for neurogenic shock and the complications of SCI as quickly as possible. Patients with a high SCI often require emergent airway inter-

Neurogenic Shock continued on page 11

Dural Venous Sinus Thrombosis

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History of Present Illness

The patient is a male in his 20s who presents to the emergency department (ED) with a chief complaint of headache. He has experienced an intermittent headache for the past month, located on the left side of his head. He describes the pain as aching and throbbing. He is unsure what has been causing the headaches and has not recognized any patterns. The headache worsened today and he had one episode of emesis prior to arrival. He also notes occasional photophobia and blurry vision in his left eye that resolves after closing the eye. He has been taking acetaminophen without relief. He denies fevers, neck pain or stiffness, and recent trauma. He denies a history of headaches and has no family history of migraines.

Past Medical History

None

Past Surgical History

None

Medications

Acetaminophen PRN
Ibuprofen PRN

Allergies

No known

Vital Signs

T	HR	BP	RR	SpO2
98.7	76	134/77	16	98%

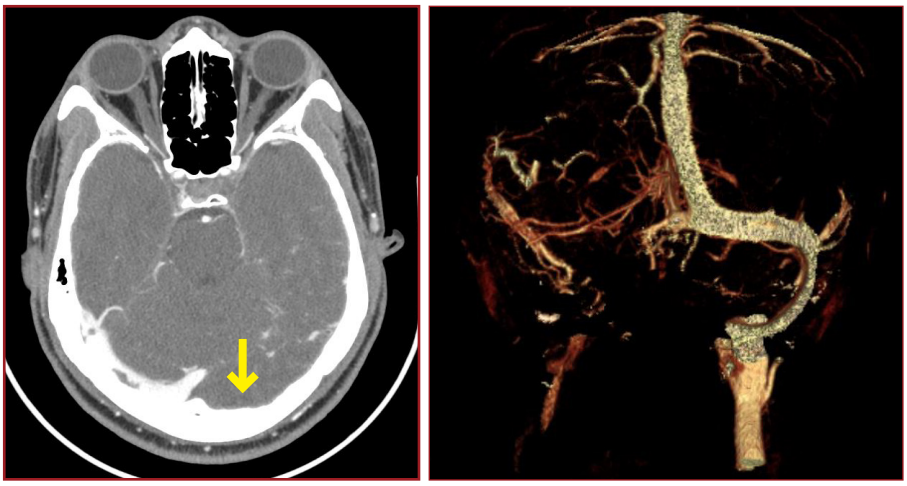
Physical Exam

The patient appears his stated age and is in no apparent distress. He has no signs of external trauma to his head. His pupils are equal, round, and reactive to light, and his extraocular muscles are intact without any notable deficits. He has mild ptosis of his left eye. His cranial nerve exam reveals numbness in the left face along the entire distribution of the trigeminal nerve. His strength and sensation testing is normal in bilateral upper and lower extremities. He performs the finger-to-nose test without difficulty. He exhibits no meningismus. He is observed ambulating in the emergency department without abnormal gait. Pulmonary and cardiac auscultation is normal. The patient's skin, vascular, and abdominal exams are normal.

Diagnostic Imaging

CT Head without contrast: mild increased density involving the left transverse sinus. CT venography is recommended to exclude venous sinus thrombosis

CT Angio Head w/wo contrast: Thrombosis of the left transverse sinus, left sigmoid sinus, and proximal left internal jugular vein.



Images 3 & 4: Left: Representative CTV, yellow arrow indicating lack of venous flow in the left transverse sinus. Right: Representative CTV of thrombosis of left transverse sinus, left sigmoid sinus

Hospital Course

The patient was treated symptomatically for his headache with 1L of lactated ringers, 10mg of prochlorperazine, and 15mg of ketorolac. The emergency department providers were concerned, given this was a new onset headache with neurologic findings including blurry vision, ptosis, and facial numbness. A non-contrast CT head showed a mild increased density involving the left transverse sinus, and radiology recommended CT angiography of the head to evaluate for venous sinus thrombosis. The patient's CT venogram showed a thrombosis of the left transverse sinus, left sigmoid sinus, and proximal left internal jugular vein. A heparin drip was started and both neurosurgery and neurology were consulted. Neurosurgery felt that no surgical intervention was necessary, and the patient was admitted to the neurology service. The patient was bridged with lovenox and was transitioned to warfarin on hospital day one. An MRI of the brain confirmed the findings seen on CT, showing an acute thrombosis of the left transverse sinus extending into the sigmoid and jugular bulb with no parenchymal abnormalities. The patient had a hypercoagulability workup that was unremarkable. He also had autoimmune testing that showed a positive ANA, dsDNA and SCL-70. These findings were felt to be non-specific and did not lead to a definitive diagnosis. He was discharged in good condition on hospital day five with outpatient rheumatology follow up.

Discussion

Cerebral venous thrombosis (CVT) is a rare disease that is challenging to diagnose. CVT is a spectrum of disease that includes thrombosis of the major dural sinuses (most common), the deep cerebral veins, and the cortical veins.[1] Although the term "dural sinus thrombosis" is often used interchangeably with CVT, it actually represents a specific subtype of CVT based on the location of the thrombosis. Anatomically, the cerebral venous drainage consists of the superficial and deep venous systems. The cortical veins drain into the major dural sinuses with a complex system of anastomosis and high variability in anatomy from person-to-person. The major dural sinuses include the superior sagittal sinus, inferior sagittal sinus, straight sinus, lateral sinus (consisting of the transverse and sigmoid sinus), cavernous sinus, and occipital sinus. All of the sinuses ultimately drain into the internal jugular vein (Figure 4).

CVT accounts for approximately 1% of all neurovascular disease and is three times more likely in women.[2,3] This female predominance is likely due to hypercoagulability secondary to pregnancy/puerperium and oral contraceptives. CVT is more common in young patients, with 80% of patients under the age of 50 and a median age of 39 years.[4] The International Study on Cerebral Vein and Dural Sinus Thrombosis identified that greater than 85% of patients with CVT have at least one risk factor.[3] Prothrombotic states such as Factor V Leiden and deficiencies of antithrombin III or protein C/S can increase the risk of CVT. Acquired conditions such as pregnancy, oral contraceptives use, or malignancy were noted in 34% of patients.[3] Infections, chronic inflammatory diseases, head trauma, and recent neurosurgical procedures were also identified as risk factors for CVT.

The pathophysiology of CVT is due to venous and CSF obstruction. Thrombosis of cerebral veins or dural sinuses obstructs blood drainage from brain tissue, resulting in increased capillary and intracranial pressure (ICP). This leads to decreased cerebral perfusion and ischemic injury to brain parenchyma. Cytotoxic edema develops and causes disruption of the blood-brain barrier. Vasogenic edema occurs from disruption of the blood-brain barrier, ultimately resulting in venous rupture and intraparenchymal hemorrhage (IPH).[5,6]

The clinical presentation of CVT is highly variable and predominantly depends on the location of the thrombosis, the time between onset of symptoms and hospital presentation, and the presence of parenchymal brain involvement. Clinical syndromes at presentation can be divided into four groups.[4,6] The first is isolated intracranial hypertension syndrome, which includes headache, vomiting, papilledema, and visual symptoms. The second syndrome consists of focal motor or sensory deficits. The third syndrome presents with new onset seizures. The final syndrome presents with global encephalopathy and is more common in elderly patients.[7]

Overall, headache is the most common symptom of CVT and is found in ~90% of patients.[3] The headache may be sudden in onset and severe, mimicking subarachnoid hemorrhage, or it may be persistent and gradually worsening. The location of the headache has no spatial relationship with the occluded sinus or parenchymal lesions.[8]

Cerebral Venous Thrombosis: Clinical Syndromes	
1	Simulates isolated intracranial hypertension: Headache, vomiting, papilledema, visual symptoms
2	Focal motor or sensory deficits
3	New onset seizures
4	Global encephalopathy *More common in elderly patients

Table 2: Cerebral venous thrombosis clinical syndromes

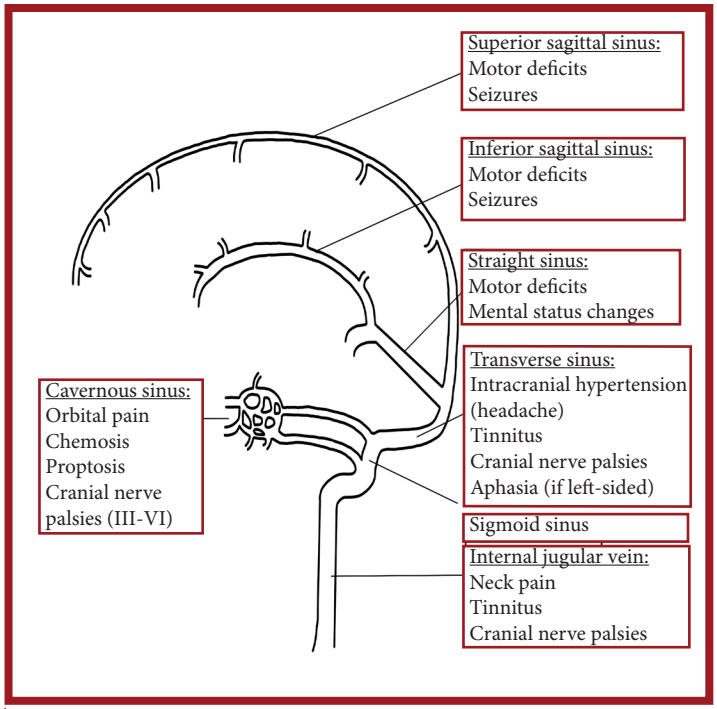


Figure 4: Anatomical locations of different venous sinuses with associated symptoms

Isolated thrombosis of a specific dural sinus produces classic symptomatology. Cortical vein thrombosis causes motor and sensory deficits with concomitant seizures. Cavernous sinus thrombosis results in ocular pain, chemosis, proptosis, and oculomotor palsy. Sagittal sinus thrombosis lead to bilateral motor deficits and seizures. Lateral sinus thrombosis presents with isolated intracranial hypertension and auditory symptoms such as tinnitus. Left transverse sinus thrombosis leads to language deficits and aphasia. Deep venous sinus thrombosis (*i.e.,* straight sinus) causes altered level of consciousness with severe cases resulting in coma. Deep venous sinus thrombosis usually results in severe motor deficits as well.

The diagnosis of CVT should be suspected in patients under 50 years of age with headaches and atypical features, including focal neurologic deficits, seizures, encephalopathy, or signs of intracranial hypertension.[6] Non-contrast head CT is the first test that should be obtained in the ED to rule out other acute or subacute cerebral disorders. 30% of CVT cases have a normal non-contrast head CT and most findings are nonspecific.[9] The gold standard for diagnosis of CVT is with MRI, as it has the highest sensitivity among imaging modalities. However, MRI availability can be limited and must be interpreted by an experienced neuro-radiologist. For this reason, CT venography (CTV) may be the preferred imaging modality due to its availability, shorter duration, and easier interpretation. Studies are conflicting on how CTV performs against MRI, but there is emerging evidence that it is as sensitive as MRI.[10]

Aside from neuroimaging, there are no lab tests that can diagnose CVT, but routine blood studies including a CBC, chemistry panel, PT, and aPTT should be obtained anticipating the patient's anticoagulation need. An elevated D-Dimer

Dural Venous Thrombosis
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Segond Fracture

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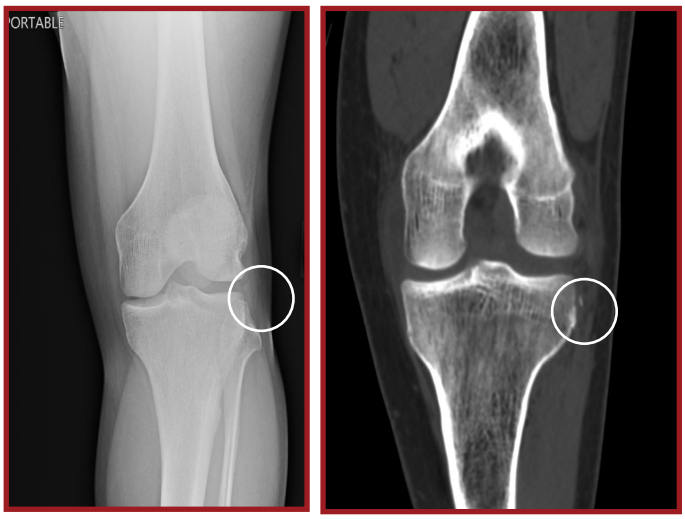
History of Present Illness

The patient is a male in his 20s with no significant past medical history who presented to the emergency department (ED) with a knee injury. He was playing soccer when he planted and internally rotated his left leg resulting in a painful pop. The pain localized to the lateral aspect of the left knee without any numbness or tingling. He was unable to ambulate after the event.

Physical Exam

The patient was well appearing and in no acute distress. Musculoskeletal exam was most notable for swelling over the anterolateral aspect of the left knee with significant tenderness to palpation over the lateral joint line. There was a mild joint effusion noted. There was increased pain with varus stress. There was also increased laxity with Lachman's maneuver on the left compared to the right. The patient was able to straighten the leg completely, but there was pain with flexion and extension.

Imaging



Images 5 & 6: Representative X-ray (left) and CT (right) demonstrating minimally displaced avulsion fracture of the lateral tibial plateau consistent with a Segond fracture (circled above).

Hospital Course

The patient was treated with oral analgesics, instructed to remain strictly non-weight bearing on the left leg, and discharged home with crutches and an orthopedic surgery referral. The patient was seen in the orthopedic clinic and an MRI was obtained that confirmed the Segond avulsion fracture with a complete tear of the anterior cruciate ligament (ACL). The patient also sustained a bucket-handle tear of the lateral meniscus with a complete tear of the posterior root attachment and medial collateral ligament (MCL) sprain. The patient underwent ACL reconstruction and lateral meniscus repair several weeks later and has since been recovering well with physical therapy.

Discussion

The Segond fracture is a type of avulsion fracture of the lateral tibial condyle of the knee. This injury pattern is the result of abnormal varus stress to the knee with associated internal rotation of the tibia. The Segond fracture is clinically significant because it is often pathognomonic for ACL tears with concomitant meniscus injuries.

Dr. Paul Segond first described Segond fractures in 1879 after observing this particular fracture pattern in cadavers who also had associated ACL tears and meniscal injuries.[1] In fact, multiple studies showed that in patients with Segond fractures, the incidence of ACL injuries was 75-100% and lateral or medial meniscal tears was 66-75%.[1] However, the Segond fracture pattern has very low sensitivity as a predictor of ACL injury with the fracture pattern only occurring in 9-12% of all ACL tears.[2]

To understand why this fracture pattern is observed it is important to understand the anatomy of the knee. The lateral aspect of the knee is complex in that there are 28 separate components that contribute to knee stability.[3] The exact cause of the Segond fracture is highly debated in the orthopedic and radiology literature, but one of the many structures associated with the lateral knee is the anterolateral ligament (ALL). The ALL runs in an anteroinferior and oblique direction from the lateral distal femur to the anterolateral proximal tibia. It is believed that the ALL contributes to rotational stability of the knee, specifically with controlling internal rotation of the tibia and locking/unlocking the knee. Disruption of this ligament is often identified with the Segond fracture on MRI.[4]

The Segond fracture, and by default ACL tear, is often caused by excessive knee internal rotation and varus stress, especially with the knee in a flexed position.[1] The injury is most commonly seen in sports injuries or falls. The patient will often have a joint effusion, ligamentous laxity specifically with varus strain, and point tenderness of the lateral joint line along the tibia. Physical exam maneuvers used for evaluation of ACL injuries are often positive, such as Lachman's, anterior drawer, and pivot shift tests.

As with most musculoskeletal injuries in the emergency department, plain films are the most appropriate initial imaging option. The fracture is often seen in the anteroposterior view of the knee on x-ray. The Segond fracture is classically associated with a small bone fragment projected parallel to the lateral aspect of the tibial plateau.[3] Although this fracture may seem small, it is imperative that the patient be referred to orthopedics for MRI to further evaluate for additional internal disruption of the knee. The patient does not need to have an MRI while in the ED as this will not change management. MRI image quality may actually improve as the swelling decreases, and many orthopedic surgeons will request improvement in swelling before any invasive procedure. There is no significant utility for CT scan unless there is high clinical suspicion for this injury and plain films are non-diagnostic, or there is a historical concern for dislocation of the knee joint.

When a patient with this fracture pattern is seen in the emergency department, the first important steps are discussing with the patient the potential extent of their injury in order to emphasize the importance of follow up with an orthopedic surgeon. If there is significant

knee instability, the patient can be placed in a knee immobilizer. Long-term use of knee immobilizers is no longer recommended as it can cause muscle atrophy and joint stiffening, ultimately leading to prolonged recovery.[5] It is imperative to counsel the patient on limiting movement on the injured knee, specifically twisting and planting movements that could worsen the injury. It is common to discharge the patient home with crutches to avoid these movements. There is no difference in outcomes of those with associated Segond fractures compared to those with ACL tears not associated with the fracture pattern.[6] The Segond fracture remains an important radiographic sign that when recognized by emergency medicine practitioners can lead to appropriate and expedited follow up.

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Neurogenic Shock

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Spinal cord injuries typically occur in two phases. The first phase of injury is the primary insult, involving some form of pathologic flexion, extension, rotation, or compression of the spinal cord with a resulting cord injury. Immediate spinal protection with a cervical collar and spinal board is used to prevent additional injury to the cord in the setting of an unstable spine fracture. Although there is no strong evidence to guide the timeline of surgical intervention, urgent stabilization and decompression of the primary injury may lead to improved neurologic outcomes compared to delayed surgical intervention.[3]

The second phase of injury is caused by the subsequent inflammatory response that results in edema, vascular congestion, cytokine release, and cellular dysfunction.[3] Hypotension from neurogenic shock results in decreased perfusion to the spinal cord and creates a local inflammatory response that worsens cellular dysfunction.[4] Injuries to the thoracic cord are most susceptible to secondary injury from hypotension given the high reliance on watershed perfusion in this area. This pathophysiological relationship serves as the theory behind a 1997 publication in the Journal of Neurosurgery, which concluded that a mean arterial pressure (MAP) greater than 85 mmHg for seven days is associated with improved neurological recovery in patients presenting with acute complete spinal cord injury. The MAP goal of 85 was arbitrarily chosen and no control group was used for comparison in this study. The seven day duration of MAP maintenance was chosen base on experimental cord injury studies which demonstrated that peak vascular congestion and edema occur in the three to day day range after injury.[10] Although this publication continues to serve as the basis behind blood pressure management in patients with spinal cord injuries, no subsequent publications have set out to refine this blood pressure goal or treatment duration.[11]

vention secondary to hypersecretion, atelectasis, bronchospasm, and respiratory failure. All of these complications can develop immediately after the injury or in a delayed fashion necessitating close observation and frequent reassessment. Because the phrenic nerve derives from the C3-C5 nerve roots, it makes sense that the risk of respiratory failure declines with lower cord injuries: 40% for C1-C4 injuries, 23% for C5-C8 injuries, and approximately 10% for thoracic injuries.[4] Respiratory failure can occur with thoracolumbar injuries due to loss of innervation to the intercostal and abdominal muscles that contribute to both inspiration and active expiration. Loss of active expiration can eliminate a patient's ability to generate an effective cough, leading to additional delayed respiratory complications.[9] Therefore, emergency physicians should consider early intubation for patients with cervical spine injuries, especially those above C5. For patients who appear to be breathing without difficulty, monitoring ventilation with end-tidal CO2 can help physicians detect impending respiratory failure requiring intubation should the patient become increasingly hypercarbic. As with all forms of shock, blood pressure support is the primary focus of management in neurogenic shock in order to improve systemic circulation and oxygen delivery.[1] This is even more important in neurogenic shock to maximize the patient's potential neurologic recovery. It is helpful to review the pathophysiology of spinal cord injuries to understand why aggressive blood pressure management is paramount.

Types of incomplete spinal cord injuries

Spinal Cord Injury	Mechanism	Symptoms	Prognosis
Brown-Sequard Syndrome	Penetrating trauma	- Ipsilateral loss of motor function, vibratory sensation and proprioception - Contralateral loss of pain and temperature sensation	Excellent prognosis 99% ambulatory at final follow up
Central Cord Syndrome	Hyperextension mechanism	- Sensory and motor deficit in upper>lower extremities	Most have moderate but incomplete recovery
Anterior Cord Syndrome	Flexion injury	- Bilateral loss of motor function, pain and temperature sensation - Spares propioception and vibratory sensation	Poor prognosis 10-20% chance of motor recovery

Table 3: Associated mechanism, symptoms and prognosis of incomplete spinal cord injuries (15)

Volume expansion with crystalloid resuscitation is first line treatment to maintain a MAP over 85 until the patient appears clinically euvolemic. Since the underlying etiology of hypotension in neurogenic shock is decreased systemic vascular resistance (SVR) secondary to loss of vasomotor tone, vasoactive agents are frequently required to further augment blood pressure. Vasoactive agents with both alpha and beta agonist properties, such as norepinephrine, are typically started first.[3] Alpha selective agonists, such as phenylephrine, are less ideal given the reflex bradycardia that often accompanies its use. Additional tools in the vasoactive arsenal include the mixed alpha and beta agonist pseudoephedrine and the alpha-selective agonist midodrine, both of which are orally administered and may facilitate weaning of intravenous vasopressors.[12]

While vasopressor administration is standard of care for MAP maintenance in SCI, some of the current literature challenges its use. One recent study theorizes that perfusion through the microvasculature of the damaged spinal cord may actually be decreased by the vasoconstriction and increased resistance to flow caused by these medications. These authors argue that more aggressive volume expansion has the benefit of improving both blood pressure and flow without the risk of vasoconstriction.[4] This debate remains largely theoretical and is unresolved, leaving clinicians with flexibility when attempting to maintain MAP above the accepted standard of 85 mmHg.

Two additional interventions that may be considered in patients with SCI include glucocorticoid administration and therapeutic hypothermia. It is important to note that neither of these treatments is considered standard of care at this time. Glucocorticoids theoretically protect the at-risk cell membranes of damaged neurons by inhibiting lipid peroxidation caused by oxygen free radicals generated during SCI. The current clinical data on glucocorticoid use in SCI are mixed. Most studies have shown that steroids—methylprednisolone in particular—have little benefit in SCI. The potential downsides of steroid administration are significant and include increased infection rates, bleeding, and steroid myopathy. The decision to initiate steroids in an otherwise healthy patient with a new SCI should be made in conjunction with the spine surgery team which will be managing the patient's long-term care.[3] Previous cardiac arrest research has demonstrated neuroprotective effects with therapeutic hypothermia by decreasing metabolic demand and prolonging recoverable ischemia time.[13,14] This raises the question of whether therapeutic hypothermia may have similar effects in the setting of spinal cord injury, especially in incomplete injuries with evidence of remaining cord function. While novel, this strategy currently lacks sufficient evidence to guide its use and should not be initiated before discussion with the spine surgery and intensive care teams.[3]

Patients with SCI and neurogenic shock are at significant risk for developing cardiovascular and respiratory complications. Patients with SCIs who are treated at Level I trauma centers with specific protocols in place for these injuries demonstrate better neurologic outcomes and lower rates of complications and mortality compared to similar patients treated at less specialized centers of care.[3,11] These patients should be admitted to an intensive care unit due to the risk of cardiovascular and respiratory instability, particularly in cervical and complete cord injuries.[8] Cord injuries that result in paralyzed abdominal musculature severely impair adequate clearance of airway secretions and make an effective cough difficult if not impossible. As a result, acute respiratory failure complicated by pneumonia is the leading cause of mortality in this patient population. Survival rates decrease significantly if mechanical ventilation is required compared to patients with similar SCIs who do not require ventilatory support.[3] Standard endotracheal suctioning only reliably clears secretions from the right mainstem bronchus and may induce bradycardia and cardiac arrest in these patients due to ongoing cardiovascular instability.[3,11] Cough-assist devices, bronchodilators, and mucolytics can help to minimize the risk of developing pneumonia, but bronchoscopy may be necessary to clear secretions.[9] Patients with a high level SCI often eventually require tracheostomy for long-term ventilator weaning and airway clearance.

Summary

Spinal cord injuries are devastating injuries and often occur in otherwise healthy individuals whose lives will be forever changed. Emergency physicians are often the first providers that come into contact with these patients, and aggressive resuscitation and minimization of secondary injury in the ED is extremely important. With early recognition of neurogenic shock and appropriate intervention, emergency physicians can truly make a difference in these patients' lives and give them the best chance at a meaningful recovery.

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Dural Venous Thrombosis

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supports the diagnosis, but a normal D-dimer evel is not sufficient to exclude the diagnosis if the physician has a high index of suspicion for CVT. In one meta-analysis, D-dimer yielded a sensitivity of 94% and specificity of 90%, but was unreliable in patients with isolated headache, subacute or chronic clinical presentations, and in those with a single affected venous sinus.[11] Another study found the false negative rate of the d-dimer to be 24%.[12] Because of the high frequency of thrombophilia among patients who develop cerebral venous thrombosis, screening for hypercoagulable conditions should be performed.[6] Testing can include antithrombin, protein C, protein S, factor V leiden, prothrombin G20210A mutation, lupus anticoagulant, anticardiolipin, and anti-beta2 glycoprotein-I antibodies. These studies should be ordered prior to anticoagulation and after discussion with both neurology and hematology.

Acute management of CVT focuses on anticoagulation, management of sequelae (such as seizures and venous infarction), and aggressive ICP management to prevent herniation.[6] Management should be performed in consultation with neurosurgery and neurology. For patients with signs of increased intracranial pressure, immediate action should be taken to reduce ICP. Head of bed elevation, hyperosmolar therapy, intensive care unit admission, and ICP monitoring may be required.

After initial stabilization, early anticoagulation is the mainstay of treatment. The rationale for anticoagulation is to prevent thrombus propagation, recanalize occluded sinuses and cerebral veins. There is also a role in preventing extra-cranial complications such deep vein thrombosis and pulmonary embolism given the relation to hypercoagulable states.[13] Anticoagulants are safe to use in patients with CVT even with associated IPH, and the presence of IPH is

not a contraindication to anticoagulation when the hemorrhage is caused by the CVT.[14] Use of either heparin or low molecular weight heparin is efficacious for initial therapy, and patients can be transitioned to warfarin once stable. While unfractionated heparin has the benefit of a shorter half-life and can be quickly discontinued, it takes longer to reach therapeutic levels compared to low molecular weight heparin. For this reason, emergency physicians should discuss the initial anticoagulation plan with the admitting team to coordinate care and avoid switching from one agent to another as in the case described above. For provoked episodes where an underlying risk factor can be identified and treated, patients should remain on anticoagulation for 3-6 months. For unprovoked episodes, oral anticoagulation should be continued for 6-12 months. Currently, there is insufficient evidence for the use of direct oral anticoagulants in CVT.[15] A systematic review of 169 patients with cerebral venous thrombosis suggested a possible clinical benefit with fibrinolysis in severe cases. However, IPH occurred in 17% of patients after fibrinolysis and was associated with clinical deterioration in 5%.[16] Endovascular thrombolysis or mechanical thrombectomy may be considered for cases of anticoagulation failure. There is limited evidence to suggest significant benefit, and this should be reserved for refractory cases.

Most patients have complete or partial recovery after CVT. In one meta-analysis including 1180 patients, only 10% had permanent neurological deficits by 12 months and the 30-day mortality rate was 5.6%.[17] The most common cause of death was brain herniation.

Summary

In summary, cerebral venous thrombosis is a rare disease that involves thrombosis in either the dural sinuses or the cortical veins. Most patients have risk factors for hypercoagulability and present most commonly with headache. Additional neurologic findings can be seen and are often related to the location of the thrombosis. Laboratory studies are not beneficial and neuroimaging must be obtained either with MRI or CTV. Anticoagulation is the mainstay of treatment even in the presence of IPH caused by the CVT, and the majority of patients have full to partial neurologic recovery. Although this is a rare diagnosis with favorable outcomes when caught early, emergency physicians must remain vigilant as morbidity and mortality rates increase substantially with delayed diagnosis.

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vessels.[8] Providers should strive to achieve lower tidal volumes (6 mL/kg of ideal body weight) to minimize pulmonary vascular resistance.[6] Decreased arterial blood pH leads to increased pulmonary vascular resistance as well, so providers should set an appropriate respiratory rate once ventilated to minimize additional respiratory acidosis.[8]

Vasopressor Support

There is only a finite amount of fluid that can be given before a patient starts to have worsening right ventricular dilation and decreased cardiac output. If judicious volume resuscitation alone does not improve the patient's hemodynamics, vasopressors should be used to support the patient's blood pressure. Canine models in prior studies have shown that norepinephrine increases mean arterial pressure and cardiac output more than phenylephrine.[9] Numerous studies have compared norepinephrine and epinephrine, and the data does not support one vasopressor over the other. Recent canine studies have shown that norepinephrine increased cardiac output and myocardial blood flow when compared to epinephrine analogs.[7,9,10] Either norepinephrine or epinephrine can be used as the first line vasopressor and depending on the patient's hemodynamic response, both can be used. If the patient's mean arterial pressure does not respond to norepinephrine or epinephrine, vasopressin can also be added. Vasopressin only increases systemic vascular resistance and has no effect on pulmonary vascular resistance. This makes vasopressin especially efficacious in the treatment of obstructive shock from pulmonary embolism.[11] In the event that further support is required, there is weak evidence for the use of low dose dobutamine (5 µg/kg/min). Dobutamine causes increased cardiac output via positive inotropy, while slightly lowering pulmonary and systemic vascular resistance.[12,13] Other positive inotropes, such as milrinone, can be used with the caveat that the hemodynamic effects will be delayed compared to dobutamine.

Nitric Oxide, Epoprostenol

There is growing evidence supporting nitric oxide and epoprostenol use in pulmonary embolism.[14,15] Pulmonary vasoconstriction is not only due to clot burden, but also from humoral factors released from platelets. These factors include vasoactive and thrombin producing peptides that cause pulmonary vasoconstriction.[3] Through the action of guanylate cyclase, nitric oxide stimulates the production of cyclic guanosine monophosphate (cGMP) which reduces calcium release from smooth muscle cells in the pulmonary vasculature.[16] Epoprostenol activates endothelial prostacyclin receptors which causes vascular smooth muscle relaxation and vasodilation. Both of these medications cause pulmonary vasodilation and decrease right ventricular afterload. Nitric oxide should be used as a salvage therapy to lower pulmonary vascular resistance in patients who are acutely decompensating despite thrombolytic and vasopressor administration. Initial starting doses begin at 5 parts per million and can be increased to 40 parts per million, similar to doses given in pulmonary hypertension. In the setting of air transportation, a respiratory therapist is needed during transport to administer the nitric oxide. Nitric oxide is a limited resource, especially in the community setting, and providers should only turn to this therapy if the patient has refractory hemodynamic collapse. It is important to note that nitric oxide is no longer available at many institutions due to cost and intense resource utilization, and

many have adopted epoprostenol as the first line inhaled pulmonary vasodilator.

Extracorporeal Membrane Oxygenation (ECMO)

If providers have attempted all of the above measures and the patient continues to have refractory shock, ECMO is the final treatment option. Patients can be cannulated prior to transport or upon arrival at the receiving facility. Venous-arterial ECMO is the modality of choice to completely bypass the pulmonary and cardiovascular systems while ongoing anticoagulation prevents further clot formation.

Conclusion

Pulmonary embolism can lead to rapid hemodynamic collapse even in the post-thrombolytic setting. The pathophysiology of the acutely decompensated patient with a pulmonary embolism is directly related to the function of the right ventricle. Fluid resuscitation should be judicious as a large volumes can lead to worsening right ventricular dilation and worsening cardiac output. Vasopressors have been shown to be effective in maintaining mean arterial pressure in these patients, specifically norepinephrine and epinephrine. Intubation should only be performed if absolutely necessary as induction and positive pressure ventilation can lead to a rapid drop in preload and subsequent cardiac arrest. The "death spiral of pulmonary embolism" can be prevented with prompt diagnosis and optimal management of the patient's hemodynamics.

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Osmotic Demyelination

continued from page 5

These alternative diagnoses can be evaluated with CT/CTA of the head and should be performed in the ED. Numerous other metabolic derangements, such as hypoxia or hypoglycemia, may present with a similar cluster of symptoms and can be detected with standard laboratory evaluation. Substance abuse, such as alcohol intoxication and/or withdrawal, can have similar presentations, but will likely fit into a toxidrome based on clinical picture. Wernicke's encephalopathy presents with the classic triad of ataxia, confusion, and nystagmus or ophthalmoplegia. Wernicke's encephalopathy is typically seen in patients with a history of chronic alcoholism, making the diagnosis of ODS even more difficult in this patient population. However, Wernicke's encephalopathy is due to thiamine deficiency, and patients frequently show improvement within hours of thiamine replacement contrary to those suffering from ODS. In summary, ODS may mimic numerous other pathologies that emergency physicians encounter on a daily basis. A recent history of hyponatremia in a normonatremic or nearly normonatremic patient is highly suspicious; however, this information is not always available. It is important to remain cognizant of this disorder and have a high level of suspicion when evaluating patients with altered mental status. Key features suggestive of ODS include dysarthria, dysphagia, flaccid paralysis, and a clinical prodrome of acute impairment followed by recovery and subsequent deterioration.

ODS is often diagnosed with cross sectional imaging, with MRI being the test of choice. Although MRI has a higher sensitivity in diagnosing this disease process, findings may not be apparent until several weeks later, whereas changes may be apparent on CT imaging sooner.[1,16,17] Some studies have demonstrated that diffusion weighted imaging (DWI) may be able to identify lesions as early as 24 hours after onset of symptoms and one case study suggests that it may also help with prognosis.[18,19] Overall, in a previously hyponatremic patient who presents with symptoms of ODS, negative imaging should not exclude the diagnosis and initiation of treatment. Repeat imaging two to three weeks later can confirm the diagnosis.[1]

Prevention of Osmotic Demyelination Syndrome

The best practice to reducing poor neurologic outcomes secondary to ODS is to avoid rapid sodium correction in chronically hyponatremic patients. While chronic hyponatremia needs to be corrected slowly over several days, acute hyponatremia can lead to cerebral edema, encephalopathy, seizures and possible cerebral herniation and death secondary to increased intracranial pressure if not treated aggressively. The most serious of symptoms of acute hyponatremia have been shown to reverse with as small as a 5 mEq/L increase in serum sodium, which can reduce intracranial pressure by up to 50% within one hour.[5,20] The current recommendation is a 100 mL bolus of 3% hypertonic saline over 10 minutes, which is estimated to increase the serum sodium by approximately 2-4 mEq/L and can rapidly abort symptoms of herniation.[20,21,22,23] This dose can be repeated twice in order to abate symptoms of herniation. Patients who are acutely hyponatremic without signs of increased intracranial pressure may be allowed to self-correct rapidly via water restriction to cause free water diuresis. In patients suffering acute hyponatremia due to the syndrome of inappropriate antidiuretic hormone, demeclocycline can be considered.[23]

Sodium correction in chronic hyponatremia should be slow to allow the brain time to adapt to the changing tonicity of its environment. Over the last several decades, there has been extensive discussion about the appropriate rate of correction in chronic hyponatremia. Several studies have demonstrated a range of anywhere between 6 to 12 mEq/L/day.[10,24,25] Other studies have demonstrated harm with correction rates of 10mEq/L/day.[24,26,27] Therefore, the current recommendation is 4-8mEq/L/day for those at low risk of ODS, and 4-6mEq/L/day in those at high risk of ODS.[23] Slow, steady correction may be difficult to accomplish as similar treatment regimens can have varying effects on serum sodium in different patients. For this reason, the patient's serum sodium level is checked every few hours to ensure that careful, steady correction is achieved, and can often be accomplished with hypotonic fluid restriction alone. Patients who are symptomatic from their hyponatremia may have their sodium level raised 4-6mEq/L over the course of several hours to abate clinical symptoms and abort impending herniation. Further correction should be delayed until the next day.[23] The effect of 1-liter of various intravenous fluids on the serum sodium can be roughly estimated with the formulas in Table 4.[28] These formulas

$$Na^{+}_{serum} = \frac{[Na^{+} + K^{+}]_{infusion} - Na^{+}_{serum}}{((*)\ x\ weight\ in\ kg) - 1}$$

The effect of 1L of infusate on serum sodium*		
	Men	Women
3% Hypertonic	+10.75mEq/L	+11.85mEq/L
0.9% NaCl	+1.17mEq/L	+1.29mEq/L
Ringer's Lactate	+0.67mEq/L	+0.74mEq/L
0.45% NaCl	-0.88mEq/L	-0.97mEq/L

*All calculations made based on a 70kg adult with an initial sodium of 110mEq/L
**use the following coefficients: 0.5 for women, 0.55 for men, 0.6 for children

Table 4: Formula to calculate rate of Na+ infusion based on adult and children weights and associated serum sodium affect of several infusates

are used to calculate the infusion rate needed to achieve a desired change in sodium in a 24-hour period. The exact results will depend on the patient's gender, body weight, and serum sodium.

Treatment

One method to treat ODS as mentioned in the patient case is to re-lower serum sodium levels if repletion is occurring too rapidly. Several animal studies have demonstrated improved outcomes following re-lowering of the serum sodium even when symptoms of ODS were already present.[30,31] Soupart et al. demonstrated complete neurologic recovery in an elderly female with hyponatremia whose serum sodium was overcorrected in the first 24 hours and subsequently re-lowered. Similar findings have been demonstrated in several other studies.[33,34] One method to re-lower the serum sodium is to administer 2-4 mcg of desmopressin IV every 8 hours with repeated 3mL/kg boluses of D5W.[23] The sodium should be checked after the administration of each D5W infusion and should be continued until the serum sodium has been re-lowered to a level beneath the therapeutic goal. Re-lowering of the serum sodium has a greater therapeutic effect when initiated earlier, and no therapeutic effect has been demonstrated when initiated more than 24 hours after the onset of ODS symptoms. Other therapies can be used when treating a patient further into their course of illness.[31]

Some animal model studies have suggested that glucocorticoids may improve outcomes in ODS by preventing blood brain barrier (BBB) disruption, limiting BBB permeability, and reducing the number of MRI detectable lesions.[35,36,37] However, re-lowering serum sodium has been shown to be more effective in improving outcomes of ODS, and the efficacy of glucocorticoids in humans has not been demonstrated and therefore is not currently a recommended treatment.[23,32,35]

Plasmapheresis is an additional therapy which is beginning to be utilized for the treatment of ODS. The proposed mechanism for this therapy is that plasmapheresis may remove myelin toxic substances.[38,39] Several studies have demonstrated significant improvement in patients with ODS after multiple sessions of plasmapheresis, even when therapy is initiated several days after the onset of symptoms.[38,39,40] The regimens in these studies vary drastically from daily treatments to biweekly treatments, and a total of anywhere from 6-10 treatments. Unfortunately, no unified recommendation exists for implementation of this therapy as the data is limited to a few case studies. However, the case reports available demonstrate promise for plasmapheresis as a treatment strategy for ODS, even when treatment is initiated over 24 hours after onset of symptoms and the patient's serum sodium has already been re-lowered with no improvement.

Summary

ODS is a demyelinating disease that most commonly develops after iatrogenic rapid correction of hyponatremia, although it can be seen in other disease states with rapid increases in serum tonicity. Patients who develop ODS have a delayed symptom onset and frequently present with spastic paralysis, dysarthria, dysphagia, movement disorders, mood and behavior disturbances, with symptoms ranging from alteration in mental status to seizures, coma, or locked in syndrome. Prevention requires careful correction of hyponatremia, with regular monitoring throughout the therapeutic course. Once overcorrection has occurred within the first 24 hours and symptoms of ODS have set in, appropriate treatment involves re-lowering of the serum sodium. Plasmapheresis has a limited amount of data but has been shown to improve outcomes and should be considered in the management of ODS.

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EKG focus

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History of Present Illness

A 16 year old female presents to the emergency department after ingesting an unknown volume of her grandmother's "heart pills" in an apparent suicide attempt. The patient is ill-appearing, tachycardic, and hypotensive with repeated episodes of nausea and vomiting. A twelve lead EKG is obtained and is notable for atrial tachycardia with a high-grade atrioventricular conduction block and frequent, polymorphic premature ventricular contractions. What did she take?

EKG Changes in Digoxin Toxicity

Digoxin is a cardiac glycoside that naturally occurs in a number of plant species, including Digitalis purpurea (common foxglove), Nerium oleander (oleander), Convallaria majalis (lily-of-the-valley), and Apocynum cannabium (dogbane). Cardiac glycosides, including digoxin, are steroid analogs that indirectly increase intracellular calcium by inhibiting adenosine triphosphate-dependent sodium-potassium antiporters. The increased intracellular calcium content increases cardiomyocyte contractility via calcium-induced calcium release from the sarcoplasmic reticulum. Concomitantly, cardioactive steroids also stimulate the vagus nerve, increasing the depolarization threshold of the atrioventricular node and slowing electrical conduction in the ventricles (negative dromotropy). These effects manifest electrocardiographically as PR interval prolongation and a characteristic "scooped" morphology of the T-wave, though these findings are not specific. It should be noted that this "digitalis effect" does not necessarily represent toxicity, and may be a benign finding in an otherwise asymptomatic patient. In toxic doses, digoxin may precipitate life-threatening dysrhythmias secondary to decreased sinoatrial and atrioventricular node conduction and increased ventricular automaticity. Though there are no pathognomic electrocardiographic findings of digoxin toxicity, highly suggestive findings include bidirectional ventricular tachycardia, atrial tachycardia with a 2:1 atrioventricular conduction, and atrial fibrillation with slow ventricular conduction. With severe toxicity, patients often degrade into ventricular fibrillation before expiring. The use of digoxin-specific antibody fragments, including DigiFab and DigiBind, are the mainstay of treating both acute and chronic digoxin toxicity.

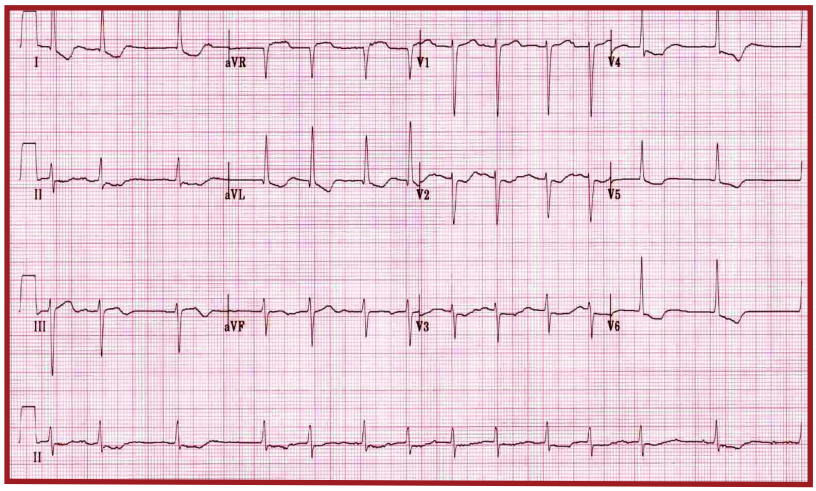

Image 7: Representative EKG with classic digitalis effect - note the "scooped" T waves

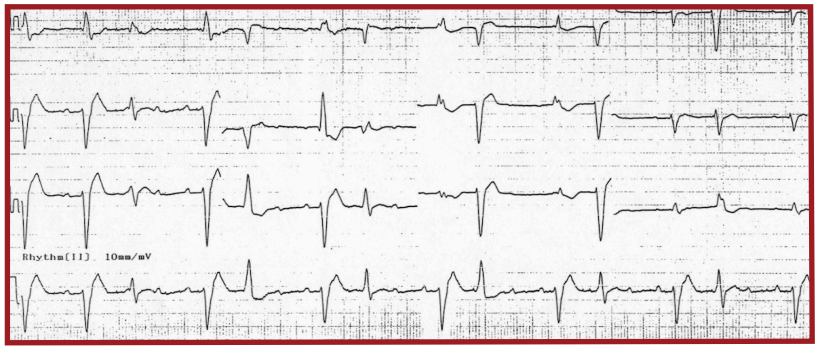

Image 8: The patient's EKG showing bidirectional ventricular tachycardia, often seen with toxic doses of digoxin

1. Goldfrank, L.R., & Flomenbaum, N. (2011) . Goldfrank's Toxicologic Emergencies, Ninth Edition. New York: McGraw-Hill.
2. Images are within the public domain, courtesy of Life In the Fast Lane.

Annals of B Pod is always looking for interesting cases to publish!

Please submit cases via EPIC In Basket message to Dr. David Habib. Make sure to include the R1/R4 involved in the case.

Submitted B Pod Cases

Case	Providers
Right Hand Injury, ICH	Burkhart/Wall
ODS	Golden/Thompson
Necrotizing Fascitis	Harrison/McDonough
Reactive Arthritis	Spigner/Thompson
Cavitary Pneumonia	Laurence/Knight
Hemolytic Anemia	Makinen/Hinckley
Depakote Overdose	Makinen/Stolz
Erythema Multiforme	Soria/Moellman
Mycoplasma Mucositis	Roblee/Roche
Anterior Spinal Infarct with PE	Irankunda/Betz
Tuberculosis	Soria/Ryan
Venous Sinus Thrombosis	Habib/Fernandez
Rectus Sheath Hematoma	Habib/Hill