

Case report

Probable *Clostridium septicum* pneumocephalus in a user of natural remedies with newly diagnosed diabetes mellitus type 1



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ABSTRACT

Clostridium septicum encephalitis is a rare cause of spontaneous, non-traumatic pneumocephalus. Systemic infections with this organism have a fulminant course, likely leading to death within 48 hours, and are commonly associated with hematological or colonic malignancies. The effectiveness of an antibacterial regimen is unknown because of a lack of studies. The best prognosis is observed in patients undergoing early surgical intervention for localized intracranial processes. Here we describe a case of rapidly developing *C. septicum* sepsis as a result of bacteremia and hematogenous spread, resulting in encephalitis and pneumocephalus in a patient without a diagnosed malignancy. The patient presented to the emergency department with diabetic ketoacidosis, which led to the diagnosis of new-onset type 1 diabetes mellitus. There are currently 19 reported cases of *C. septicum* central nervous system infections in the literature, with 12 of them having pneumocephalus. Natural remedies, such as drinking kombucha tea and performing coffee enemas, that were used by our patient may have played a role in the dissemination of *C. septicum*. In survivors of this fulminant illness, colonic and hematologic malignancies should be excluded because of their association with such infections. Type 1 diabetes mellitus, drinking kombucha tea, and performing coffee enemas may be newly recognized risk factors associated with the dissemination of *C. septicum*.

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Introduction

Pneumocephalus refers to air in the cranial cavity, typically due to head trauma, tumors, or iatrogenic following neurosurgery. *Clostridium septicum* infection is a rare cause of spontaneous, non-traumatic pneumocephalus [1]. Infections with this organism are rare, causing only 1.3% of all clostridial infections [2]. However, it is an important pathogen due to its strong association with colonic and hematologic malignancies, and its fulminant course seen in the limited number of cases of *C. septicum* central nervous system (CNS) infections reported in the literature to date [2]. Here we report a case of rapidly developing *C. septicum* pneumocephalus in a patient presenting to the emergency department (ED) with

diabetic ketoacidosis (DKA), which additionally led to the diagnosis of new-onset type 1 diabetes mellitus (DM).

Case report

A 55-year-old Caucasian female presented to the ED via emergency medical services (EMS) complaining of abdominal pain, weakness, and occasional confusion. Her initial finger-stick blood glucose level was 555 mg/dL. According to her family members, the patient had been “sick” for the prior week, being too weak to eat or get out of bed. However, she refused to come to the hospital. She had been constipated and seeking relief for her abdominal discomfort through natural remedies, including giving herself coffee enemas daily and drinking kombucha tea twice a day. She had no significant past medical history, and her surgical history included a previous appendectomy and an exploratory laparotomy after a car accident many years prior.

Physical examination in the ED revealed a blood pressure of 94/60 mmHg, pulse rate 101 bpm, respiratory rate 28, and temperature 96.6 °F. Glasgow Coma Scale (GCS) was 15. Neurologic examination showed grossly intact cranial nerves, motor strength,

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and sensation. Psychiatric examination was positive for mental confusion. Her cardiac examination revealed a regular rhythm with no murmurs, and the abdominal examination showed normal bowel sounds with no tenderness or guarding. Significant laboratory test results included hemoglobin A1c of 13.4% with glucose 589 mg/dL, ionized calcium 1.35 mmol/L, chloride 111 mmol/L, potassium 4.1 mmol/L, sodium 130 mmol/L, lactic acid 1.3 mmol/L, beta-hydroxybutyrate >2 mmol/L, hemoglobin 9.1 g/dL, hematocrit 32.5%, and platelet count $712 \times 10^3/\mu\text{L}$. Arterial blood gas showed pH of 6.9, CO₂ 12.6, and pO₂ 190 mmHg. Urinalysis showed white blood count of 2 cell per high power field, specific gravity 1.018, protein 30, ketones 80, glucose >1,000, with positive yeast and hyaline cast. Her urine also tested positive for cannabinoids.

Patient was diagnosed with DKA and new-onset DM type 1 with sepsis secondary to urinary tract infection. She was started on intravenous fluids, insulin drip, the broad-spectrum antimicrobials vancomycin and piperacillin-tazobactam, and intravenous fluconazole. Computed tomography (CT) head imaging upon arrival showed no significant findings (Fig. 1) and chest x-ray was normal. CT abdomen/pelvis without contrast revealed dilated small bowel loops with possible obstruction, and an orogastric (OG) tube was placed to suction. With that treatment, the patient began to show improvement in her laboratory findings by the following day. However, she continued to have worsening confusion and weakness with septic shock necessitating vascular pressor initiation with norepinephrine. On the second day, she developed significant weakness and inability to overcome gravity in all four extremities. Blood pressure continued to decline despite the infusion of norepinephrine and phenylephrine, and she was intubated for airway protection due to unresponsiveness. GCS was 3 with no motor function.

On the third day, the patient had an episode of cardiopulmonary arrest and was resuscitated. Following the episode, she had no cough, gag, or corneal reflex. There was no pain response and

pupils were fixed. Bowel sounds were noted to be absent in all four quadrants with a distended and rigid abdomen. Due to her decline, she was taken to the operating room and underwent exploratory laparotomy with right hemicolectomy for what appeared to be ischemic right colon with perforation of the cecum. She underwent an ileostomy and a Hartman procedure.

A follow up CT head scan was performed after surgery, which showed pneumocephalus (Fig. 2). There was a right frontal lesion with intraparenchymal gas. There was a mass effect with a 6 mm right-to-left midline shift, transtentorial herniation, and herniation through the foramen magnum. Subarachnoid hemorrhage was seen bilaterally with diffuse cerebral edema. Results of the CT were discussed with the family, and the decision was made to withdraw care, extubate, and provide comfort care. The patient passed away minutes after extubation. Blood cultures 24 hours post-mortem grew *C. septicum*. Peritoneal fluid cultures grew *Streptococcus agalactiae*, *Prevotella intermedia*, *Bacteroides uniformis*, and *C. septicum*. Her urine culture did not grow any yeast.

Discussion

C. septicum is an obligate anaerobic, gram-positive, spore-forming, exotoxin and gas producing bacillus [1]. The organism was first isolated by Pasteur and Joubert in 1877 [1]. Due to its ability to form endospores, it is widespread in nature, primarily being found in soil and potentially the gastrointestinal (GI) tract of humans, although recent studies show the organism may not actually colonize the human GI tract [3]. It is capable of infecting normal tissues due to being more aerotolerant than other *Clostridium spp.*, and *C. septicum* infections are particularly important due to their association with malignancies and their fulminant course [2]. The organism is capable of causing tissue necrosis through production of multiple exotoxins with alpha toxin being the most lethal [1].

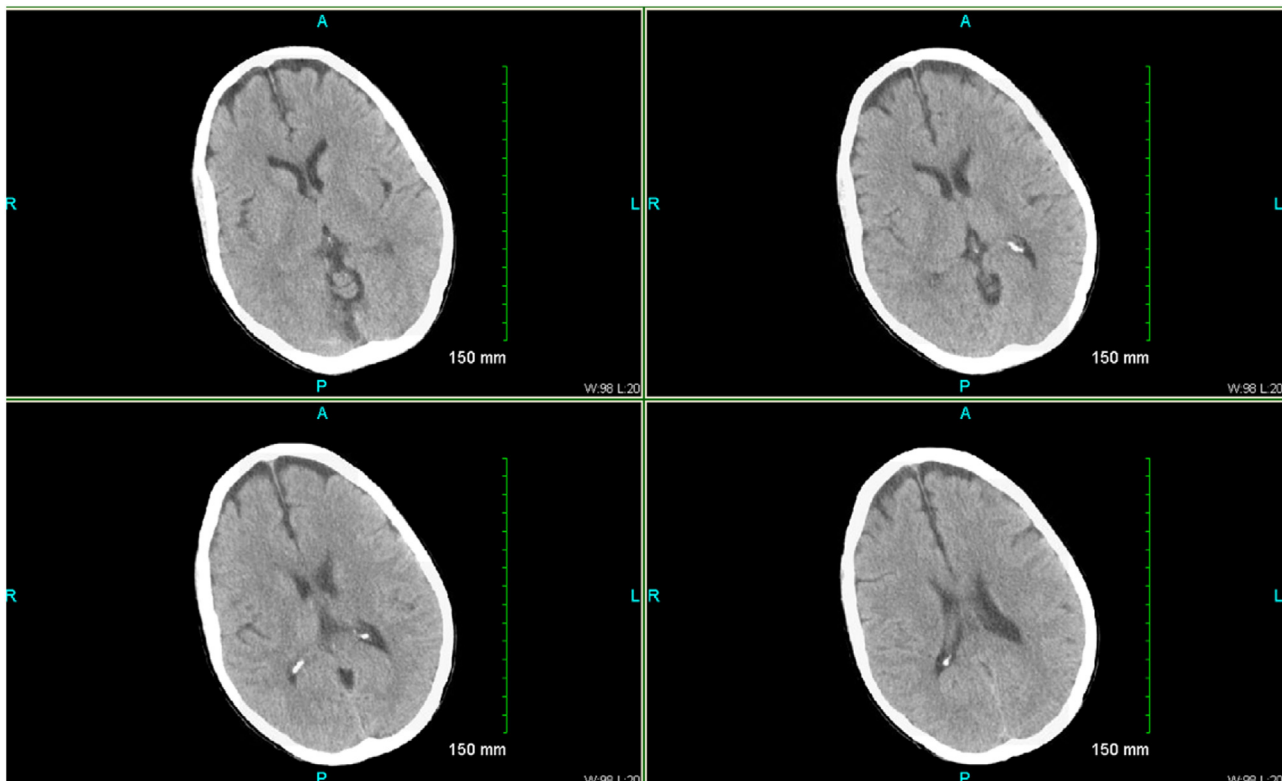


Fig. 1. Initial CT head with no significant findings.

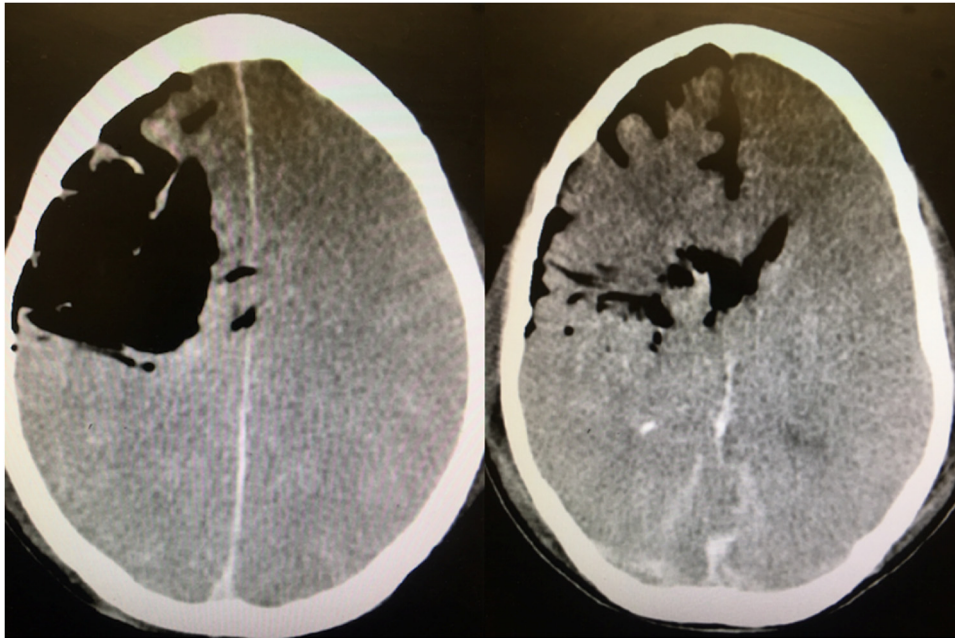


Fig. 2. Follow-up CT head showing pneumocephalus.

The terminal ileum and cecum are believed to provide the most favorable environment for colonization by *C. septicum*. The current thought is that disruption of the bowel mucosal barrier allows hematogenous spread of the organism [2]. This would be supported by the rapid deterioration seen in our case following perforation of her cecum due to obstruction. Risk factors for dissemination include colonic or hematologic malignancies, inflammatory bowel disease, neutropenia, and DM [1]. It is our thought that the new onset of type 1 DM with DKA contributed to the rapid dissemination in our patient.

The correlation between drinking kombucha tea or the use of coffee enemas daily in promotion of possible *C. septicum* dissemination in our patient is not clear. These are concomitant cofactors never discussed in previously published cases of *C. septicum* infections. Kombucha tea is prepared by fermenting sugared black or green tea by a consortium of acetic acid, bacteria, and yeast [4]. It is regarded as one of the foods with the potential of enhancing human health and treating AIDS, aging, anorexia, arthritis, atherosclerosis, cancer, constipation, and diabetes, but there is no evidence to support any of these claims [5]. The microbial dynamics of this drink are not uniform as research shows that not only do the tea components vary across Kombucha products, they can vary throughout the course of the fermentation process as well [6]. The yeast component of the tea generally includes *Saccharomyces cerevisiae* among other species, and the bacterial component almost always includes *Gluconacetobacter xylinus* to oxidize yeast-produced alcohols to acetic acid [7]. Recent literature has shown antimicrobial activity among components produced during the tea fermentation process, however, there remains the risk of bacterial contamination of the tea during the brewing process due to the use of bacteria [4].

Coffee enemas are a more likely contributor to the dissemination in this case, shown by previous literature on coffee enema-related septicemia, and similar to the transient enteric bacteremia seen during colonic instrumentation in sigmoidoscopy or barium enemas [8]. The daily use of coffee enemas in our patient could have disrupted the bowel mucosal barrier as previously discussed, further contributing to the translocation of bacteria and hematogenous spread. Overall, the medical literature remains clear in that

the alleged health benefits of this natural remedy remain unfounded and consequentially can cause more harm.

C. septicum is the primary cause of spontaneous gas gangrene or atraumatic myonecrosis in addition to an uncommon but fatal cause of sepsis with mortality rates of up to 60–70% [1]. Hematogenous spread to the CNS is rare and manifestations can include meningitis, cerebritis, and brain abscess. Due to the ability of the organism to produce gas, pneumocephalus may result; however, it is rarely the primary manifestation [3]. Additionally, infection by gas-forming bacteria is a rare cause of pneumocephalus with a review of 295 cases showing the causes to be trauma in 73%, tumors in 12.9%, surgery in 8.8%, and unknown in 0.6% [2].

According to a recent literature review by Macha et al., and further review by us, there are currently 19 reported cases of *C. septicum* CNS infections with 12 of them having pneumocephalus as a manifestation. The overall mortality in these patients has been high (74%) with most dying within the first 48 hours (79%) [3]. The rapid progression of the infection can be seen in a recent case report by Katyal and Dmello where CT head findings changed from abnormal hypodensity to pneumocephalus within an 8 hours period, similar to our case where CT head upon arrival was normal compared to the severe pneumocephalus seen on follow up imaging 3 days later. It should be noted that the presence of *C. septicum* in the brain was not confirmed with any cultures although it is very likely secondary to the growth of *C. septicum* on blood cultures and the overall progression of the infection.

Treatment of *C. septicum* CNS infections mainly consists of high-dose penicillin in combination with clindamycin, gentamicin, or metronidazole for a duration of 4–6 weeks, although the effectiveness of this therapy is uncertain due to lack of human trials [1]. Better prognosis is seen in patients undergoing surgery for a localized process such as brain abscess as compared to antibacterials alone for meningoencephalitis [3]. DM might infer a worse prognosis with these infections although a recent study by Hermesen et al. showed that DM had no effect on survival as compared to non-DM patients (46% vs. 49%) [9]. Among survivors of *C. septicum* infections, colonic and hematologic malignancies

must be excluded due to their close association. In our case, the patient did not have any colonic malignancy, but rather cecal ischemia and perforation most likely caused the dissemination.

C. septicum is an uncommon cause of pneumocephalus, often with a fulminant course leading to death. Early diagnosis is key with initiation of antimicrobial therapy and surgical intervention when possible. It is important to have a high index of suspicion and perform frequent imaging for pneumocephalus when patients begin to deteriorate, and infection is suspected.

Author statement

Ahmad Oussama Rifai, MD and **Shana Webb** were part of the team managing the patient. **Shana Webb** collected, organized, and de-identified patient data. **Saeid Mirzai** analyzed data and wrote the original draft. **Kareem Rifai** and **Amanda Reiner** aided with paper drafting and editing. **Saeid Mirzai** and **Ahmad Oussama Rifai, MD** critically reviewed and edited the paper. **Ahmad Oussama Rifai, MD** approved the final version to be published. All authors contributed extensively to the work presented in the paper.

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