Alshmandi et al. Scr Med. 2025 Nov-Dec;56(6):1265-9. DOI:10.5937/scriptamed56-61265

CASE REPORT

Serotonin Syndrome: A Clinical Case Report

Mohamed Alshmandi,[1] Haider Ali Tariq Butt,[1] Julia Kiernan[2]

1. Department of Medicine, Midland Regional Hospital of Portlaoise, Portlaoise, Ireland.
2. Department of Emergency Medicine, Perth Children's Hospital, Perth, Western Australia, Australia.

Citation: Alshmandi M, Butt HAT, Kiernan J. Serotonin syndrome: a clinical case report. Scr Med. 2025 Nov-Dec;56(6):1265-9.

Corresponding author:
MOHAMED ALSHMANDI
E: malshmandi@gmail.com
T: +353852431204

Received: 3 September 2025
Revision received: 5 October 2025
Accepted: 5 October 2025

Abstract

Serotonin syndrome is characterised by high levels of serotonin, a neurotransmitter in the nervous system. A 36-year-old male was hospitalised due to generalised weakness, loss of appetite, jaundice, abdominal pain, recurrent fever and delirium. Diagnoses of serotonin syndrome, peptic ulcer disease and metabolic-associated fatty liver disease (MAFLD) were confirmed. Management required withdrawal of the causative agent and administration of intravenous fluid support and benzodiazepines to control agitation and neuromuscular symptoms. This case clearly demonstrates the critical importance of thorough history-taking, careful clinical examination and reassessment of provisional diagnoses when initial treatments prove ineffective.

Key words: Serotonin syndrome; Autonomic nervous system diseases; Hyperthermia; Neuromuscular diseases; Tremor.

Introduction

Serotonin syndrome is characterised by high levels of serotonin, a neurotransmitter in the nervous system. Patient presents with symptoms of autonomic instability, neuromuscular hyperactivity and altered mental status.[1] Common causative agents include selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs) and other serotonergic drugs.[1, 2] Serotonin syndrome is rarely caused by monotherapy of SSRIs.[1] It usually occurs with the use of a combination of several serotonergic medications; the combination of an SSRI and MAOI poses the greatest risk.[3] Early recognition of a disease is essential to prevent serious adverse outcomes.

Case history

A 36-year-old male presented with symptoms of generalised weakness, loss of appetite, jaundice, abdominal pain, recurrent fevers and delirium. He was admitted under the surgical team for further investigation and workup. His past medical history included pan-hypopituitarism, Charles Bonnet syndrome, metabolic syndrome (diabetes mellitus type II, hypercholesterolaemia and high body mass index (BMI) with increased waist circumference), heterozygotic hemochromatosis and bilateral optic atrophy. The physical examination demonstrated a confused patient with jaundice and mild upper abdominal discomfort.

Relevant diagnostic blood investigations were carried out (Table 1). Both chest and abdominal X-rays demonstrated no abnormalities. An ultrasound of the abdomen showed low-grade hepatosplenomegaly with fatty infiltration of the liver and a small amount of sludge in the neck of the gallbladder. However, there was no evidence of ascites, gallstones, cholecystitis or common bile duct dilation. A magnetic resonance cholangiopancreatography (MRCP) and an abdominopelvic computed tomography (CT) scan confirmed these findings. Brain CT and pituitary magnetic resonance imaging (MRI) showed no

new abnormalities. The full septic screen was negative.

The gastroenterology team subsequently took over the patient's care. An echocardiogram (ECHO) was normal and a lumbar puncture ruled out meningitis. A comprehensive liver workup, including testing for Wilson's disease and autoimmune hepatitis, was negative. The leading impression was metabolic-associated steatohepatitis (MASH), formerly known as non-alcoholic steatohepatitis, accounting for the patient's abnormal liver function tests, which were later confirmed by liver biopsy. Liver biopsy revealed normal hepatic architecture, moderate hepatic steatosis with some lipofuscin pigment and minimal portal lymphocytic inflammation; normal bile ducts with normal iron stores and no interface hepatitis; no fibrosis and negative stain for copper. Dry weight copper was 16 mcg/g.

Despite empirical antibiotic therapy, the patient's abdominal discomfort and febrile episodes persisted, prompting further assessment and investigation, including an oesophagogastroduodenoscopy (OGD) and medication review. The OGD revealed *Helicobacter pylori*-associated gastritis and a duodenal ulcer in the first part of the duodenum (D1). Upon careful history-taking, it was discovered that the patient was initiated on sertraline by his primary care physician for anxiety and was also started on regular tramadol during admission for pain management.

Table 1: Blood analyses

Parameter	Value
Haemoglobin (Hb)	8.8 g/dL
White blood cells (WBC)	7.6 $\times 10^9$/L
Neutrophils	4.14 $\times 10^9$/L
Platelets	75 $\times 10^9$/L
Urea	9.1 mmol//L
Creatinine	89 umol/L
Estimated glomerular filtration rate (eGFR)	> 90 mL/min/1.73 m^2
Sodium	154 mmol/L
Potassium	3.3 mmol/L
Alanine aminotransferase (ALT)	104 IU/L
Aspartate aminotransferase (AST)	106 IU/L
Alkaline phosphatase (ALP)	152 IU/L
Gamma-glutamyl transferase (GGT)	2148 IU/L
Total bilirubin	117.1 umol/L
Albumin	37 g/L
C-reactive protein (CRP)	57 mg/L
Calcium	2.28 mmol/L
Magnesium	0.95 mmol/L
Phosphorous	0.79 mmol/L
International normalised ratio (INR)	1.1
Activated partial thromboplastin time (APTT)	28 s
D-dimer	1.34 mg/L FEU
Thyroid-stimulating hormone (TSH)	0.183 mIU/L
Free thyroxine	10.2 pmol/L
HbA_1C	52 mmol/mol
Human growth hormone	0.9 mL U/L
Insulin-like growth factor 1 (IGF1)	31.0 ug/L
Anti-nuclear antibody (Ab)-IgG	Negative
Anti-mitochondrial Ab	Negative
Anti-smooth-muscle Ab	Negative
Anti-liver/kidney microsome Ab	Negative
Anti-parietal-cell Ab	Negative

Anti-glutamic acid decarboxylase (Anti-GAD) Ab	Negative
Anti-neuronal Ab	Negative
Voltage-gated Ca and K channel Ab	Negative
Contactin 2 associated protein	Negative
Leucine-rich glioma intact 1	Negative
N-methyl-D-aspartate (NMDA) receptor Ab	Negative
Iron	19.6 umol/L
Transferrin	1.7 g/L
IgG	5.70 g/L
IgM	2.01 g/L
IgA	1.38 g/L
α 1 antitrypsin	1.8 g/L
Alpha-fetoprotein	11.0 ng/mL
Urine copper	3.64 umol/24 h
Caeruloplasmin	0.38 g/L
CMV, EBV, HBsAg, HAV Ab, Anti-HCV, HIV and syphilis	Not detected
COVID-19	Not detected
Blood film	Hypochromia, macrocytosis, anisocytosis, stomatocytes and teardrop cells

CMV: cytomegalovirus; EBV: Epstein–Barr virus; HAV: hepatitis A virus; HCV: hepatitis C virus;

On re-examination, the patient exhibited tremors, both spontaneous and inducible clonus and hyperreflexia. These findings met the Hunter Criteria for serotonin syndrome. Consequently, sertraline was discontinued and treatment was initiated with cyproheptadine, lorazepam, intravenous fluids and external cooling using cooling blankets. The patient's symptoms resolved entirely within 48 hours. He subsequently returned to his baseline clinical status and was discharged to a convalescence facility before returning home.

Discussion

Serotonin syndrome is a serious condition caused by the overstimulation of 5-HT receptors in the central nervous system. Five-A classic triad of symptoms characterises it: cognitive effects such as agitation or confusion; autonomic instability, including hyperthermia, hypertension and tachycardia; neuromuscular signs, including tremor, clonus and hyperactive reflexes.[4]

Diagnosis is clinical and based on the Hunter Serotonin Toxicity Criteria, which is considered more specific and sensitive than older methods.[5] According to these criteria, an individual exposed to serotonergic medication is diagnosed with serotonin syndrome if they display one of the following: spontaneous clonus; inducible clonus with agitation or diaphoresis; eye clonus with agitation or diaphoresis; tremor with hyperreflexia; hypertonia with temperature > 38 °C and eye clonus or inducible clonus.

In this case, the patient demonstrated tremors, hyperreflexia and fever, all of which meet Hunter's criteria when considered in the context of recent sertraline use—a serotonergic agent. This confirmed the clinical suspicion of serotonin syndrome.

Due to the nonspecific nature of many of its symptoms and their overlap with those of other medical conditions, a detailed history and clinical assessment are necessary for a timely and definitive diagnosis. This highlights the critical role of clinicians in ensuring patient safety through careful evaluation. Pharmacologic agents commonly implicated in serotonin syndrome include SSRIs, serotonin-norepinephrine reuptake inhibitors (SNRIs), MAOIs and tricyclic antidepressants. Other high-risk agents include tramadol, ondansetron, linezolid, lithium, 3,4-methylenedioxymethamphetamine (MDMA) and cocaine, mainly when used in combination with serotonergic drugs.[6,7]

Management requires withdrawal of the causative agent, administration of intravenous fluids support and benzodiazepines to control agitation and neuromuscular symptoms. Temperature

management is crucial for hyperthermia.[1] In moderate to severe cases, cyproheptadine, a serotonin receptor antagonist, may be administered.[1, 2] Most patients show significant improvement within 24 h of treatment, although severe cases may require ICU admission for close monitoring and management of complications. Early recognition and timely management are crucial for ensuring a full recovery and preventing adverse outcomes.[1]

Conclusion

This case highlights the importance of conducting a comprehensive history, careful clinical examination and reassessment of the provisional diagnosis when initial treatments prove ineffective. It underscores the need for early recognition of serotonin syndrome to prevent serious complications. Additionally, it demonstrates that multiple coexisting pathologies can contribute to a patient's hospital admission. Healthcare providers must remain vigilant when prescribing even a single serotonergic medication and should always evaluate potential drug interactions to minimise the risk of serotonin toxicity.

Ethics

Our institution does not require ethics approval for reporting individual cases or case series. Written informed consent for the anonymised patient's information to be published in this article was obtained from the patient.

Acknowledgement

We acknowledge the support of the medical staff for their role in managing this case.

Conflicts of interest

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

Author ORCID numbers

Mohamed Alshmandi (MA):
0009-0009-5225-7821
Haider Ali Tariq Butt (HATB):
0009-0007-6794-2325
Julia Kiernan (JK):
0009-0009-0156-1962

Author contributions

Conceptualisation: MA
Writing - original draft: HATB
Writing - review and editing: MA, JK
Supervision: MA

References

1. Boyer EW, Shannon M. The serotonin syndrome. N Engl J Med. 2005 Mar 17;352(11):1112-20. doi: 10.1056/NEJMra041867.
2. Sternbach H. The serotonin syndrome. Am J Psychiatry. 1991 Jun;148(6):705-13. doi: 10.1176/ajp.148.6.705.
3. Wang RZ, Vashistha V, Kaur S, Houchens NW. Serotonin syndrome: Preventing, recognizing, and treating it. Cleve Clin J Med. 2016 Nov;83(11):810-7. doi: 10.3949/ccjm.83a.15129.
4. Maitland S, Baker M. Serotonin syndrome. Drug Ther Bull. 2022 Jun;60(6):88-91. doi: 10.1136/dtb.2021.000032.
5. Dunkley EJ, Isbister GK, Sibbritt D, Dawson AH, Whyte IM. The Hunter Serotonin Toxicity Criteria: simple and accurate diagnostic decision rules for serotonin toxicity. QJM. 2003 Sep;96(9):635-42. doi: 10.1093/qjmed/hcg109.
6. Garel N, Greenway KT, Tabbane K, Joober R. Serotonin syndrome: SSRIs are not the only culprit. J Psychiatry Neurosci. 2021 May 27;46(3):E369-E370. doi: 10.1503/jpn.210001.
7. Buckley NA, Dawson AH, Isbister GK. Serotonin syndrome. BMJ. 2014 Feb 19;348:g1626. doi: 10.1136/bmj.g1626.