

## Case Report

# Auto-brewery syndrome caused by oral fungi and periodontal disease bacteria

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**Background:** Auto-brewery syndrome (ABS) is often caused by fungi in the intestinal tract. We describe a rare case of alcohol production by *Candida albicans* and periodontal disease bacteria in the oral cavity.

**Case Presentation:** A man aged in his 60s had a car accident, and alcohol was detected on his breath. At the time, he exhibited alcohol overdose seizures with no alcohol consumption. We carried out a gastrointestinal endoscopy, detected esophageal candidiasis, and diagnosed ABS. His seizures continued despite using miconazole oral gel. Significant tooth decay, periodontal disease, and high *C. albicans* levels were observed in his oral cavity. Alcohol production was confirmed from periodontal bacteria and *C. albicans* cultures and alcohol-degrading enzyme functions were poor. Dental treatment and antifungal drugs reduced seizures, and improved his fatty liver.

**Conclusion:** Alcohol can be produced by microorganisms in healthy individuals. Therefore, blood alcohol levels and alcohol-degrading enzyme functions should be examined in patients with unexplained liver dysfunction.

**Key words:** Alcohol, auto-brewery syndrome, *Candida albicans*, fatty liver, periodontal disease

## INTRODUCTION

PREVIOUS REPORTS SUGGEST that auto-brewery syndrome (ABS) is caused by alcohol produced by fungi in the stomach and intestines.<sup>1</sup> We encountered a unique ABS case, which was caused by periodontal disease and oral candidiasis.

## CASE REPORT

THE CASE INVOLVES a man aged in his 60s with height 170 cm and body weight 63 kg. He had a medical history of fatty liver, and his family history was unremarkable.

In 2016, the patient had a car accident and alcohol was detected on his breath. He had not been drinking for more than 12 h prior to the accident. He was admitted to the department of gastroenterology at our hospital after confirming that he had not brought alcoholic beverages. During his stay, his alcohol overdose seizures persisted once every 1–3 days, and a 100–300 mg/dL alcohol range was detected. We carried out upper and lower gastrointestinal endoscopy, capsule-type endoscopy, and gastric juice and stool microbiology cultures. No gastrointestinal tract abnormalities, that is, diverticula, which accumulate food residues and fungi, were confirmed. Mild esophageal candidiasis was detected in the upper esophagus, with *Candida albicans* detected in the patient's gastric juices. He was subsequently diagnosed with ABS caused by esophageal candidiasis. After taking 2% miconazole oral gel for 7 days, his seizures temporarily disappeared, but they recommenced once every 1–3 days. After discharge, his seizures continued and he repeatedly appeared at our emergency center. In 2020, at the time of emergency transport, he developed neuropathy when a drip needle was inserted into his upper limb, therefore, he was admitted.

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Received 7 Dec, 2020; accepted 31 Mar, 2021

### Funding information

No funding information provided.

Even after admission, the patient's seizures recurred once every 1–3 days. As we planned another gastrointestinal endoscopy, we observed significant tooth decay and periodontal disease in his oral cavity (Fig. 1). Thus, we suspected periodontal disease bacteria and *C. albicans* had colonized this environment. Samples were collected and cultures carried out. We observed high *C. albicans* densities of 20 colonies/medium from buccal mucosa. Furthermore, although bacterial counts were unknown, the following were detected in periodontal lesions: *Streptococcus sanguinis*, *Streptococcus parasanguinis*, *Streptococcus mitis*, *Leuconostoc lactis*, *Corynebacterium sp.*, *Klebsiella pneumoniae*, and *Enterobacter cloacae*. We immediately extracted several decayed/decaying teeth, and orally administered 2% miconazole oral gel and povidone-iodine gargle. On day 7 of treatment, the miconazole oral gel was switched to amphotericin B syrup due to the appearance of a mild drunkenness seizure. The patient also continued with oral micafungin at 100 mg/day for 4 weeks. On day 10 of treatment, *C. albicans* densities decreased to one colony/medium and his seizures almost disappeared (Fig. 2). Currently, with ongoing dental treatment and regular culture testing, his periodontal disease has improved and *C. albicans* levels have not increased.

## DISCUSSION

IN JAPAN, ABS was reported as “meiteisho” by Sato *et al.* in 1952. This condition is also called gut fermentation syndrome or endogenous ethanol fermentation, however, no unified clinical nomenclature has been proposed. The underlying ABS mechanism is believed to be caused by *C. albicans*<sup>2</sup> and/or *Saccharomyces cerevisiae*,<sup>3</sup> which



**Fig. 1.** Maxillary teeth of a man aged in his 60s with auto-brewery syndrome. Defects of teeth are due to decay on the back teeth, misalignment of the front teeth, and periodontal disease.

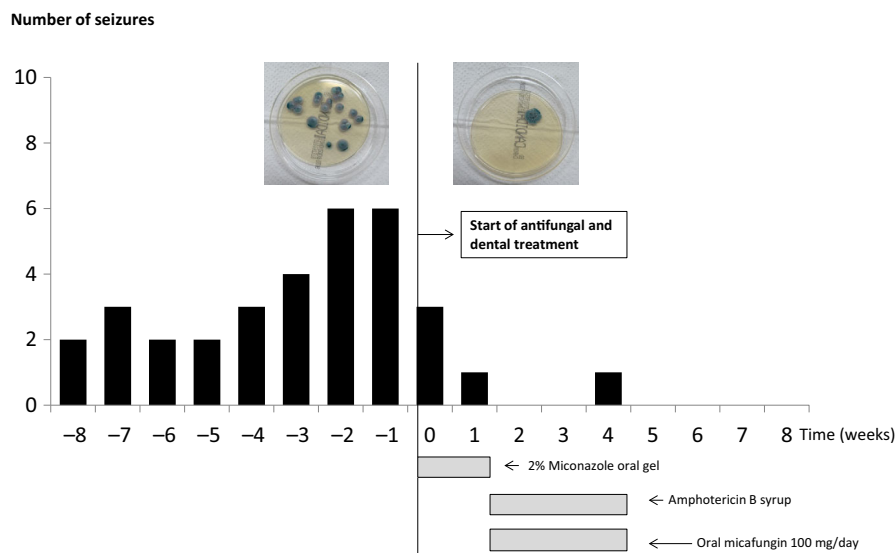
colonize the stomach and intestines and react with glucose to produce alcohol, leading to alcohol overdose seizures. Potential ABS causes are linked to antibiotic use,<sup>4</sup> depression of the anastomotic site due to gastrointestinal surgery, and gastrointestinal and urinary bladder<sup>5</sup> diverticulum. Treatments include the surgical excision of food residue accumulation sites, oral antifungal drugs, and low-carbohydrate diets.

During initial ABS stages, we suspected a diverticulum in the patient's gastrointestinal tract. We carried out endoscopic examinations but the cause of his seizures remained undetermined. Antifungal drugs improved symptoms but only for a few days, as his seizures soon recurred. We noted extensive tooth decay in the oral cavity and speculated this poor oral environment was associated with his seizures. Dental treatment, antifungal drugs, and gargling with povidone-iodine were administered, and his seizures subsided. In addition, the blood alcohol levels at the time of seizures decreased significantly ( $222.1 \pm 13.3/139.8 \pm 18.7$  mg/dL before/after treatment,  $P < 0.05$ , *t*-test).

To confirm alcohol production from the oral cavity, we examined alcohol-producing abilities of fungi and periodontal disease bacteria from the oral cavity. First, we supplemented sugar to the patient's *C. albicans* culture as well as to the *C. albicans* cultures from two healthy subjects. We then assessed alcohol levels after 12 h of incubation (Appendix 1). Patient cultures did not show high alcohol-producing abilities when compared with the two healthy subjects. Subsequently, *Streptococcus* and *K. pneumoniae* collected from periodontal disease lesions of this patient were added to his samples, cultured for 12 h, and assessed for alcohol production. Interestingly, *Streptococcus*- and *K. pneumoniae*-added samples detected much higher alcohol levels than *C. albicans*-only samples. Similar results were obtained when *K. pneumoniae* was collected from healthy subjects. Thus, periodontal disease bacteria such as *Streptococcus* and *K. pneumoniae* had higher alcohol-producing capabilities than fungi.

To rule out alcohol production from the intestinal tract, we thoroughly washed the oral cavity, gave 40 g of glucose to the patient, and measured hourly blood alcohol levels. No blood alcohol levels were detected for 6 h after oral glucose had been given. Therefore, for this patient, alcohol production from the intestinal tract was ruled out as a cause of his seizures.

Oral candidiasis is not rare. Chika *et al.* reported that approximately 30% of healthy individuals,<sup>6</sup> regardless of age, experienced *Candida* colonization in their oral cavities. We know that *Streptococcus* and *K. pneumoniae* are present in the oral cavity and intestinal tract of many humans, suggesting most could be producing endogenous alcohol after



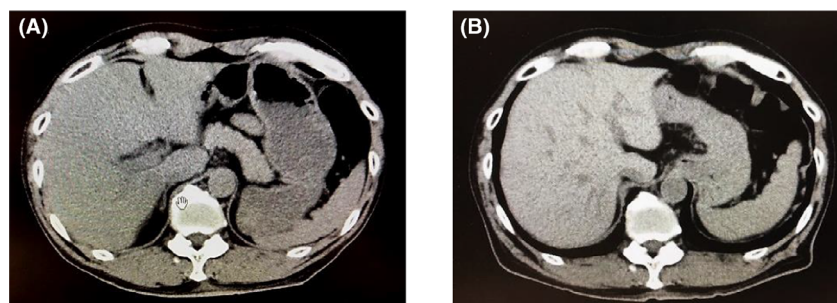
**Fig. 2.** Frequency of alcohol overdose seizures before and after the start of antifungal and dental treatment in a man aged in his 60s with auto-brewery syndrome. A few days from starting treatment, mild seizures were observed. On day 7 of treatment, a mild seizure was observed; 2% miconazole oral gel was discontinued, and amphotericin B syrup and micafungin 100 mg/day was started. Seizures were suppressed after discontinuing oral medication and syrup. The number of *Candida* colonies was 20 before the start of treatment, but decreased to one on day 10 of treatment.

ingesting sugar. Another study reported that up to 3.5 mg/dL alcohol was detected in 1,557 healthy alcohol-free individuals, due to fungal parasitization of the gastrointestinal tract, presumably due to fermentation.<sup>7</sup> In another study where an alcohol-degrading enzyme inhibitor was orally administered, blood alcohol levels were increased when apple juice was ingested without alcohol in healthy subjects.<sup>8</sup> These reports support the notion that endogenous alcohol production occurs in healthy humans.

So why did we observe severe alcohol overdose seizures in this patient? To address this issue, buccal mucosa cells were genetically tested for common polymorphisms in alcohol and acetaldehyde-degrading enzymes (Appendix 1). Alcohol-degrading enzymes had very low activity, and toxic acetaldehyde-degrading enzymes had very high activity in this patient. These polymorphism types are prevalent in 2.8% of the Japanese population, and are considered very rare.<sup>9</sup> Therefore, in this patient: (i) *Candida* and periodontal disease bacterial levels in the oral cavity were originally high due to excessive tooth decay and periodontal disease, (ii) acetaldehyde, which adversely affects bacterial growth, was easily degraded, potentially permitting bacteria growth in this cavity, (iii) the alcohol-degrading activity in the oral cavity was very poor. Thus, when these factors were combined, we repeatedly observed his seizures.

Currently, patient dental treatment and gargling with povidone-iodine are ongoing, oral antifungal drugs have been discontinued, and seizures have not recurred. *Candida albicans* is now not detected in the oral cavity, nor the intestinal tract. In addition, *Streptococcus* and *K. pneumoniae* are not detected in the oral cavity. However, *Streptococcus* and *K. pneumoniae* are likely present in the intestinal tract, and *C. albicans* is ingested from many foods, so these microbes could recolonize the oral cavity. Long-term oral antibiotic and antifungal treatments are not appropriate, therefore, complete seizure suppression might be impossible. However, seizure frequency and severity can be controlled by continuing oral care with appropriate antibiotics and antifungals based on symptoms.

Low alcohol levels are typically produced in the oral cavity and digestive tract of healthy individuals, but when enzymatically controlled by alcohol-degrading enzymes or diluted by body fluids, alcohol overdose seizures are rare. When alcohol-degrading enzyme activity is poor, some individuals might be constantly exposed to trace alcohol levels. For our patient, although the direct relationship with this treatment was unclear, his fatty liver improved considerably, even though no changes in body weight were recorded (Fig. 3). Prolonged exposure to alcohol in the oral cavity could have been the cause of his fatty liver. A recent report<sup>10</sup> suggested that endogenous alcohol produced by



**Fig. 3.** Computed tomography (CT) images of a man aged in his 60s with auto-brewery syndrome. (A) Abdominal CT image before the start of antifungal and dental treatment. (B) Abdominal CT image taken 33 days after the start of antifungal and dental treatment. Fatty liver improved on the image.

*K. pneumoniae* caused non-alcoholic fatty liver. Thus, in cases where unexplained headaches or liver dysfunction persist, blood alcohol levels, bacterial and fungal levels in the oral cavity, and alcohol and acetaldehyde-degrading enzyme functions should be explored.

## ACKNOWLEDGMENTS

WE ARE DEEPLY grateful to Professor Mitsuo Kishi who provided advice on dental treatments.

## DISCLOSURES

Approval of the research protocol: N/A.

Informed consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Registry and the registration no. of the study/trial: N/A.

Animal studies: N/A.

Conflict of interest: None.

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## APPENDIX 1

### ALCOHOL PRODUCTION TEST

FIVE MICROLITERS OF a solution prepared by adjusting *Candida albicans* (from the patient and two healthy controls) to McFarland 0.5 was added to 1 mL brain heart infusion broth containing 5% glucose. The mixture was incubated at 37°C for 12 h and further cultured. The alcohol levels in our patient were 71 mg/dL, whereas healthy control I was 36 mg/dL and healthy control II was 59 mg/dL. In addition, the alcohol level from *C. albicans* and *Streptococcus* in the patient was 191 mg/dL, and the alcohol concentration of *C. albicans* and *Klebsiella pneumoniae* was 220 mg/dL.

Blood alcohol levels were measured on a LABOSPECT 008 $\alpha$  instrument (Hitachi, Tokyo, Japan).

### TESTING OF GENES RELATED TO ALCOHOL METABOLISM

**T**HE ARG47HIS POLYMORPHISM of alcohol dehydrogenase 1B (*ADH1B*) and the Glu487Lys

polymorphism of aldehyde dehydrogenase 2 (*ALDH2*) were investigated by EBS (Hiroshima, Japan) on a Mass ARRAY System (Agena Bioscience, San Diego, CA, USA). A genetic polymorphism in *ADH1B* was identified as Arg/Arg, which was a homo-hypoactive type. A genetic polymorphism in *ALDH2* was identified as Glu/Glu, which was a homo-active type.