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Case Report

Gangrenous cholecystitis due to rare actinomyces odontolyticus infection in patient with pancreatic adenocarcinoma: A case report

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ABSTRACT

Introduction: Gangrenous cholecystitis is a life-threatening complication of acute cholecystitis. Although typically associated with Bacteroides infection, immunocompromised patients, such as those receiving chemotherapy, are more susceptible infection with uncommon organisms. To our knowledge, there are no previously reported cases of gangrenous cholecystitis secondary to actinomyces odontolyticus, which we present here.
Case: A 48 year-old male with risk factors for cholecystitis including male sex, ERCP with stent placement, and immunocompromised state secondary to chemotherapy for pancreatic adenocarcinoma presented with worsening abdominal pain and altered mental status. Over the prior 2 months, he had recurrent episodes of abdominal attributed to the pancreatic cancer. Laboratory values were remarkable for leukocytosis and elevated alkaline phosphatase and lactic acid. He was administered antibiotic therapy with piperacillin-tazobactam and urgently underwent a sub-total open cholecystectomy. Intra-abdominal fluid cultures grew actinomyces odontolyticus. In addition to piperacillin-tazobactam, he was subsequently administer vancomycin for clostridium difficile infection and micafungin. De-escalating antibiotics resulted in worsening leukocytosis. Per his previously expressed wishes in the setting of pancreatic cancer, he was discharged to home hospice and expired afterwards.
Discussion: This is the first reported case of gangrenous cholecystitis secondary to infection with actinomyces odontolyticus. The patient's immunosuppressed state made him susceptible to rare organisms and likely delayed the appearance of symptoms, which are also similar to the symptoms of pancreatic cancer causing biliary obstruction. Cholecystitis should be included in the differential diagnosis of epigastric pain for immunocompromised patient with pancreatic cancer and history of ERCP.

Introduction

Gangrenous cholecystitis is characterized by necrosis of the gallbladder wall that can progress to perforation, pneumoperitoneum, and life-threatening sepsis [1]. Imaging findings of intramural gas and asymmetric wall thickening, especially with pericholecystic fluid accumulation, seen on computed tomography. are concerning. Typical lab results are similar to acute cholecystitis and include elevated liver enzymes and leukocytosis. Patients often present with fever, peritonitis, and right upper quadrant pain, and depending on the degree of sepsis, altered mentation; of note, pain may limited due to focal denervation caused by ischemia.

Risk factors include male sex, diabetes, and cardiovascular disease [1]. Because cholecystitis can progress to gangrenous disease, factors that predispose to cholecystitis, such as pancreatitis or prior instrumentation of the biliary tree such as endoscopic retrograde cholangiopancreatography (ERCP) with metal stent also increases the likelihood of gangrenous cholecystitis [2].

Cholecystitis is most commonly attributed to e. coli, klebsiella, acinetobacter, and enterobacter [3], whereas gangrenous cholecystitis is more frequently associated with Bacteroides, all of which are gram negative anaerobes [4]. Actinomyces is rarely isolated as the cause of cholecystitis, with only 23 reported cases, and only one other case reported to be specifically caused by actinomyces odontolyticus [5]. Actinomyces odontolyticus is a particularly rare gram positive filamentous bacillus (facultative anaerobe) with only 47 cases of infection reported from its discovery in 1958 to 2019 [6].

Herein we present the case of a patient who presented with acute gangrenous cholecystitis who subsequently underwent open subtotal cholecystectomy with the culprit organism found to be actinomyces odontolyticus.

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Case

A 48-year-old male with severe bullous emphysema on home oxygen therapy (former smoker, 29 pack-years) and T2N1M0 pancreatic adenocarcinoma on chemotherapy presented with worsening right upper quadrant abdominal pain and altered mental status over a course of 24 h. Because of prior obstruction of the common bile duct (CBD) from his known pancreatic head adenocarcinoma, he had previously undergone (ERCP) with covered metal stent placement in the CBD 7 months prior to his presentation. He completed 3 cycles of neoadjuvant chemotherapy with gemcitabine/abraxane 2 months before his presentation. Prior to presentation, it has been reported that the patient had a history of recurrent abdominal pain attributed to his pancreatic adenocarcinoma disease process. 3 months before he arrived to the emergency department, he was hospitalized for suspected bacterial superimposed onto COVID pneumonia and treated with antibiotics.

Per report from his family, additional symptoms included lethargy, diarrhea, and loss of appetite. On presentation, vital signs were stable, but laboratory evaluation was significant for leukocytosis (23,500/mm^3), elevated alkaline phosphatase (206 units/liter), and elevated lactic acid (2.90 mmol/l). He was initially given vancomycin, cefepime, and metronidazole at an outside hospital before being transferred for surgical evaluation. At our emergency department, blood cultures were taken and the patient was started on a piperacillin-tazobactam antibiotic regimen. He was then taken to the operating room for surgical exploration.

Upon entering the peritoneum, murky ascites was immediately encountered and was sent for culture and cytology. There were extensive fibrin deposits overlying the gallbladder and throughout the upper abdomen, suggesting that the process had been occurring for several days. The patient's omentum was plastered over the gallbladder and liver. Through blunt dissection the omentum was taken down to the infundibulum to expose a distended gallbladder with a thickened rind. While gently dissecting the omentum medially, the bile duct stent became visible. It became immediately apparent that the common bile duct was similarly ischemic and gangrenous and had perforated over the stent.

Given the extent of the inflammation and the defect in the bile duct, a subtotal cholecystectomy was performed. There was insufficient viable tissue around the ischemic common bile duct to perform an end-to-end choledochostomy. Given the small defect and healthy duodenum adjacent, the edge of the duct was sutured to the duodenum, additionally buttressed with a second layer of duodenum to healthy duct for a serosal patch and covered with a graham patch.

The patient was taken to the intensive care unit (ICU) following surgery and was started on micafungin in addition to piperacillin-tazobactam. Blood cultures grew only pan-susceptible Klebsiella pneumoniae. Intra-abdominal fluid cultures grew predominantly actinomyces odontolyticus, as well as Streptococcus anginosus and prevotella denticola, all of which were susceptible to piperacillin/tazobactam. On postoperative day (POD) 2, the patient's central venous catheter was removed and he was weaned off of vasopressors. His mental status also improved to baseline. His leukocytosis consistently improved until POD 5 when he developed copious watery diarrhea. In the setting of recent C. difficile infection and confirmed polymerase chain reaction analysis of a stool sample, vancomycin was added to the patient's antibiotic regimen and his condition improved briefly; however, efforts to de-escalate antibiotics were met with worsened leukocytosis and further clinical deterioration, including severely altered mentation. In the setting of the patient's pancreatic cancer and in keeping with his previously discussed wishes as relayed by the family, he was discharged to home hospice without further antibiotic therapy and expired shortly thereafter.

Discussion

Our case is unique because our patient presented with gangrenous cholecystitis and cultures growing the actinomyces odontolyticus species. We found only one other case report of actinomyces cholecystitis secondary to the odontolyticus species [5], and no reported cases of gangrenous cholecystitis with this bacteria. The patient presented with several risk factors for gangrenous cholecystitis, including male sex, stent placement of common bile duct via ERCP, and immunocompromised state secondary to his neoadjuvant chemotherapeutic regimen. Additionally, the patient's history of recurrent abdominal pain was attributed to his pancreatic adenocarcinoma disease process, which may have caused providers to overlook the possibility of cholecystitis, hence allowing the disease to progress to gangrenous cholecystitis. Although he did receive piperacillin-tazobactam, assessment of his treatment response was particularly difficult given his co-infection with C. difficile; however, actinomyces are well-known to be particularly difficult to eradicate. Furthermore, source control via subtotal rather than total cholecystectomy may have been inadequate.

Actinomyces is a gram-positive filamentous facultative anaerobe that generally occupies the genitourinary and upper gastrointestinal tract as commensals and can cause infection when spreading to deep tissues such as bone and muscle [6]. Infection is typically in immunocompromised patients, most often in the cervicofacial area. Only 5 % of infections involving actinomyces species are found in the hepatobiliary system [7]. The rarity of hepatobiliary infection from actinomyces may be associated with bile salts inhibiting actinomyces proliferation [8]. Because of coinfection with other oral flora, including Streptococcus anginosus and prevotella denticola, a possible etiology for our patient's gallbladder infection could include seeding of actinomyces odontolyticus via the ERCP procedures he underwent. A similar mechanism has been postulated for abdominal actinomyces infection following endoscopic pancreatic stenting [9]. Inflammatory disease in the gastrointestinal tract can increase susceptibility to actinomyces infection, which can explain why rare cases of pancreatic actinomyces infection occur in the context of chronic pancreatitis [10]. Our patient had risk factors for actinomyces infection, including poor dentition, significant smoking history, COPD, and recent COVID and superimposed bacterial pneumonia [11]. In the single case of actinomyces cholecystitis reported by Furuya et al., the authors postulated that coinfection with aerobic bacteria like MRSA can consume oxygen and hence provide a more favorable environment for the proliferation of actinomyces [5]. Our patient did not have evidence of co-infection with aerobic bacteria, making the bile salt environment more unfavorable for actinomyces growth.

Actinomyces is generally treated with IV penicillins for 2–6 weeks, then oral penicillin for 6–12 months [6]. National Institute for Clinical Excellence (NICE) recommends using amoxicillin-clavulanate or piperacillin-tazobactam as the initial therapy to include Staphylococcus aureus and gram-negative bacilli coverage [6]. The average treatment duration for cholecystitis caused by actinomyces infections was reported to be 109 days [5]. Despite a relatively long antimicrobial course, infection with actinomyces generally has a good prognosis when treated. One study of 94 patients with pulmonary actinomyces infection had a 98 % cure rate [12]. On the contrary, gangrenous cholecystitis has a poorer prognosis, with a mortality reported to be 17.8 % in a study of 107 patients [1] and up to 40–50 % in other studies [13,14]. Therefore, our patient's poor outcome can be collectively attributed to his comorbidities, and infection with a pathogen that requires a long duration of antibiotic therapy to eradicate.

To our knowledge, this is the first case report of gangrenous cholecystitis caused by actinomyces odontolyticus. This patient was at particularly high risk due to his immunosuppressed state and recent, prior C. difficile infection, and his demise was likely related to his overall frailty and inability to clear a durable and difficult-to-treat pathogen. Physicians should be aware of the potential of infection by rare but commensal organisms in immunosuppressed patients undergoing invasive procedures such as ERCP. In addition, cholecystitis should remain on the differential of epigastric pain in patients with pancreatic adenocarcinoma, including those who underwent ERCP stent

placement and chemotherapy. This would allow a more prompt evaluation of symptoms and informed treatment decisions.

Author's contributions

Chadi Nahal was involved in the patient's care, contributed to the literature review, and wrote and edited the case report. Phillip Blotevogel edited the case report and was the resident involved the patients pre-operative, operative, and post-operative care. Vidyaratna Fleetwood was the attending surgeon who directed the patient's pre-operative, operative, and post-operative care and edited the case report.

Author statements

We would like to submit our case report "Gangrenous cholecystitis due to rare actinomyces odontolyticus infection in patient with pancreatic adenocarcinoma: A Case Report" to be considered for publication in *IDcases*.

We confirm that this work is original and not published elsewhere, nor is it currently under evaluation for publication elsewhere.

To our knowledge, this is the first reported case of gangrenous cholecystitis by actinomyces odontolytius. We hope this will contribute to the armamentarium of knowledge necessary for diagnosing and managing these rare infections in patients with elevated risk.

Each of the authors contributed substantially to the care of this patient and to the writing and editing of this case report. Artificial intelligence has not been used to write or edit this manuscript.

We have no conflicts of interest to disclose. We have approval for publication per Saint Louis University Institutional Review Board Guidelines.

CRediT authorship contribution statement

Chadi Nahal: Writing – review & editing, Writing – original draft. **Vidyaratna A. Fleetwood:** Writing – review & editing, Writing – original draft, Supervision. **Phillip Blotevogel:** Writing – review & editing, Writing – original draft, Supervision.

Ethics approval and consent to participate

The Saint Louis University Institutional Review Board has determined that a descriptive report of observations on up to 5 people or organization(s), in which the observations were retrieved in a retrospective manner and no research questions/hypotheses are being tested, does not meet the definition of research, and may be considered a "case report". In such cases, SLU investigators are not required to obtain IRB approval prior to beginning the activity.

Consent for publication

The authors are permitted to publish this case report under the guidelines of the Saint Louis University Institutional Review Board.

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Conflicts of interest/Competing interests

The authors have no conflicts of interest, financial relationships, or in-kind support to disclose.

Data availability

Not applicable.

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