



Clostridium ventriculi infection may be associated with rectosigmoid adenocarcinoma: a case report

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Abstract: Various bacterial species have been directly correlated with specific gastrointestinal (GI) tumors. However, the malignant nature of *Clostridium ventriculi*, a CO₂ producing bacterium known for causing emphysematous gastritis, remains unclear. Our primary aim is to highlight the association between *C. ventriculi* and rectosigmoid adenocarcinoma. A case of a 79-year-old Caucasian man with chronic obstructive pulmonary disease (COPD) who presented to the emergency department with shortness of breath and mild abdominal distention. The day after he was treated for acute exacerbation of his COPD, he developed coffee-ground emesis. The results of a non-contrast computed tomography (CT) of the abdomen and pelvis revealed emphysematous gastritis. Upper endoscopy revealed *C. ventriculi* infection on hematoxylin and eosin (H&E) stain. Following treatment with antibiotics and discharge, the patient presented to the emergency department 1-week later with rectal bleeding. A colonoscopy was performed revealing well-differentiated rectosigmoid adenocarcinoma. To the best of our knowledge this is the first association of rectosigmoid adenocarcinoma in the presence of *C. ventriculi* infection. This case not only serves clinicians in the urgent initiation of antibiotics due to the serious morbidity and mortality of emphysematous gastritis, but also to promote monitoring and colon cancer screening of this cohort with their primary care physicians and gastroenterologists once a diagnosis is established.

Keywords: Case report; *Clostridium ventriculi*; emphysematous gastritis; adenocarcinoma; colon cancer

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Introduction

C. ventriculi, identified as a human pathogen over a century ago, is a spore forming, gram positive and anaerobic coccus with a carbohydrate fermenting metabolism as its sole energy source (1-3). The pathogenesis of this organism has been speculative since its discovery, however, several cases of gastric perforation, emphysematous gastritis, and peritonitis have been described (1). It remains one of the few infectious causes of emphysematous gastritis treatable with antibiotics. The long-term clinical implications of this

pathogen have only recently been emphasized, including associations with gastric adenocarcinoma (1). This case is unique in its association of *C. ventriculi* with rectosigmoid adenocarcinoma. We discuss what may serve as risk factors in relation to this organism with most evidence advocating an original insult or pathology, such as delayed gastric emptying seen most commonly in *C. ventriculi* infected patients (4,5)

We present the following article in accordance with the CARE reporting checklist (available at <http://dx.doi.org/10.21037/dmr-20-76>).

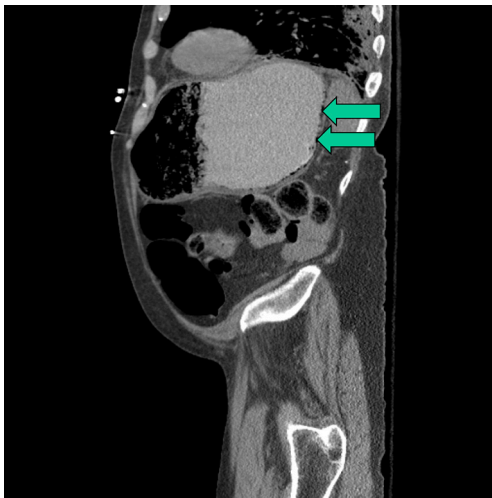


Figure 1 Sagittal computed tomography at the level of the stomach demonstrates nondependent air within the posterior wall of the gastric body consistent with emphysematous gastritis.

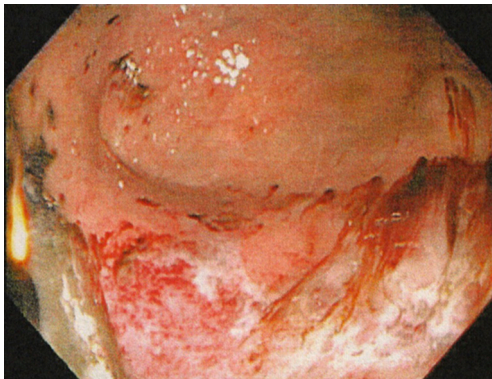


Figure 2 Upper endoscopy image of the stomach demonstrating diffuse gastritis and a gastric body mass.

Case presentation

A 79-year-old Caucasian man with a 55-pack-year smoking history, squamous cell carcinoma of the neck status post radiotherapy in 2015 in remission and chronic obstructive pulmonary disease (COPD) requiring 2L O₂ via nasal canula at night, presented to the emergency department with worsening shortness of breath and acute abdominal distention of 2 days duration. He denied unintentional weight loss, hematemesis, abdominal pain, and melena. He had not undergone colon cancer screening with colonoscopy, and was retired from meaningful employment for 5 years, spending most of his time at home with his wife

tending to his horses. The patient quit smoking 5 year prior and consumed one beer per day for the past 3 years. There was no family history of colon cancer, polyps, liver disease or emphysema.

The patient was found to be saturating 87% on 5L nasal canula with his remaining vital signs within normal limits. Physical examination revealed mild retractions with wheezing and rhonchi bilaterally, in addition to mild abdominal distention. Laboratory investigation revealed a hemoglobin of 14.6 g/dL, creatinine of 1.5 mg/dL and blood urea nitrogen of 26 mg/dL. Arterial blood gas displayed a pH of 7.38, pCO₂ 40 mmHg, pO₂ 64 mmHg. There were no acute cardiopulmonary findings seen on chest X-ray. The patient was initiated on high flow nasal canula, intravenous fluids, macrolide antibiotics and received 125 mg methylprednisolone prior to admission for suspected COPD exacerbation.

He developed new onset coffee ground emesis 6 hours following admission for COPD exacerbation. Physical exam revealed worsening abdominal distention, which was non-tender to palpation without peritoneal signs. Repeat laboratory values displayed a hemoglobin of 13.2 g/dL, creatinine of 1.4 mg/dL, blood urea nitrogen of 36 mg/dL. An abdominal radiograph demonstrated mild gaseous distention of multiple bowel loops. The following day, a computed tomography (CT) without contrast of the abdomen and pelvis was obtained. Gastric pneumatosis with wall thickening and adjacent fat stranding in the greater curvature (*Figure 1*) was noted. Gastric distention was also noted, suggestive of gastroparesis, with left lower lobe pneumonia superimposed with emphysematous change. Azithromycin was discontinued and intravenous piperacillin/tazobactam 3.375 g every 8 hours was added. After, a nasal gastric tube was placed with a nothing per oral (NPO) diet, as his abdominal distention worsened his dyspnea.

The Gastroenterology consult service performed an upper endoscopy which showed Los Angeles Grade D esophagitis with a medium sized bezoar in the stomach. A large, infiltrative and ulcerated, non-circumferential mass was found and biopsied in the greater curvature, which appeared to be a malignant gastric tumor (*Figure 2*). The examined duodenum was normal. Intravenous proton pump inhibitor and metoclopramide were initiated. Gastric biopsy results found marked ulcerative and hemorrhagic gastritis with tissue necrosis and numerous bacterial organisms whose morphologically was consistent with *C. ventriculi* (*Figure 3*).

The Infectious disease consultants, recommended

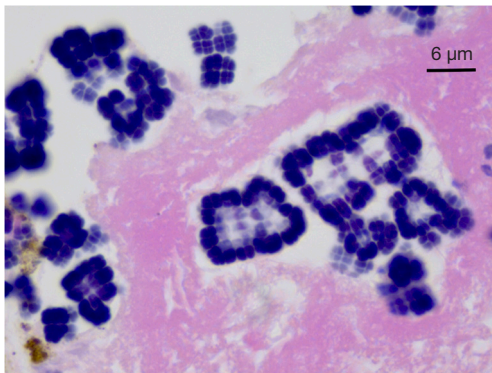


Figure 3 Hematoxylin-eosin stained gastric mass biopsy revealing basophilic-cuboidal *Sarcina* organisms in tetrad arrangement and background submucosal necrosis in a patient with idiopathic gastric outlet obstruction.

continuation of the piperacillin/tazobactam for 9 more days, in addition to starting a 14-day course of oral metronidazole 500 mg four times per day. A CT with contrast of the abdomen and pelvis was performed 72-hours following the initiation of metronidazole, which revealed resolution of the pneumatosis. Six days after CT imaging, intravenous piperacillin/tazobactam was completed and metronidazole frequency was reduced to three times per day. The results of repeat upper endoscopy revealed many non-obstructing, non-bleeding serpiginous gastric ulcers at the location of the previous mass without evidence of perforation. The ulcers were biopsied which revealed ulcerative gastritis with reactive epithelial changes and no evidence of the previously seen organisms. At the time of discharge, the patient tolerated a full diet and metronidazole was continued outpatient for 4-days with a follow up clinic visit thereafter. Six days following discharge, the patient returned to the emergency department with bright-red blood per rectum and acute blood loss anemia. Colonoscopy revealed a well-differentiated mass in the rectosigmoid, in which biopsies proved to be adenocarcinoma. A follow up CT with contrast of the chest revealed numerous pulmonary nodules scattered bilaterally, in which the patient declined biopsy to confirm metastatic disease. The patient agreed to systemic chemotherapy for 8 cycles, after declining surgical intervention. He underwent appropriate follow up after chemotherapy and later succumbed to his disease after transitioning to hospice care shortly after.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and

with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient's spouse for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Discussion

C. ventriculi (formerly *Sarcina ventriculi*), is a strictly anaerobic, carbohydrate-fermenting and CO₂ producing bacterium known for its characteristic tetrad arrangement (6). It is particularly capable of thriving in environments with a low pH ~2 (6-8). *C. ventriculi* infection carries an association with life-threatening complications, such as emphysematous gastritis, diagnosed by imaging, clinical and endoscopic findings. When such complication arise, urgent initiation of antibiotics is required given the high mortality rate. However, scant literature confronts the long-term complications of this organism, including the risk of cancer (9). It was first discovered as a potential human pathogen in 1842 by Goodsir and has since been seen in the feces of healthy human host, particularly those with vegetarian diets (2,10). However, Canale-Parola and Lam-Himlin confront the mechanism of this hypothesis, stating such a bacterium being present is pathological. Canale-Parola strongly suggested that *C. ventriculi* has been visualized in various stomach contents after invading the mucosa, that it is not found in the healthy human stomach (4). Lam-Himlin *et al.*, state that as opposed to mucosal invasion, an initial insult to the gastric mucosa precedes the invasion of the *Sarcina* species (5). Given the isolation challenges of culture and the lack of molecular biological test available, theories assessing the etiology of this microorganism remain elusive, which may prove to be a developing area of biological research (1).

Most noteworthy in our case, *C. ventriculi* has been more recently associated with adenocarcinoma, particularly gastric and pancreatic (5). The potential mechanism and etiology this organism has in relation to adenocarcinoma remains unclear but draws particular resemblance of proposed locations affected by *H. pylori*. It is important to consider the patients social factor of owning livestock, which has particularly been described in the involvement of acute gastric dilation of equines seen in veterinary literature (11). In addition, the patient was found to have gastric distention suggestive of gastroparesis on imaging, possibly contributing to his infection. What makes this case unique is the association with rectosigmoid adenocarcinoma, the first association described to the best of our knowledge.

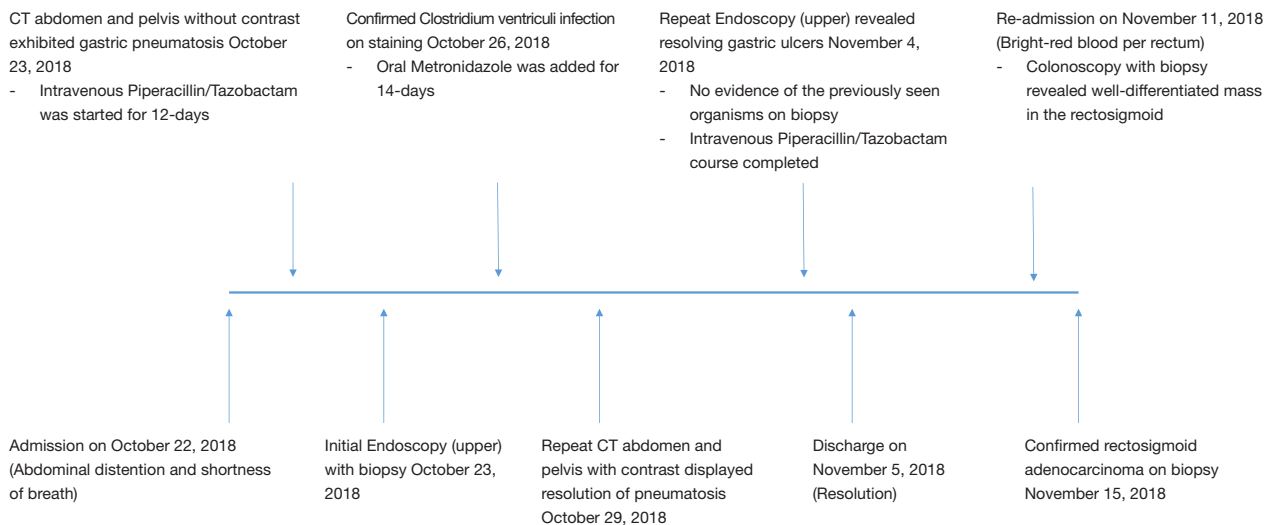


Figure 4 Historical and current information from this episode of care organized as a timeline.

Of course, one cannot infer correlation or causation, particularly in consideration of the limitations including the patient's age, cancer history, radiation exposure and lack of colon cancer screening. Further research with regards to the prevalence of *C. ventriculi* in the community, etiology and association with gastrointestinal (GI) adenocarcinoma is needed, as more bacterial species are found in correlation with GI malignancy. Furthermore, there remains considerable inconsistency on the type and duration of treatment, seen in Haroon Al Rasheed-Senseng's systematic review of treatment (1). Medlicott and Adams have compiled various approaches to treatment based upon clinical status, none of which provides a "gold standard" (12). It should be noted that we used a combination of intravenous piperacillin/tazobactam and oral metronidazole, which revealed evidence of eradication of the organisms on repeat endoscopy following 9–12 days. For ease of reference, the episodes of care are organized as a timeline from historical to current information (Figure 4).

Conclusions

C. ventriculi should be considered in the differential diagnosis of patients with a history of gastroparesis or gastric outlet obstruction who present with life-threatening complications such as emphysematous gastritis or acute blood loss anemia, particularly in the setting of livestock exposure. Due to lack of available culture and molecular testing, endoscopic biopsy with histopathological evaluation

remains the gold standard for diagnosis. Patients infected with *C. ventriculi* should be provided counseling on preventive measures for patients affected with colorectal cancers, including lifestyle modifications such as weight reduction, regular exercise, higher consumption of nutrient-dense foods and limited exposure to environmental risk factors such as smoking and alcohol.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <http://dx.doi.org/10.21037/dmr-20-76>

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Ethical Statement: The authors are accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient's spouse for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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