OBSERVATION: CASE REPORT

Urinary Auto-brewery Syndrome: A Case Report

Background: Auto-brewery syndrome is a rare medical condition in which intoxicating quantities of ethanol are produced by specific types of yeast or bacteria through endogenous fermentation in the digestive system (1).

Objective: To alert clinicians to the possibility of a previously unrecognized auto-brewery syndrome in which ethanol is produced through endogenous fermentation in the urinary system.

Case Report: A 61-year-old woman with cirrhosis and poorly controlled diabetes presented to our center for placement on the liver transplant waitlist. Previously, clinicians at another hospital advised her to obtain treatment for alcohol addiction instead of placing her on their center's liver transplant waitlist because urine tests for alcohol were repeatedly positive. Initially, our encounters were similar, leading our clinicians to believe that she was hiding an alcohol use disorder. However, we noted that plasma test results for ethanol and urine test results for ethyl glucuronide and ethyl sulfate, which are the metabolites of ethanol (2), were negative, whereas urine test results for ethanol were positive (**Table**). In addition, the patient did not have alcohol intoxication symptoms during clinic visits, despite urine ethanol values greater than 39.1 mmol/L (>180 mg/dL). Moreover, she consistently denied alcohol consumption. Besides these discrepancies, we also noticed that she frequently had hyperglycosuria (≥55.5 mmol/L [≥1000 mg/dL]) with abundant budding yeast in urine samples (**Table**). These findings led us to test whether yeast colonizing in the bladder could ferment sugar to produce ethanol (3). The **Figure** describes the in vitro experiment we used to demonstrate remarkably high levels of ethanol production

Table. Laboratory Findings

Analytes	Results	Reference Values
Alcohol		
Ethanol (plasma)	Negative	Negative (cutoff = 2.2 mmol/L [10 mg/dL])
Ethanol (urine)	Positive	Negative (cutoff = 4.4 mmol/L [20 mg/dL])
Ethyl glucuronide (urine)	Negative	Negative (cutoff = 500 ng/mL)
Ethyl sulfate (urine)	Negative	Negative (cutoff = 100 ng/mL)
Serum chemistry		
Sodium, *mmol/L*	137	136–146
Potassium, *mmol/L*	4.0	3.5–5
Chloride, *mmol/L*	101	98–107
Bicarbonate, *mmol/L*	22	21–31
Urea nitrogen		
mmol/L	4.6	2.9–9.3
mg/dL	13	8–26
Creatinine		
μmol/L	44.2	44.2–123.8
mg/dL	0.5	0.5–1.4
Glucose		
mmol/L	16.3	3.9–5.5
mg/dL	293	70–99
Total protein, *g/L*	68	63–77
Albumin, *g/L*	35	34–50
Aspartate aminotransferase, *U/L*	23	15–41
Alanine aminotransferase, *U/L*	12	14–54
Total bilirubin		
μmol/L	61.6	5.1–25.7
mg/dL	3.6	0.3–1.5
Direct bilirubin		
μmol/L	17.1	1.7–8.6
mg/dL	1.0	0.1–0.5
Alkaline phosphatase, *μkat/L*	2.98	0.65–2.14
Diabetes		
Hemoglobin A_{1c}, %	8.6	<5.7
Urinary analysis		
Clarity	Cloudy	Clear
Bilirubin	Negative	Negative
Blood	Negative	Negative
Ketone	Negative	Negative
Protein	Negative	Negative
Glucose		Negative
mmol/L	≥55.5	
mg/dL	≥1000	
Microscopic analysis	Numerous budding yeast	

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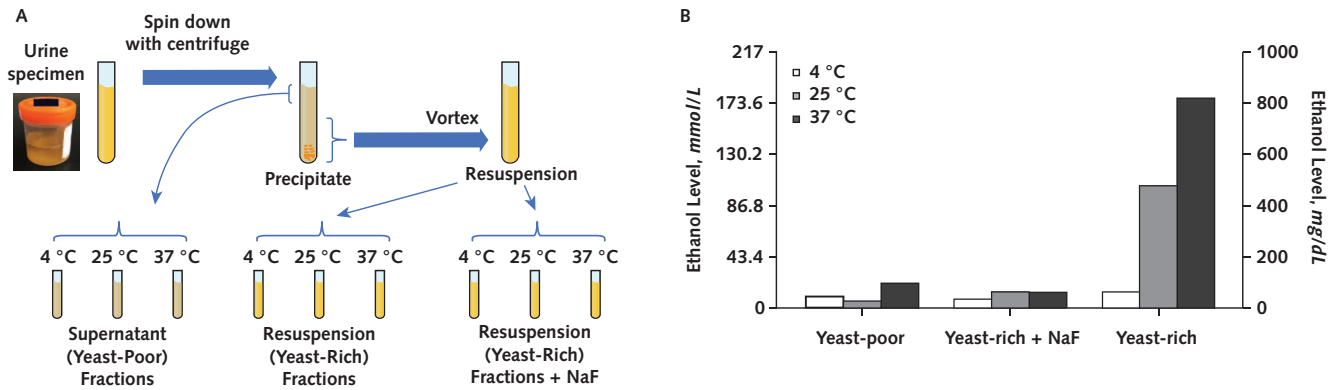
Figure. Ethanol production by fermenting yeasts.



A. Outline of the experiment. In this experiment, the freshly voided urine sample was immediately transported to the laboratory on ice. The specimen was centrifuged into yeast-poor and yeast-rich fractions for incubation at 3 temperatures (4 °C, 25 °C, and 37 °C) for 24 h. The yeast-rich fraction was also incubated in the presence of 1% sodium fluoride, a fermentation inhibitor. The ethanol level was determined using headspace gas chromatography. **B.** The ethanol levels in the urine sample after 24 h incubation. The ethanol level increased from 9.6 mmol/L (44 mg/dL) (baseline before incubation) to 103.3 mmol/L (476 mg/dL) and 177.1 mmol/L (816 mg/dL) after 24-h incubation at 25 °C and 37 °C, respectively. In contrast, minimal ethanol production was seen in the yeast-poor fraction and sodium fluoride and 4 °C conditions. No ethanol production was seen after 24-h incubation at 37 °C in the negative control urine (data not shown).

(3.9 mmol/L [18 mg/dL] per hour at 25 °C and 6.9 mmol/L [32 mg/dL] per hour at 37 °C) in the patient's freshly voided urine. As a result, we concluded that the discrepant test results were best explained by yeast fermenting sugar in the bladder. We identified the yeast as *Candida glabrata*, which is part of the normal body flora and is closely related to brewer yeast or *Saccharomyces cerevisiae* (4). We tried eliminating this yeast using an oral antifungal regimen but it was unsuccessful, presumably because of the patient's poorly controlled diabetes. As a result of our experiment and new appreciation for her pathophysiology, she was reconsidered for liver transplantation.

Discussion: Production of ethanol through fermentation of yeast in the urine of patients with poorly controlled diabetes has been reported elsewhere, but these reports are limited to 1 postmortem case and in vitro conditions (3). We have not found a similar report of yeast producing ethanol by fermenting sugar in the bladder. We propose calling this phenomenon "urinary auto-brewery syndrome" or "bladder fermentation syndrome." This syndrome is similar to but distinct from the traditional auto-brewery syndrome, which is also known as "gut fermentation syndrome" (1), whereby alcohol is generated by fermenters in the gastrointestinal tract, producing a positive plasma ethanol level and causing symptoms of intoxication.

The experience we describe here of 2 liver transplant teams at different institutions demonstrates how easy it is to overlook signals that urinary auto-brewery syndrome may be present. Acquiring all of the data necessary to evaluate a transplant candidate is complicated because of the high stakes, time constraints, and workload of the persons acquiring the data. Proper processing of data is even more difficult—it is all too easy to order alcohol monitoring tests inconsistently, overlook discrepancies in the results, and allow bias to enter and persist in the decision-making process. Standardized guidelines for abstinence monitoring laboratory interpretation are needed.

We remind clinicians of the importance of recognizing urinary auto-brewery syndrome when it is present. Abstinence monitoring is involved in many medical and legal contexts. For example, abstinence monitoring is part of some addiction treatment programs and is ordered by some courts to help determine custody in family disputes. It is also part of many pretransplant evaluations (5). Clinicians must be diligent about paying close attention to medical record documentation and laboratory results and should always investigate in the event of incongruences.

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