

Introduction

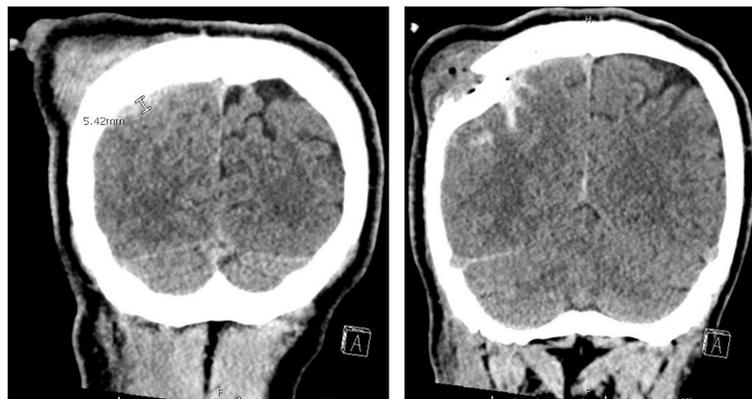
Traumatic Brain Injury (TBI) often involves a sequelae of medical and neurologic complications.^{1,2} The use of serotonergic medications to treat complications such as agitation, seizures, mood disorders, infections, and pain are common.³ Unfortunately, the signs and symptoms of serotonin syndrome have significant overlap with the complications of TBI.⁴ We present a case where this overlap in clinical presentation created a challenging, and therefore delayed, diagnosis.

Case Presentation

A 20-year-old male presented to the ED after sustaining a bean bag bullet wound to his head. The patient arrived with an initial GCS of 4 and was subsequently intubated in the ED. CT of his head showed a depressed right parietal lobe skull fracture, subarachnoid hemorrhage, and a 5 mm subdural hemorrhage. He underwent emergent craniotomy and hematoma evacuation on hospital day (HD) 1. Patient was noted to have multiple seizures on HD1 that were refractory to levetiracetam but improved with initiation of valproic acid.

On HD6, patient developed MRSA pneumonia. He was initially started on vancomycin, however he developed severe tongue swelling, protrusion, and dystonia. Given concern for vancomycin-induced angioedema, his antibiotic was changed to linezolid.

Fig 1: CT Head showing right parietal skull fracture, subarachnoid hemorrhage, and subdural hemorrhage.



Case Presentation (Continued)

PM&R was consulted on HD11. At this time, the patient continued to have low grade fevers despite antibiotic treatment. He also developed intermittent agitation and confusion. Examination was notable for diffuse hyperreflexia, bilateral wrist extension clonus, spasticity, and tremors. On HD12 the patient developed nausea and emesis secondary to ileus. He was started on metoclopramide by the primary team. Patient was also restarted on his home fluoxetine and trazodone medications.

Psychiatry was consulted on HD19 for progressive agitation and confusion. They noted that he was on several serotonergic medications concurrently which increased his risk for serotonin syndrome. Linezolid, fluoxetine, trazodone, metoclopramide, valproic acid, and opioid medications were immediately held.

Discontinuation of these medications resulted in an improvement of his agitation, confusion, fevers, clonus, and muscle rigidity within one day. Subsequent examination the next day showed marked improvement in spasticity and clonus, along with resolution of his tongue dystonia. He progressed from non-ambulatory to ambulating 40 feet with minimal assistance using a walker by time of discharge to inpatient rehab on HD 22.

Table 2: Common medications used to treat sequelae of TBI that have been implicated in serotonin syndrome.^{4,5}

Sequelae of TBI	Medications implicated in Serotonin Syndrome
Agitation	Ziprasidone, Lithium
Seizures	Carbamazepine, Valproate
Depression / Anxiety / Insomnia	SSRI, SNRI, MAOI, TCA, Trazodone
Pain	Fentanyl, Oxycodone, Tramadol, Methadone
Cognitive/Motor Deficits	Sinemet, Methylphenidate
Nosocomial Infection	Linezolid, Clarithromycin, Isoniazid
Nausea/Vomiting	Ondansetron, Metoclopramide
Headache	Triptans

Discussion

Serotonergic medications are commonly used to treat TBI sequelae such as agitation, pain, sleep disturbance, depression/anxiety, cognitive deficits, seizures, headache, and nosocomial infections. Unfortunately, the signs and symptoms of serotonin toxicity, including altered mental status, neuromuscular abnormalities, and autonomic dysfunction, have significant overlap with the clinical picture seen in TBI patients, which makes the diagnosis challenging. Key findings that may help differentiate serotonin syndrome include hyperthermia without infection, mydriasis, and ocular clonus. Serotonin syndrome is a life-threatening yet preventable syndrome with a favorable prognosis if treated. Thus, physicians must remain astute when prescribing serotonergic agents for TBI patients.

Table 1: Overlap of TBI sequelae vs. serotonin syndrome.^{1,3}

Sequelae of TBI	Signs/Symptoms of Serotonin Syndrome
Confusion	Confusion
Agitation	Agitation
Hyperreflexia, Clonus, Tremors	Hyperreflexia, Clonus, Tremors
Dystonia	Dystonia
Tachycardia, Hypertension	Tachycardia, Hypertension
Headache	Headache
Autonomic Dysfunction	Autonomic Dysfunction
Nosocomial Infection	Hyperthermia
Impaired sleep/wakes cycle	Insomnia
	Diarrhea
	Mydriasis, Ocular Clonus
	Temperature > 104 F
	Diaphoresis

Conclusion

Serotonin syndrome may be difficult to diagnose due to its similarities with severe TBI sequelae. Given the widespread use of serotonergic medications to treat neurocognitive and neuropsychiatric disorders after TBI, clinicians must maintain a high level of suspicion for serotonin syndrome. When the diagnosis is unclear, serotonergic agents should be discontinued. Serotonin syndrome is a life-threatening yet preventable syndrome with a favorable prognosis if treated, and early recognition can prevent significant morbidity and mortality in the TBI population.

References

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