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Auto-brewery syndrome in a 50-year-old woman

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A 50-year-old woman was referred to a gastroenterology clinic after 7 presentations over the previous 2 years to emergency departments (EDs) with alcohol intoxication despite her report of no alcohol consumption. Over the preceding 5 years, she had had recurrent urinary tract infections (UTIs), which required frequent courses of ciprofloxacin and nitrofurantoin, as well as gastrointestinal reflux disease, treated with dexlansoprazole. In the past, she would drink a glass of wine at holidays; however, in recent years, she had stopped drinking altogether because of her religious beliefs. She lived with her husband and children.

Two years previously, the patient started to have excessive somnolence and episodes of falling asleep suddenly while getting ready for work or preparing meals. She presented to her family physician several times with excessive somnolence and to EDs with slurred speech, the smell of alcohol on her breath, and falls caused by somnolence. On her ED visits, she was discharged with the diagnosis of alcohol intoxication, despite her reports of no alcohol intake, corroborated by her family. During her initial ED visit, her alcohol level was elevated at 39 (normal < 2) mmol/L, with normal liver enzymes. A non-contrast computed tomography (CT) scan of her head showed no acute intracranial findings. During subsequent ED visits, she had 3 separate assessments by psychiatrists who provided care related to addiction medicine at the hospital. During these assessments, she scored zero on the CAGE (Cut, Annoyed, Guilty, and Eye) screening questionnaire for alcohol use disorder. Notably, during her third ED visit, she received certification under the *Mental Health Act* (Form 1), as the treating emergency physician had concerns for self-neglect when the patient initiated discharge before psychiatry assessment.

After each ED visit, the patient needed 1–2 weeks off work because of persistent lethargy and somnolence. During this time at home, she ate little, given her suppressed appetite from somnolence. Her lethargy would then resolve over 1–2 weeks, with subsequent improvement in appetite. Her lethargy and somnolence recurred in an episodic manner every 1–2 months thereafter.

On her seventh ED visit, the patient presented with slurred speech, alcohol odour on her breath, and an elevated ethanol level of 62 mmol/L. A diagnosis of auto-brewery syndrome was considered by the emergency physician, who prescribed oral fluconazole (100 mg, twice daily) and sent a gastroenterology referral.

At the gastroenterology clinic, the patient was assessed by a dietitian, who suggested a low-carbohydrate diet (Table 1). A CT enterography scan did not show any small bowel pathology indicative of stasis or microbial overgrowth. After completing a 1-month course of fluconazole and adhering to the low-carbohydrate diet,

Key points

- Auto-brewery syndrome involves endogenous alcohol fermentation by fungi in the gut.
- Diagnostic evaluation includes collateral history, ethanol level measurements with an oral glucose challenge, and, potentially, fungal culture and susceptibility testing of gastrointestinal secretions.
- Management involves longitudinal, multidisciplinary care involving specialists in primary care, gastroenterology, infectious diseases, and mental health, as well as dietitians, with a strategy of antifungal therapy and a low-carbohydrate diet.
- Auto-brewery syndrome may carry substantial social, legal, occupational, and medical consequences for patients, and awareness of this syndrome is essential for clinical diagnosis and management.

Table 1: The low-carbohydrate diet prepared by a dietitian for a 50-year-old woman with auto-brewery syndrome

Meal type	Suggested meal content options
Breakfast	Vegetarian patty, boiled egg, egg omelette with vegetables (spinach, onion, bell peppers, and tomatoes), avocado, roasted cauliflower, dry almonds
Lunch	Barbecue chicken with cucumber and lettuce, or lentil soup
Dinner	Chicken, salmon, or lamb, with 1 tablespoon of rice or 1 tablespoon of dahl or salad
Fluids	Water, coffee or tea with no sugar

her symptoms resolved and remained absent for 4 months. The patient then started increasing her carbohydrate intake. One month after increasing carbohydrate intake, she had recurrence of slurred speech and drowsiness, which led to a fall. She was reassessed in the gastroenterology clinic, restarted on fluconazole, advised to revert to the low-carbohydrate diet, and referred to our infectious diseases clinic. After 2 weeks of fluconazole and a low-carbohydrate diet, her symptoms resolved.

On consultation with the patient in our infectious diseases clinic, we agreed with the diagnosis of auto-brewery syndrome based on her recurrent intoxication presentations with elevated ethanol levels and consistent self- and corroborated reporting of no alcohol consumption. Moreover, the complete resolution of symptoms and absence of detectable alcohol levels after treatment with fluconazole and a low-carbohydrate diet provided additional support for the diagnosis. We stopped the patient's fluconazole after 6 weeks because of symptom resolution and an elevated alanine transaminase level of 217 (normal 17–63) IU/L, attributed to the fluconazole. Her alkaline phosphatase and total bilirubin levels remained normal. A gastroenterologist performed esophagogastroduodenoscopy and colonoscopy 3 days after she completed the fluconazole course. Fungal cultures from duodenal and terminal ileum aspirates showed no growth; however, the likelihood of isolating fungi in cultures obtained after the course of fluconazole was low.

We started the patient on *Lactobacillus acidophilus* probiotics to replenish gut microbiota. To reduce further gut dysbiosis, we advised the patient and her family physician to use narrow-spectrum antibiotics only after confirming a UTI diagnosis with urine culture and compatible symptoms.

The patient remained asymptomatic for 6 months, after which we conducted an oral glucose challenge test to evaluate the safety of carbohydrate consumption. She was given 150 g of oral glucose after we determined an undetectable baseline level of ethanol. Subsequent measurements taken at 0.5, 1, 2, 3, 4, 5, 24, and 48 hours after glucose intake showed no detectable ethanol levels (< 2 mmol/L). Based on these results, we advised her to gradually increase her carbohydrate intake, and she will continue follow-up with our infectious diseases clinic, the gastroenterologist, and the dietitian.

Discussion

Auto-brewery syndrome is a rare syndrome of endogenous alcohol fermentation. A 1948 report of a boy with a ruptured stomach whose contents smelled of alcohol was the first to describe gut fermentation.[1] Auto-brewery syndrome as a diagnostic entity was first described in 1952 in Japan, where it bears the layman term *Meitei-sho*, which translates as "alcohol auto-intoxication syndrome."[2] The first cases in North America were published in the United States in the 1980s.[3,4] A 2020 systematic review identified 20 patients reported in the English medical literature since 1974.[5]

Auto-brewery syndrome is thought to result when microorganisms capable of fermenting alcohol from carbohydrates outgrow normal gut flora.[6] Although population-based studies have shown that gut alcohol fermentation with low levels of endogenous ethanol can occur even among healthy people, blood ethanol levels rarely reach concentrations high enough to cause intoxication.[7] Auto-brewery syndrome is uncommon because it requires several host factors to interact with substantial overpopulation of fermenting microorganisms, and high carbohydrate consumption.[6] Comorbidities such as diabetes, liver disease, gut dysmotility disorders, and inflammatory bowel disease are associated with auto-brewery syndrome through mechanisms contributing to increased levels of blood glucose and decreased ethanol metabolism.[6,7] Genetic predisposition for inactive aldehyde dehydrogenase enzyme and subsequent inefficient alcohol metabolism, may also play a role.[6] In our patient, we suspect her recurrent antibiotics for UTI and dexlansoprazole use led to gut dysbiosis with potential contribution of genetics, resulting in auto-brewery syndrome.

Commonly implicated fungi responsible for outgrowing normal gut flora in auto-brewery syndrome are *Saccharomyces cerevisiae* and *Candida* species including *C. albicans, C. tropicalis*, *and C. glabrata*.[2] Bacteria have also been cultured from patients with auto-brewery syndrome. Although the role of bacteria remains unclear, a recent case–control study proposed *Klebsiella pneumoniae* as an important culprit.[7–9]

No standardized diagnostic algorithms are available for auto-brewery syndrome and years of delay to diagnosis are common.[8,9] When auto-brewery syndrome is suspected, the diagnostic framework includes performing a history (from the patient and close contacts), physical examination, blood work, glucose challenge test, and microbiological assessments (Figure 1). A CAGE screening questionnaire should be performed and blood ethanol and liver enzyme levels should be measured.[3]

Protocols for glucose challenges include obtaining a baseline level of ethanol from blood or via a breathalyzer, followed by ingestion of a high load (100–200 g) of glucose. Ethanol levels are obtained at 1, 2, 4, 8, 16, and 24 hours after glucose ingestion. The glucose challenge should be conducted in a monitored setting to ensure no consumption of ethanol and safety in the event of intoxication.[3,8] Undetectable ethanol levels at baseline, followed by detection of ethanol after glucose ingestion, can confirm the diagnosis.

Fungal and bacterial cultures of gastrointestinal secretions obtained through esophagogastroduodenoscopy or colonoscopy can help identify culprit pathogens with antimicrobial susceptibility.[3] Stool fungal cultures can also be obtained as an adjunct test.[6,8] The diagnostic yield of the glucose challenge and microbiologic evaluations will decrease if these are conducted after administration of empiric antifungal agents, as with our patient. Therefore, prompt arrangements for these diagnostics are crucial when auto-brewery syndrome is suspected, as delays in treatment can prolong its physical, social, and financial ramifications.

Management of auto-brewery syndrome lacks established guidelines. Antifungal therapy and low-carbohydrate diets have been the primary treatments in documented cases. If a microbiologic diagnosis is established, an antifungal agent can be chosen based on susceptibility. Otherwise, fluconazole is a reasonable empiric choice given that *S. cerevisiae* and *C. albicans* are the most commonly implicated fungi.[2,7]

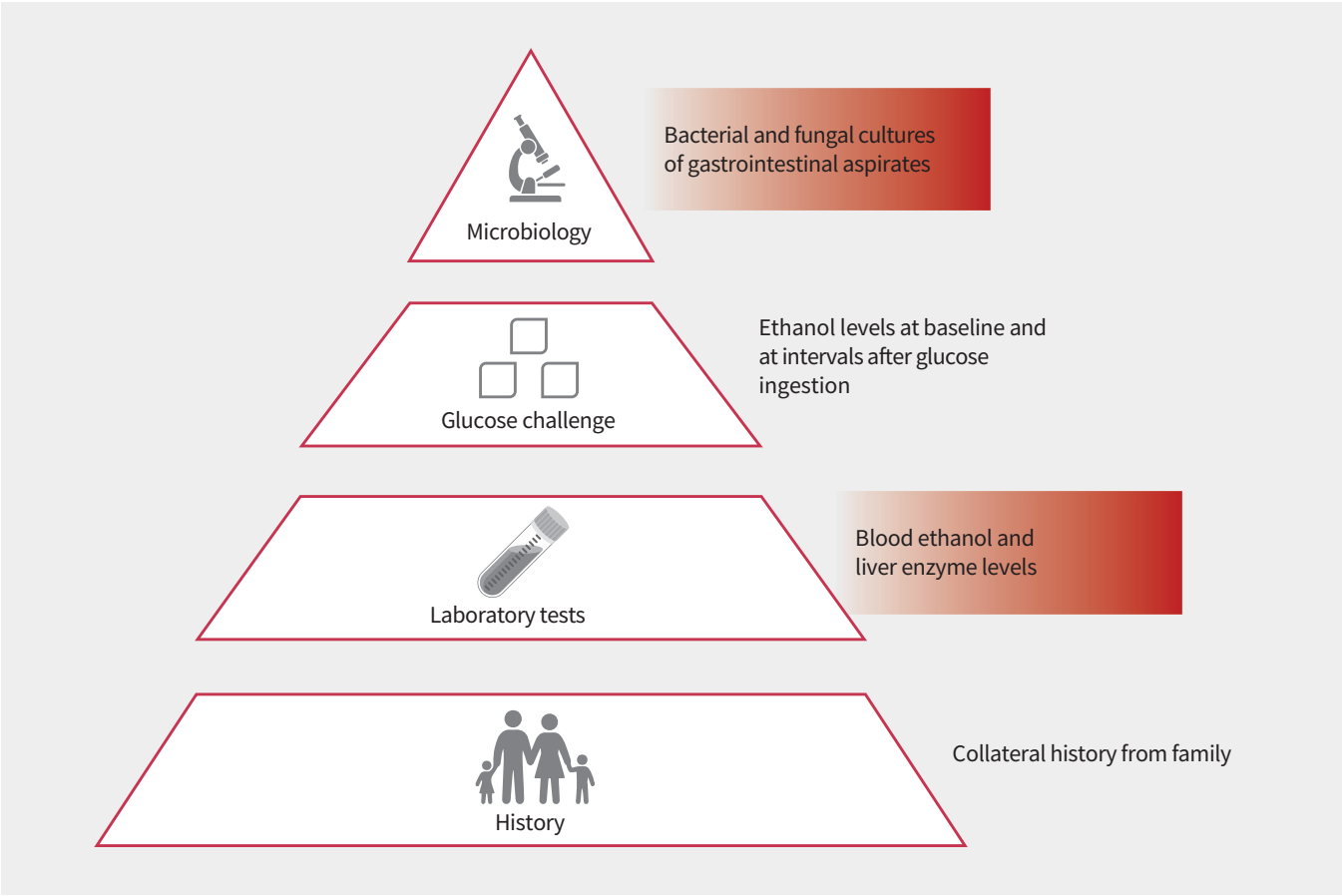

Figure 1: Diagnostic framework for suspected auto-brewery syndrome.

Relapse after antifungal treatment, in the absence of dietary nonadherence, should prompt endoscopic evaluation for culture and susceptibility testing. Echinocandins, itraconazole, voriconazole, and amphotericin B have been successfully used in cases of relapse after fluconazole.[7,8] One patient who had refractory symptoms despite trials of several antifungals received a fecal microbiota transplant with effective symptom resolution.[10]

Clinical and biochemical resolution of auto-brewery syndrome has been reported with 3 weeks of fluconazole (100–150 mg/d).[3,7] Among patients with relapsing disease, antifungal durations of 6–8 weeks have been successful.[3] In addition to antifungals, probiotics may provide benefit by replenishing gut bacteria as competitive flora to fungi.[3,8] Levofloxacin therapy resolved auto-brewery syndrome in a patient in whom *K. pneumoniae* was identified as a culprit pathogen.[9] Management of auto-brewery syndrome should include evaluation for hepatic effects of ethanol similar to those with alcohol use disorder.

Auto-brewery syndrome carries substantial social, legal, and medical consequences for patients and their loved ones. Our patient had several ED visits, was assessed by internists and psychiatrists, and was certified under the *Mental Health Act* before receiving a diagnosis of auto-brewery syndrome, reinforcing how awareness of this syndrome is essential for clinical diagnosis and management.

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