A rare case of typhoid fever encephalopathy presenting as Cotard's Syndrome.

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Background

- Typhoid fever, caused by *Salmonella enterica* serotype Typhi, is a systemic infection that can present with a spectrum of complications, including typhoid encephalopathy
- In the United States, typhoid fever is rare – approximately 400–450 cases are reported annually – and the vast majority (about 80–85%) are associated with international travel to endemic regions (especially South Asia). Typhoid fever encephalopathy is a recognized complication in about 21% of hospitalized patients [1,2]
- Psychiatric manifestations of typhoid fever are rare, and Cotard's syndrome—a condition characterized by nihilistic delusions such as believing one is dead or rotting—has been described in only two prior cases associated with typhoid fever.[3]

Case Presentation

25-year-old woman with a history of asthma and prior episodes of malaria and **no prior psychiatric history** presented to the emergency department with three days of subjective fevers, generalized body aches, diffuse abdominal discomfort, nausea, and vomiting. She had **returned from travel to Ghana approximately one month prior to presentation**.

On presentation, she was febrile (39.4°C) and tachycardic at 110 bpm. **She was alert and fully oriented on arrival.** Physical examination was notable for diffuse abdominal tenderness, but no focal neurologic deficits. Subsequently **admitted for gastrointestinal infection** and started empirically on piperacillin-tazobactam.

Over the next 3 days, malaria was ruled out, but **blood cultures grew Salmonella species**, later confirmed as Salmonella Typhi, susceptible to ceftriaxone. A CT angiography of the chest/abdomen/pelvis revealed diffuse circumferential wall thickening of the terminal ileum with mild inflammatory changes, a pattern highly suspicious for **typhoid ileitis**.

Evaluation and Treatment

DAY 4: Nursing staff noted that the patient began exhibiting new-onset anxiety that was out of character and unrelated to her medical condition

DAY 5: Despite defervescence and marked improvement in gastrointestinal symptoms, her **anxiety had intensified** and was accompanied by severe insomnia. The patient became **increasingly perseverative** on exact details of care

DAY 6: Uncharacteristic anxiety with ruminations, obsessive fixation, and insomnia persisted despite trials of hydroxyzine and melatonin. MRI of the brain obtained which showed a Chiari I malformation but no other abnormalities

DAY 8 (~12:30AM): Psychiatry first consulted when the patient unexpectedly insisted on immediate discharge from the hospital. Patient described as being intermittently disoriented (not recognizing she was in hospital), making infrequent eye contact and scanning the room anxiously, her affect ranging from worried and tense to inappropriate smiling. Haloperidol IM, and later oral olanzapine 5mg and 10mg administered due to agitation and attempts at elopement.

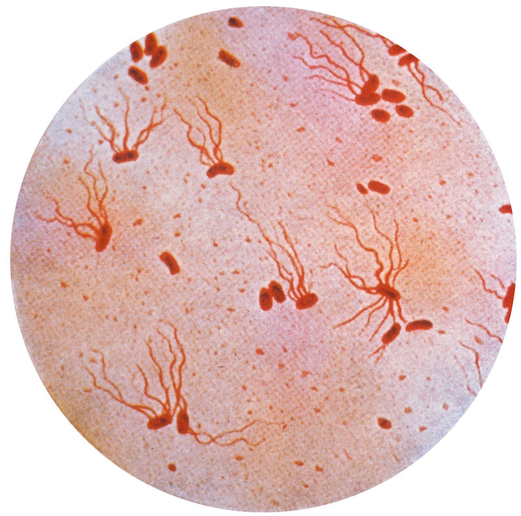
DAY 8 (mid-morning): Psychiatry re-evaluation. Patient fully regained orientation X 3. However, she begins describing an **unrelenting sense of dread and hypervigilance**. She verbalizes **extreme shame** about an **olfactory hallucination** that she was emitting a foul odor and that she was **"rotting internally".** She demonstrated appropriate, articulate speech with no observable dysarthria. Thought content was dominated by **nihilistic and self-deprecatory themes**: she repeatedly voiced **guilt** about being a burden to her family and **unworthy** of care, at times stating that she **felt she had already died**. Telemetry readings mirroring anxious themes. Her thought process was perseverative and fixated on her health and guilt. She denied any visual or auditory hallucinations. She **endorsed a passive wish for death**, but she denied any active suicidal intent or plan. Started on scheduled olanzapine, 5mg nightly.

DAY 10: After three doses of scheduled olanzapine (48 hours later) and continuation of treatment with ceftriaxone she had a complete resolution of the delusional belief that she was rotting or dead, the olfactory hallucination disappeared, and her sense of hopelessness and guilt resolved. Her thought process became linear and reality-based, and her affect returned to normal as corroborated by her father (who noted that she had returned to her usual baseline personality).

DAY 11: Discharged home; olanzapine taper not filled by patient

5 WEEKS LATER: No psychiatric symptoms reported at ID follow-up

"I feel like I am rotting internally and emitting a foul odor as if I've already died. I am a burden to my family and do not deserve care"



Photomicrograph of Salmonella enterica serovar Typhi, the causative agent of typhoid fever.[4]

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Discussion

- In this patient, a confirmed S. Typhi infection was associated with an atypical neuropsychiatric course that included Cotard's syndrome – a rare delusional belief of being dead or decaying. While delirium alone could explain some of her symptoms, the prominence of nihilistic delusions (e.g. "I am rotting internally"), self-deprecatory guilt, and severe anxiety is highly unusual.
- A growing body of literature shows that various infections can precipitate neuropsychiatric sequelae via mechanisms such as direct central nervous system infection, neuroinflammation, molecular mimicry, and autoimmune responses.
- A 2025 study by Zhao et al. showed that the typhoid toxin produced by S. Typhi can disrupt the blood–brain barrier (BBB) by injuring vascular endothelial cells, leading to inflammation, cerebral edema, and neurological dysfunction. Further research in mice models suggest a potential valuable role for corticosteroids in the management of typhoid encephalopathy.[5, 6]

Conclusion

This case highlights the importance of considering typhoid encephalopathy when a patient with Salmonella Typhi infection shows acute psychiatric symptoms, even bizarre symptoms like nihilistic delusions and in the absence of any prior psychiatric history.

Clinicians must remain vigilant for presentations such as acute delirium, psychosis, or Cotard's syndrome in the setting of severe infections.

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