A Case Series of 25 Auto-Brewery Syndrome patients: A single community hospital experience

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ABSTRACT

Introduction

Auto-brewery syndrome (ABS) is a rare condition where ingested carbohydrate is converted to alcohol by enteric fungi; a diagnosis often discounted by medical personnel. The goal of our study was to confirm or refute the diagnosis of ABS with a systematic investigative and treatment plan. Initial success caused patients from across the country to seek our center.

Methods

Criteria for evaluation were as follows: alcohol abstinence, positive breathalyzer without alcohol ingestion, concomitant elevated blood alcohol level, corroboration of abstinence from family member or close friend, and prior medical evaluation for an alternative cause of symptoms.

If patient met criteria, they underwent endoscopic evaluation for collection of gastrointestinal secretions. Collected samples were sent for culture with sensitivities. After endoscopy, patient submitted to a Carbohydrate Challenge Test (CCT), which involved breathalyzer as well as initial serum glucose and ethanol levels. Then ingestion of 200g of glucose, followed by serial monitoring of breathalyzer, serum glucose and serum ethanol levels for 8 hours.

Then patients started on antifungal therapy, carbohydrate free diet for 6 weeks and serial breathalyzer monitoring, followed by reintroduction of carbohydrates to diet. If breathalyzer turned positive, then antifungal regimen was adjusted based on cultures.

Results

The 25 patients included 20 males and 5 females, age range 20-63(41.8) years. All patients had antibiotic exposure prior to symptoms. 16(64%) had a positive CCT. 11(69%) patients had antifungal therapy prior to CCT. Cultures revealed a variety of fungi with multiple patients harboring multiple fungi. *Saccharomyces cerevisiae* was most common, present in 7(28%) patients. Also noteworthy was 1 patient with positive CCT had negative cultures.

Significant associations were noted with esophagitis 12(48%) and Barrett's esophagus 7(28%). Lastly, all patients suffered from complications including: multiple hospitalizations for alcohol intoxication 8(32%), end stage liver disease 4(16%), arrest for driving under the influence 6(24%), pancreatitis 2(8%), and traumatic subdural hemorrhage 1(4%).

Discussion

ABS represents a challenge in establishing diagnosis and administering effective treatment. These cases demonstrate ABS's varied presentation, shows our testing and treatment methodology, and highlights areas for further research both in diagnostic modalities and treatment protocols to more effectively manage this orphan disease

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INTRODUCTION

Auto-brewery syndrome (ABS) is a rare medical condition where ingested carbohydrate is converted to alcohol by enteric fungi. In our patient cohort of 25, this condition was triggered by prior exposure to antibiotics. Antibiotics are known to change the gut microbiome allowing fungal overgrowth. There is one series of ABS where klebsiella species were implicated in alcohol production from carbohydrates [1]. To date there has been no such case series investigating fungi causing ABS. This diagnosis was often not accepted even by medical personnel. To validate this diagnosis, we performed a standardized Carbohydrate Challenge Test (CCT) in 25 patients from 2014 to the 2022. The purpose of our study was to confirm or refute the diagnosis of ABS, and to have a rational investigative and a treatment plan. This case series details the results of our investigative protocol, patient comorbidities, the fungal species identified, and complications of ABS in our cohort.

METHODS

Inclusion Criteria: Positive breathalyzer in the absence of any alcohol ingestion, a concomitant elevated blood alcohol level, and if possible, a family member or friend to corroborate abstinence..
We were contacted by more than 300 patients complaining of ABS symptoms. Only 25 fit our inclusion criteria and were accepted into our investigational protocol.
First upper and lower endoscopy were performed for collecting gastrointestinal secretions for pH, gram stain, culture and sensitivity and bacterial and fungal studies. After endoscopic evaluation CCT was initiated.
CCT: Initial serum glucose and ethanol levels as well as breathlyzer levels were taken. Next patients ingested 200g of oral glucose. Then serum glucose and ethanol levels were monitored at 30 minutes, 1 hours, 2 hours, 4 hours, and 8 hours. During the test patients were allowed a regular diet. If no ethanol was detected in blood samples at 8 hours patients could opt to return sample collection 16 hours and 24 hours.
Following CCT: Patient's adhered to empiric antifungal therapy, a carbohydrate free diet, and alcohol abstinence for 6 weeks, while regularly monitoring breathalyzer levels. After completing the antifungal therapy carbohydrates were slowly and successfully reintroduced into their diet. If breathalyzer results turned positive, antifungal therapy was resumed, this time tailored based on fungal cultures.

RESULTS

25 patients including 20 males and 5 females with an age range of 20-63(41.8) years. 16(64%) had a positive CCT. 24 patients had at least one fungal species identified on culture of gastrointestinal secretions. It is also noteworthy that in our entire cohort only 1 patient did not demonstrate any fungal or Klebsiella growth from secretion specimens, however that patient did have a positive CCT. Below is detailed the funal species identified, patient comorbidities, and complications from ABS.
Fungal cultures revealed a wide variety of fungi with multiple patients demonstrating multiple fungi present. Saccharomyces cerevisiae (brewer's yeast) was the most common species identified, present in 7(28%) of our patients. Candida was the most common genus identified. A complete list of the fungi identified is included in Table 1.
Numerous comorbidities were noted with the most common being esophagitis, Barrett's esophagus, hypertension, and obesity. A summary of comorbidities in included in Table 2.
Lastly, all patients suffered from complications from ABS. The most common being multiple hospitalizations for acute alcohol intoxication 8(32%). Other serious complications notably included end stage liver disease 4(16%), traumatic subdural hemorrhage 1(4%), and arrest for driving under the influence of alcohol 6(24%). A complete listing of complications from ABS is listed in Table 3.

Table 1. Fungal Species Detected

Fungal Species Identified	Frequency
Aspergillus versicolor	1
Candida albicans	5
Candida dubliniensis	2
Candida glabrata	2
Candida guillienmondii	1
Candida intermedia	1
Candida lambica	1
Candida lusitaniae	1
Candida parapsilosis	4
Candida sojae	1
Cryptococcus albidus	1
Geotrichum klebahnii	1
*Klebsiella Species**	4
Penicillium	3
Pichia manschurica	1
Rhodotorula minuta	1
Rhodotorula mucilaginosa	4
Rhodotorula species	1
Saccharomyces cerevisiae	7
None	1

*Bacteria implicated in ABS in literature

Table 2. Comorbidities

Obesity	5
Hypertension	6
Hyperlipidemia	1
Diabetes Mellitus	2
Cirrhosis	2
Multiple Sclerosis	1
Asthma	2
Coronary Artery Disease	1
Inflammatory Bowel Disease	1
Barrett's Esophagus	7
Esophagitis	12
Peptic Ulcer Disease	2

Table 3. Complications from ABS

Anxiety	3
Aspiration Pneumonia	1
Depression	5
DWI	6
End Stage Liver Disease	4
Mechanical Fall	4
Multiple Hospitalizations	8
Pancreatitis	2
Seizures	1
Traumatic Subdural Hemorrhage	1

DISCUSSION

During the past 10 years we have been treating these patients, we have come to learn that successfully treated patients could relap. If and when this happened these patients were restudied as before to detect presence of fungi or high alcohol producing klebsiella in their GI secretions and then retreated appropriately. Many of these were due to antibiotic exposure or unknown trigger which required retreatment with antifungals. We have come to learn ABS could be a recurrent or relapsing condition and each new episode would have to be reinvestigated and retreated. If our treatment failed, we offered a Brazilian dietary supplement protocol as another option. This was carried out with the assistance of a local nutritionist. We only had access to commercial laboratories for bacterial and fungal studies. These commercial laboratories would only detect about 30-35% of gut Fungi. We are hoping to have access to genomic studies in the future for better identification for gut microbiome and mycobiome [2-3]. We are also hoping to be able to send stool samples for sophisticated genomic studies on gut mycobiota and microbiota.
We have only just started to understand this complicated condition of ABS and more research is needed. The role of probiotic use and fecal transplantation in this condition has yet to be elucidated as well. This study opens up a myriad of investigational avenues for others to follow. The terms of legality with regard to DWI could also be a subject for future discussions. It is our hope our understanding of ABS diagnosis and treatment will continue advance with new technological advances with increasing fungi detection.
Patients with ABS represent a unique challenge both in establishing their diagnosis as well as regarding administering effective treatment. The cases presented in this case series demonstrate ABS's varied presentation, highlights how we have been treating our patients, and finally where further research both in diagnostic modalities as well as treatment protocols in order to more effectively treat patients with this orphan disease should be directed.

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