

Serotonin Syndrome and Intrahepatic Cholestasis of Pregnancy: A Case of Drug Toxicity

Livia Samara, Abigail Oliver
University Hospitals Bristol and Weston NHS Foundation Trust

INTRODUCTION

- Intrahepatic cholestasis of pregnancy (ICP) affects 0.7% of pregnancies in the UK
- ICP is characterized by pruritus in the absence of a primary skin condition with abnormal bile acid concentrations [1]
- 20-80 % of patients with ICP have abnormal liver function tests (LFTs) [2]
- 3.3% of pregnant women in the UK are prescribed selective serotonin re-uptake inhibitors (SSRIs) and its prevalence is rising [3,4]
- The increasing use of SSRIs and antipsychotic medications during pregnancy raises concerns about serotonin syndrome, a known complication of this medication
- This is characterised by a classic triad, shown in figure 1. [5]

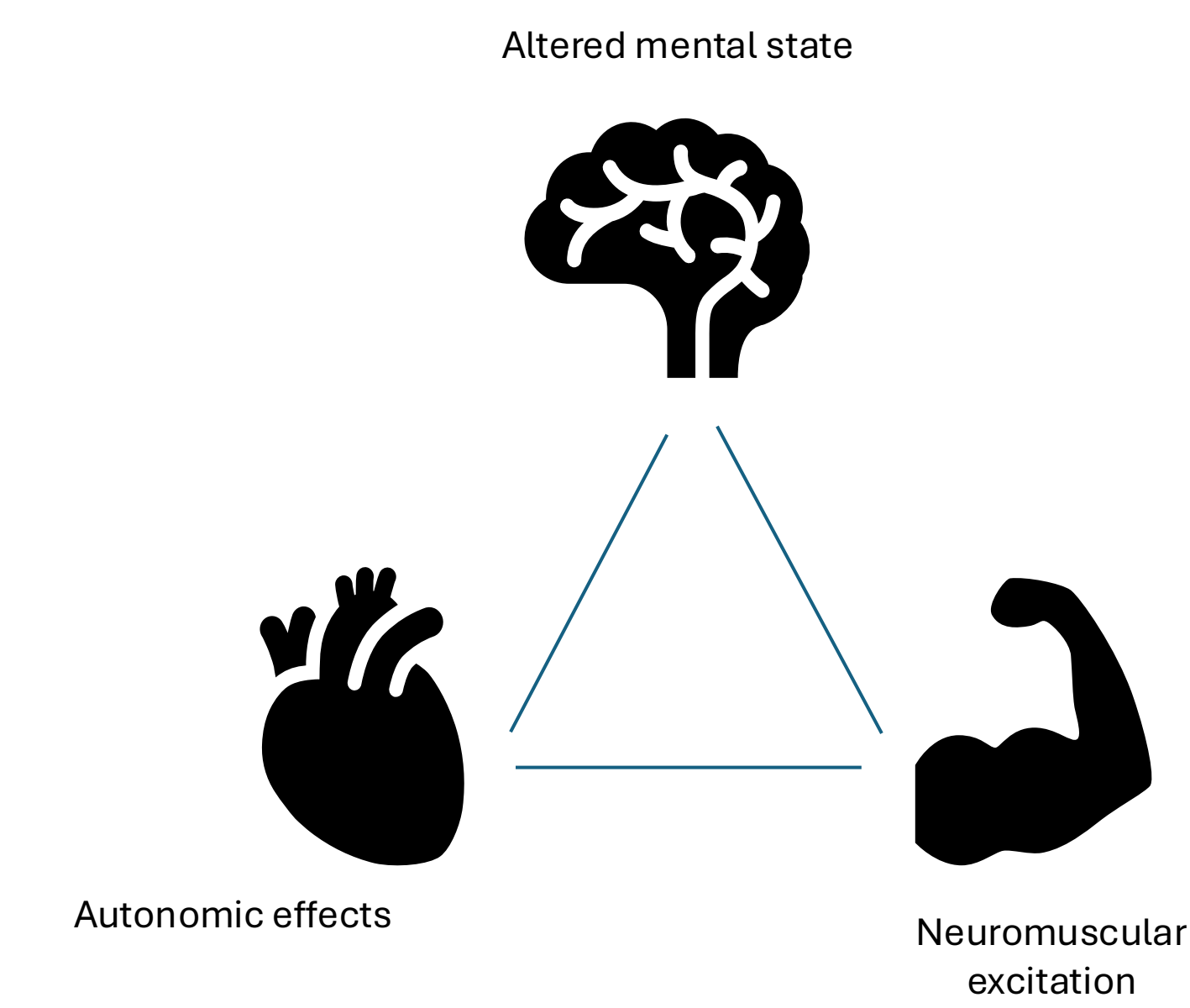


Figure 1. Classic triad of serotonin syndrome

Figure 2. Chemical structure of serotonin

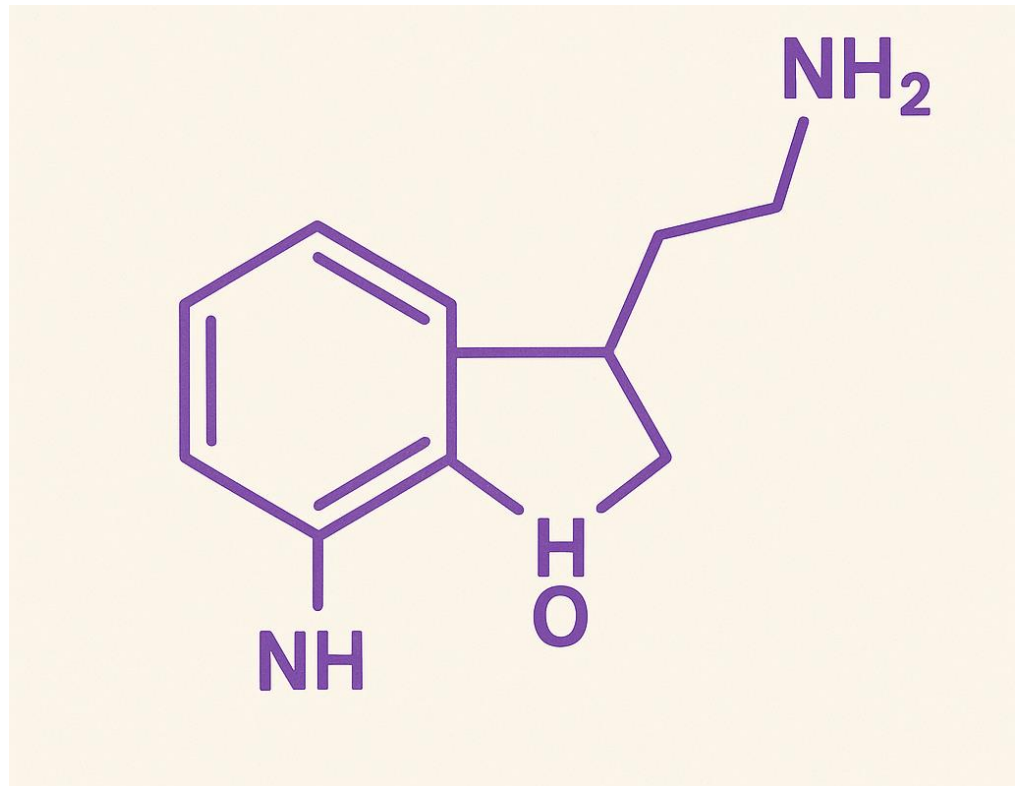


Table 1. Investigations performed and results

CTG	Uncomplicated fetal tachycardia
ECG	Sinus tachycardia
Echocardiogram	Normal
CTPA	No evidence of pulmonary embolism
Urine toxicology	Negative
Autoimmune profile	Normal
Hepatitis screen	Normal
Urine PCR	17

CASE

- Background:
- 32 years old
 - G2 P0 (previous termination of pregnancy at 8 weeks)
 - History of bipolar disorder, post-traumatic stress disorder and previous suicide attempts
 - Medication history – Quetiapine 150 mg OD, duloxetine 120 mg OD
 - Booked her pregnancy at 9+3
 - Under consultant led care due to mental health history
- 31+4:
- Saw her community midwife and reported itching
 - Bloods were taken which showed total bile acids of 82 µmol/L and ALT of 734 U/L
- 31+5:
- Seen in DAU by consultant
 - On review reported 3-day history of itchy hands and feet with no rash which had progressed to all over her body. This was worse at night and in the evenings. She was also feeling nauseous and had on occasion vomited. She denied any other symptoms
 - Repeat bloods showed total bile acids of 40 µmol/L and ALT of 848 U/L
 - Due to severely deranged LFTs was admitted for further investigation
- 31+6:
- Reviewed by SpR overnight due to tachycardia and hypertension
 - Observations: HR 150, BP 162/95, RR 20, SpO2 98% on air, temperature 36.2
 - On review she was agitated and reported a 3-day history of periods of chest heaviness and palpitations occurring 10 times per day
 - On examination she was hyperreflexic, 1 beat of clonus in left foot only, dilated pupils and normal tone
 - Investigations shown in table 1
 - She required a stat dose of labetalol
 - Given her medication history and new derangement in liver function in the presence of the classic triad of symptoms she was diagnosed with serotonin syndrome
 - Duloxetine dose reduced
- 32+3:
- ALT improving and discharged home

- 36+3:
- Consultant antenatal clinic review
 - Induction of labour booked for 37+3 – 37+5
- 36+6:
- SRM confirmed
- 37+0:
- Augmented with oxytocin
 - Category 2 caesarean section for abnormal CTG in labour

DISCUSSION

Serotonin syndrome is defined as an excess of serotonin in the central nervous system and is characterised by a triad of neuromuscular excitation, autonomic effects and an altered mental state. It is a clinical diagnosis[5]. It is typically associated with recent increases or overdose of serotonergic medications, such as SSRIs and atipsyhcotics. However, in the setting of liver impairment, drug metabolism may be slowed, leading to elevated drug levels and toxicity. Both duloxetine and quetiapine are metabolized by the liver, and in this case, ICP-induced liver dysfunction likely contributed to drug accumulation, precipitating serotonin syndrome[6]. This is the first reported case of serotonin syndrome in the context of liver dysfunction in ICP. Given the rising number of antenatal patients on SSRIs in the UK, it is important for obstetricians to be familiar with this rare, but potentially life-threatening complication.

CONCLUSION

This case demonstrates the need to consider the diagnosis of serotonin syndrome in patients with ICP and abnormal liver function tests on psychiatric medications presenting with unusual symptoms.

REFERENCES

[1] Girling J, Knight CL, Chappell L. Intrahepatic cholestasis of pregnancy: Green-top Guideline No. 43 June 2022. BJOG: An International Journal of Obstetrics & Gynaecology. 2022 Dec 1;129(13).

[2] Dajti E, Bruni A, Barbara G, Azzaroli F. Diagnostic approach to elevated liver function tests during pregnancy: a pragmatic narrative review. Journal of Personalized Medicine. 2023 Sep 16;13(9):1388.

[3] Molenaar NM, Bais B, Lambregtse-van den Berg MP, Mulder CL, Howell EA, Fox NS, Rommel AS, Bergink V, Kamperman AM. The international prevalence of antidepressant use before, during, and after pregnancy: A systematic review and meta-analysis of timing, type of prescriptions and geographical variability. Journal of affective disorders. 2020 Mar 1;264:82-9.

[4] Gray K. Medicines Used in Mental Health – England – 2015/16 to 2021/22 | NHSBSA [Internet]. www.nhsbsa.nhs.uk. 2022. Available from: <https://www.nhsbsa.nhs.uk/statistical-collections/medicines-used-mental-health-england/medicines-used-mental-health-england-201516-202122>

[5] Boyer EW, Shannon M. The serotonin syndrome. New England Journal of Medicine. 2005 Mar 17;352(11):1112-20.

[6] Huddart R, Hicks JK, Ramsey LB, Strawn JR, Smith DM, Babilonia MB, Altman RB, Klein TE. PharmGKB summary: sertraline pathway, pharmacokinetics. Pharmacogenetics and genomics. 2020 Feb 1;30(2):26-33.