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An Unusual Case of Auto-brewery Syndrome Secondary to *Candida glabrata*

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Abstract

Auto-brewery syndrome occurs when ethanol concentrations increase in the body without alcohol consumption. This has been associated with a disruption in the gut microbiota leading to a prevalence of specific fungi which ferment carbohydrates into alcohol. Patients are clinically present with symptoms of acute alcohol intoxication and withdrawal whilst denying any alcohol consumption. This is a challenging diagnosis as diagnostic tests are not always reliable in proving the patient has not consumed alcohol. Once diagnosed, patients are managed with a complex interdisciplinary approach that involves a sugar-free diet with low carbohydrates and high protein concentrations, probiotic consumption, stool softeners, laxatives, antifungals, consistent monitoring of blood alcohol concentration (BAC), and fecal microbial transplantation if all other measures are unsuccessful. Non-medical management includes abstinence from driving and other tasks affected by alcohol intoxication. This case report presents an unusual case of a patient with auto-brewery syndrome secondary to *Candida glabrata* after prolonged exposure to amoxicillin. The patient was diagnosed after numerous unremarkable diagnostic tests, multiple visits to the emergency room, and failure to respond to traditional antifungal treatment.

Keywords: autobrewery syndrome, Candida glabrata, alcohol ethics, alcohol intoxication

Introduction

Auto-brewery syndrome (ABS), also known as gut fermentation syndrome, occurs when there is an increase in ethanol concentration in the body despite minimal alcohol consumption **[1,2]**. This occurs due to fungi such as *Saccharomyces cerevisiae*, *Saccharomyces boulardii*, or *Candida glabrata*, which convert carbohydrates into ethanol **[3]**. These fungi are part of the normal flora, however, antibiotic use can often sterilize the gut microbiome and lead to an imbalance of microorganisms in the gut. Blood alcohol levels are usually above 200 and can further increase with excessive consumption of carbohydrates or prolonged transit time of stool (e.g. chronic obstruction, hypomotility), causing increased fermentation **[4]**. Patients generally present with symptoms suggestive of acute alcohol poisoning, such as fatigue, memory loss, aggressive behavior, and depressive episodes despite denying any alcohol consumption. Diagnosis of ABS is usually delayed due to challenges in proving that patients have not consumed alcohol. Patients suspected of having ABS are given a provocative carbohydrate test, and alcohol levels are monitored at various intervals **[3]**. This case report presents a patient who was found to have auto-brewery syndrome due to *Candida glabrata* after multiple visits to the emergency room.

Case Description

A 59-year-old Caucasian male with a past medical history notable for hypertension, type 2 diabetes mellitus, fatty liver disease, and obesity presented to the hospital in April 2021 for confusion and inability to swallow. He was noted to have normal glucose levels of 101 mg/dL, a normal anion gap of 20, aspartate aminotransferase (AST) of 171 units/L, alanine aminotransferase of 207 units/L, lipase of 67 units/L. Most notably, his blood alcohol level (BAC) was 419 mg/dL on admission. A chest x-ray **(Figure 1)** was only remarkable for mild bibasilar atelectasis. He was admitted for acute alcohol intoxication and was treated symptomatically with aggressive intravenous **[5]** fluid hydration until his mental status improved. Despite his documented BAC, the patient's family was adamant that he had not consumed any alcohol. They reported a past history of multiple admissions for acute alcohol intoxication including facing stigma from healthcare providers who did not trust their denial of alcohol consumption. They further explained that he was undergoing a workup for a suspicion of underlying auto-brewery syndrome (ABS). The following description is the patient's clinical presentation and

workup that began in June 2020 up until our encounter with the patient in April 2021.

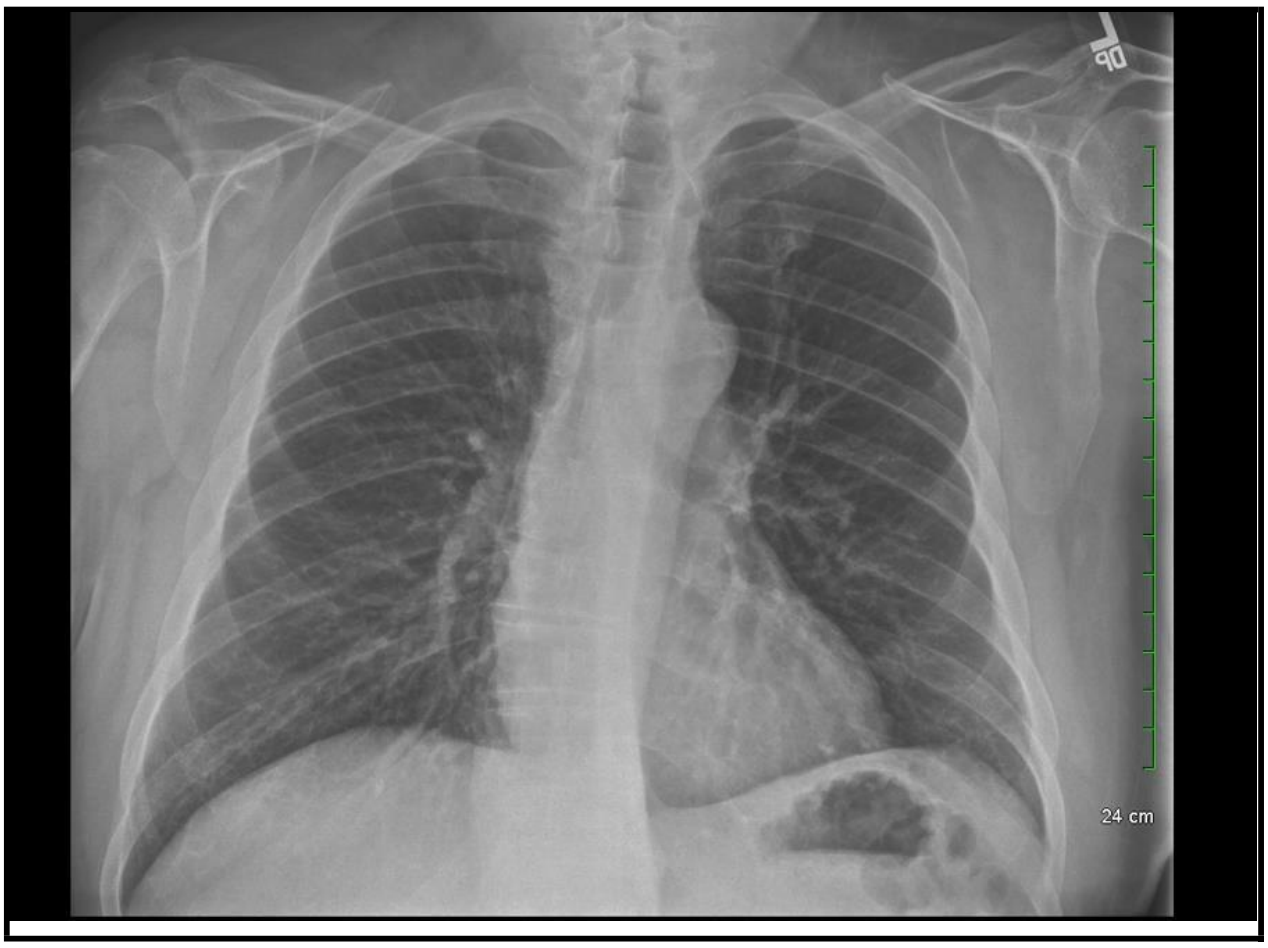

Figure 1: Patient's normal chest radiograph

Starting back in 2020, the patient's wife states that he was given a course of 875 mg of amoxicillin twice daily for two weeks to treat sinusitis. His wife noted initial symptoms of fatigue, confusion, and unsteady gait in early July 2020 after course completion. An incident was thereafter reported where the patient was found in a stupor with slurred speech and unsteady gait after an afternoon of swimming in the pool without alcohol. He was brought to the emergency department and was found to have a BAC of 343 mg/dL. The patient was observed for a decrease in BAC before being discharged after improvement of mental status. Given no proper explanation for his condition and the wife's insistence that he had not consumed alcohol, she began investigating other causes of alcohol intoxication and came across auto-brewery syndrome.

The patient continued to have elevated BAC levels despite a lack of alcohol consumption. He was seen in October 2020 at an outside hospital for a workup for auto-brewery syndrome consisting of a glucose tolerance test, esophagogastroduodenoscopy (EGD), colonoscopy, stool cultures, blood cultures, and labs that were all found to be normal. Though these tests were normal, the patient's wife reported that he continued to be symptomatic, and outside providers agreed with the diagnosis of auto-brewery syndrome based on clinical suspicion. He was started on 750,000 units of nystatin three times per day for a few days and then increased to 1,000,000 units three times per day.

In February 2021, the patient was started on fluconazole and switched to 100 mg of IV micafungin after symptoms did not improve with the hopes that escalation would resolve his symptoms. Despite this treatment, the patient was found to be confused and unable to swallow in April 2021. He was brought to the emergency department which was our team's first meeting with the patient. He was treated with IV fluids and subsequent workup was unremarkable for other etiologies of encephalopathy. After he achieved baseline mental status, he was discharged from the hospital and advised to follow up with another team for a workup of ABS on the off-chance that the initial workup was a false-negative.

After discharge, the patient underwent further endoscopy with duodenal biopsies obtained, and fluid cultures positive for *Candida glabrata*. He was started on 100 mg of IV micafungin daily via a peripherally inserted central catheter line (PICC) in the outpatient setting and after six days was escalated to 150 mg of IV micafungin daily for six weeks given he had no improvement on the lower dose of micafungin. He had a BAC of zero for 41 days on daily point-of-care breathalyzer checks. On the 42nd day, his PICC line was pulled, and his BAC subsequently increased. In September 2021, the patient was given a trial of oral amphotericin B, which was unsuccessful as the mixture was compounded with glycerin triggering carbohydrate conversion to ethanol. The patient's BAC was managed with water, and he was unable to tolerate any foods or liquids without elevating his BAC.

In October 2021, the patient presented to the emergency room after he was found to be unresponsive and was found to have a BAC of 411. He was managed with fluids until his BAC decreased, and he was discharged with plans to undergo evaluation for a fecal matter transplant.

At this point, the family managed him conservatively on a low carbohydrate and high protein diet with a dietician whilst undergoing

evaluation for a fecal matter transplant. His wife had joined multiple support groups and found that probiotics, Unicleinic acid, and frequent bowel movements helped to manage his symptoms. Prior to the patient's formal evaluation for a fecal matter transplant, his wife started to notice bottles of alcohol around the house. She was sure these were new bottles as he had not consumed alcohol before. He was found to start seeking alcohol and showing signs of cravings for alcohol consumption despite the adverse health effects. His fecal matter transplant evaluation was delayed, and ultimately, he was deemed to not be candidate, given the concern for auto-brewery syndrome versus alcohol use disorder. The wife described that the patient unsuccessfully went through Alcoholics Anonymous and a separate rehabilitation program, ultimately leading to negative changes in his mental behavior.

Discussion

Auto-brewery syndrome, or gut-fermentation syndrome, occurs when there is an increase in ethanol concentrations in the body without consumption of alcohol **[1,2]**. Fungi commonly associated with this syndrome include *Saccharomyces cerevisiae, Saccharomyces boulardii, and Candida glabrata* **[3]**.In the aforementioned case, the blood alcohol content did not rise during the glucose tolerance test and the cultures were negative, which did not confirm a diagnosis of ABS but triggered treatment initiation due to high clinical suspicion. With an increase in the dose of micafungin and eliminating dietary triggers such as carbohydrates, the patient's symptoms improved. His improvement with dietary modification as well as the family's consistent insistence of his not having consumed alcohol supported our hypothesis of auto-brewery syndrome secondary to *Candida glabrata*. To further support our hypothesis, there have been other case reports linking *Candida glabrata*to autobrewery syndrome **[4]**. The patient experienced a significant delay in diagnosis which is thought to be secondary to stigmatization as the burden of diagnosis relies in the trust of the patient's denial of alcohol **[3]**. In addition, there is a limit in test capability to differentiate between endogenous alcohol production versus exogenous alcohol consumption. In our patient, the *Candida glabrata* test was performed at an outside facility as the patient and their family were looking for alternative providers given the stigma they faced. The specific assay used was unable to be determined, however, the detection rate for *C. glabrata* was reported at 37.5% in one study, and in another study, the sensitivity was reported to be 73.9% **[6,7]**.

The delay in diagnosis also increased the time that the patient was exposed to high levels of alcohol, partly due to the difficulty in eliminating *Candida* glabrata. **[8,9]**. *Candida glabrata*is also known to have reduced azole susceptibility adding to the challenges in treatment **[10]**. In addition, other studies have shown that an increased dose of micafungin is needed to treat *C. glabrata*, as was seen in our patient **[5,7]**.

Taken together, the decreased detection rate and low sensitivity in the identification of *C. glabrata*led to the conclusion that the patient's first initial negative biopsy result was a false negative. Furthermore, there have been other case reports linking *Candida glabrata* to as an endogenous fermenter in autobrewery syndrome, further supporting our hypothesis that this micro-organism was the culprit **[4]**. This, in combination with the patient's improvement on an increased dose of micafungin, as reported by other studies, lead to our conclusion that the patient's ABS was due to overgrowth of *Candida glabrata.*

Auto-brewery syndrome is also difficult to treat as there are a broad range of triggers, which serves as a platform for future research. Most of the information for patients is also through case reports that can vary based on the patient's co-morbid conditions. There are many triggers for increased BAC such as diet, intestinal obstruction, and hypomotility **[4]**. Our patient also anecdotally reported constipation as a trigger for an ABS flares **[11]**. Taken together, this suggests that probiotics, stool softeners, and laxatives should be considered in the management of patients with ABS. Other considerations in managing ABS should include an interdisciplinary approach with a dietician to ensure patients receive adequate nutrition on a low-carbohydrate, high-protein, and sugar-free diet **[12]**. For patients who struggle to eradicate the fungi, fecal matter transplantation has been shown to be successful to restore balance in the gut microbiota **[8,13]**.

This case also highlighted not only the challenges in a delayed diagnosis, but also the consequences such as alcohol dependence and cravings. Patients who are diagnosed or suspected of having ABS should undergo a prompt workup and closely followed to prove lack of alcohol consumption. As seen in our patient, a delay in diagnosis can lead to unintended ethanol dependence due to prolonged exposure to high levels of alcohol. This not only has medical and/or legal implications, but also societal and familial implications associated with stigma and associated behavioral changes, respectively.

Conclusion

This case of auto-brewery syndrome secondary to *Candida glabrata* highlights the challenges of diagnosis, as the burden of proof relies on subjective reports from the patient. Furthermore, this case highlights the importance of reporting such cases of *Candida glabrata* to increase awareness of the syndrome and reduce future delays in diagnosis. Taken together, this also highlights that negative biopsy results in the setting of high clinical suspicion should prompt providers to consider treatment initiation, and to be aware that *Candida glabrata* can be challenging to eliminate.

References

1. Tameez Ud Din A, Alam F, Tameez-Ud-Din A, Chaudhary FMD (2020) Auto-Brewery Syndrome: A Clinical Dilemma. Cureus. 12(10): e10983.
2. Paramsothy J, Gutlapalli SD, Ganipineni VDP, Okorie IJ, Ugwendum D, et al. (2023) Understanding Auto-Brewery Syndrome in 2023: A Clinical and Comprehensive Review of a Rare Medical Condition. Cureus. 15(4): e37678.
3. Malik F, Wickremesinghe P, Saverimuttu J (2019) Case report and literature review of auto-brewery syndrome: probably an underdiagnosed medical condition. BMJ Open Gastroenterol. 6(1): e000325.
4. Welch BT, Coelho Prabhu N, Walkoff L, Trenkner SW (2016) Auto-brewery Syndrome in the Setting of Long-standing Crohn's Disease: A Case Report and Review of the Literature. J Crohns Colitis. 10(12): 1448-1450.
5. Dinis-Oliveira RJ (2021) The Auto-Brewery Syndrome: A Perfect Metabolic “Storm” with Clinical and Forensic Implications. Journal of Clinical Medicine. 10(20): 4637.
6. García-Salazar E, Acosta-Altamirano G, Betancourt-Cisneros P, Reyes-Montes MDR, Rosas-De-Paz E, et al. (2022) Detection and Molecular Identification of Eight Candida Species in Clinical Samples by Simplex PCR. Microorganisms. 10(2): 374.
7. Wang K, Huo L, Li Y, Zhu L, Wang Y, et al. (2022) Establishment of a rapid diagnosis method for Candida glabrata based on the ITS2 gene using recombinase polymerase amplification combined with lateral flow strips. Front Cell Infect Microbiol. 12: 953302.
8. Vandekerckhove E, Janssens F, Tate D, De Looze D (2020) Treatment of Gut Fermentation Syndrome With Fecal Microbiota Transplantation. Ann Intern Med. 173(10): 855.
9. Kruckenberg KM, DiMartini AF, Rymer JA, Pasculle AW, Tamama K (2020) Urinary Auto-brewery Syndrome: A Case Report. Ann Intern Med. 172(10): 702-704.
10. Xiao M, Fan X, Chen SC, Wang H, Sun ZY, et al. (2015) Antifungal susceptibilities of Candida glabrata species complex, Candida krusei, Candida parapsilosis species complex and Candida tropicalis causing invasive candidiasis in China: 3 year national surveillance. J Antimicrob Chemother. 70(3): 802-10.
11. Altomare DF, Portincasa P, Rinaldi M, Di Ciaula A, Martinelli E, et al. (1999) Slow-transit constipation: solitary symptom of a systemic gastrointestinal disease. Dis Colon Rectum. 42(2): 231-40.
12. Painter K, Cordell BJ, Sticco KL (2022) Auto-brewery Syndrome. StatPearls. Copyright © 2022, StatPearls Publishing LLC., Treasure Island (FL).
13. Malikowski T, Khanna S, Pardi DS (2017) Fecal microbiota transplantation for gastrointestinal disorders. Curr Opin Gastroenterol. 33(1): 8-13.