Hypermucoviscous Klebsiella Pneumoniae Liver Abscess in a Previously Healthy Burmese Male

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Introduction

Discovered over 100 years ago, Klebsiella pneumoniae is a gram-negative pathogen found in the environment and on mammalian mucosal surfaces1. In the Western world, K. pneumoniae most commonly infects the lungs and urinary tract. The majority of these infections occurs in hospitals and long-term care facilities2. However, over the past 20 years, considerable attention has been focused on community-acquired pyogenic liver abscesses (CA-PLA) caused by a hypervirulent variant of K. pneumoniae with a tendency for metastatic spread2,3. Most of these cases have
been reported from Taiwan, where this organism is the leading cause of PLA. Since the mid-1980s, over 900 patients with PLA due to K. pneumoniae were reported from East and Southeast Asian countries. Nonetheless, K. pneumoniae CA-PLA is becoming a global issue as evidenced by confirmed cases in North America and Europe with the majority of hosts being of Asian descent. A total of fifteen cases of hypermucoviscous K. pneumoniae CA-PLA have been reported in the United States4-9. Purported theories for the stratified prevalence of K. pneumoniae pyogenic liver abscesses include genetic susceptibility, socioeconomic factors, and interaction between bacterial and host variables2. The hypermucoviscous strain of K. pneumoniae is an emerging phenotype with very critical distinguishing features. These include a community-acquired origin, absence of underlying hepatobiliary disease in the host, and invasive complications, such as meningitis, brain abscess, endophthalmitis, endovascular infections, and colon cancer. This report details the first reported case of hypermucoviscous K. pneumoniae CA-PLA in the state of Missouri identified in an otherwise healthy individual of Asian descent.

Case Presentation

A 38 year-old Asian male with no previous medical diagnoses presented to the emergency department (ED) with right upper quadrant abdominal pain, headache, and myalgia. He denied recent abdominal surgery, biliary disease, diabetes mellitus, recent travel, or sick contacts. The patient was examined in the ED and discharged home with a diagnosis of viral syndrome. However, the patient’s symptoms became more severe and he returned to the ED three days later reporting fevers up to 102.5°F, a severe left-sided tension-type headache, pleuritic chest pain, dyspnea, and anorexia.

The patient was born and raised in Burma and moved to Malaysia later in life. He emigrated from Malaysia to the United States 5 years ago and had not left the United States since then. He had no history of significant childhood illnesses. He reported recent contact with visitors from Thailand, who were all healthy at the time of interaction.

Significant findings on physical examination included extreme tenderness to palpation of the right upper quadrant. Laboratory studies were remarkable for leukocytosis (WBC 12,100/mm3 with 73.4% granulocytes and 11.9% monocytes), hyperbilirubinemia (1.4 mg/dL), mild transaminitis (ALT 63 U/L, ALP 166 U/L), and evidence of inflammation with an ESR of 57 mm/hr and CRP of 9.1 mg/dL. Urinalysis was notable for amber colored urine, presence of bilirubin, 2.0 Ehrlich U/dL urobilinogen, 20-30 RBCs/hpf, 30mg/dL protein, and 15 mg/dL ketones.

A CT of the abdomen and pelvis with intravenous contrast revealed a peripherally enhancing hypodense mass in hepatic segment IVa with no significant central enhancement on delayed phase imaging. Approximately 20 mL of purulent fluid was removed from the abscess via IR-guided biopsy and drainage. An abscess drainage catheter was not introduced secondary to the high puncture with possibility of pleural reflection transgression.

The patient was started on IV ceftriaxone and metronidazole, diagnostic testing was ordered, and an abscess gram stain and anaerobic culture was performed to identify the culprit pathogen.
Results of diagnostic laboratory testing are as follows:

HIV 1,2 Antigen Antibody: Nonreactive
Cryptosporidium: Negative
Giardia Antigen by EIA: Negative
Stool ova and parasites :Negative
Quantiferon-TB Gold: Negative
Abscess culture – anaerobic Hypermucoviscous K. pneumonia

Culture plate demonstrating the hypermucoviscous characteristics of the isolate. Strains of Klebsiella with the hypermucoviscosity phenotype are identified with the string test. A colony is lifted off the growing medium with an inoculation loop. A string greater than 5 mm is considered a positive result.

On follow-up ultrasound of the right upper quadrant the following day, the liver abscess had not significantly changed in size compared with the initial CT scan. However, no new fluid collection or perihepatic free fluid was visualized and the patient’s headache and abdominal pain had improved. Another 20mL of purulent fluid was drained from the abscess and a silicon drain was placed.

The patient was discharged on hospital day 7 on a six-week course of oral ciprofloxacin. Five days after discharge he presented to the clinic for follow up with his silicon drain in place. Symptomatically the patient seemed to be improving. However, since discharge, the patient was continuing to drain approximately 20 mL of fluid each day. A colonoscopy was scheduled in one month to screen for colorectal malignancy.

Discussion

This previously healthy 38 year-old patient initially presented to the hospital with symptoms consistent with a viral illness. However, worsening abdominal pain and fevers led to further workup and identification of a hepatic abscess of the right lobe. The patient’s history of inhabitance in Malaysia five years prior and an otherwise unremarkable past medical and social history increased suspicion for a primary pyogenic liver abscess caused by K. pneumoniae. Clinical features of pyogenic liver abscess include fever, chills, right upper quadrant tenderness, abdominal pain, leukocytosis, elevated ALT and AST, elevated ALP, and hyperbilirubinemia12.
In the United States, pyogenic liver abscesses are most often polymicrobial with streptococci and Escherichia coli being the most common pathogens. However, monomicrobial liver abscesses caused by Klebsiella pneumoniae infection have become more prominent in recent years. K. pneumoniae infection occurs most commonly in individuals with a compromised immune response, such as diabetes, malignancy, and alcoholism. It is also more common in patients with hepatobiliary disease, colorectal disease or a history of intraabdominal disease or trauma. K. pneumoniae can also occur in the absence of hepatobiliary disease.

The prevalence of hypermucoviscous K. pneumoniae CA-PLA in individuals of Asian descent is not well understood. It is hypothesized that an undetermined host genetic factor may predispose these individuals to intestinal colonization by more virulent strains of K. pneumoniae. It is posited that liver abscess may occur when this more virulent strain of bacteria translocates across the intestinal epithelium to the liver. Interestingly, individuals colonized with this more virulent strain of K. pneumoniae do not always develop infection. However, the associated risk factors, mechanisms of infection, and outcomes of K. pneumonia liver abscesses remain largely unclear.

Studies have shown that the mucoviscosity-associated gene A (magA) and regulator of the mucoid phenotype A (rmpA) are the main contributors to the increased virulence of the hypermucoviscosity phenotype of K. pneumoniae that causes CA-PLA in Taiwan. Specifically, magA+ K. pneumoniae strains demonstrate increased serum resistance, greater resistance to phagocytosis, and greater lethality in mice. RmpA is a regulator gene for the synthesis of the extracapsular polysaccharide and positively controls the mucoid phenotype of K. pneumoniae. Overproduction of polysaccharide is responsible for the mucoid phenotype of K. pneumoniae. The bacterial chromosome encodes the rmpA gene, but the mucoid phenotype itself is regulated by rmpA located in a plasmid. In addition, this strain of K. pneumoniae can more efficiently acquire iron for the purposes of growth and replication. Overall, both rmpA and magA genes are essential for the induction of the hypermucoviscosity phenotype by K. pneumoniae.

Thus far, only 15 cases of K. pneumoniae strains with the hypermucoviscosity phenotype have been reported in cases of CA-PLA in the United States. Despite the small number of reports, the incidence of this disease is rising. Furthermore, more than one-third of individuals infected with hypermucoviscous strains of K. pneumoniae are more likely to develop complications, such as meningitis, endocarditis, subcutaneous muscular abscesses, osteomyelitis, pulmonary emboli, pleural empyema or endophthalmitis as compared than individuals infected with hypermucoviscous-negative strains. Even more concerning is the finding that these serious, life-threatening complications can develop in young, previously healthy individuals. The current mortality rate for hypermucoviscous K. pneumoniae infection ranges from 3-42%. Currently, this hypervirulent strain of K. pneumoniae remains uniformly resistant to ampicillin, but is susceptible to most antibiotics, including third and fourth-generation cephalosporins, monobactam, carbapenems, and ciprofloxacin. However, it is possible that as the disease becomes more prominent, this strain will become resistant to antimicrobials leaving few options for treatment other than supportive care.

Conclusion
We report the case of a 38 year-old previously healthy Burmese man who presented with abdominal pain, headache, myalgia, and back pain. He was found to have leukocytosis, transaminitis, hyperbilirubinemia, and evidence of systemic inflammation. A hypodense hepatic mass was identified with a CT of the abdomen. The patient was ultimately diagnosed with hypermucoviscous K. pneumoniae CA-PLA.

This case provides additional evidence for the emergence of hypermucoviscous K. pneumoniae CA-PLA outside of East Asia and supports the need for continued research to gain a better understanding of its pathogenesis predilection for individuals of Asian decent. This report also delineates the importance of acknowledging the dynamic state of infectious disease, the shifting racial demographics in the Western world, and the ever-present potential for antibiotic resistance. With this information clinicians will be more equipped to identify and treat a potentially fatal disease in individuals with symptoms of a seemingly self-limiting infection.

References
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Introduction

Osteoporosis occurs with increased prevalence in individuals with inflammatory bowel disease (IBD), and as such, these patients are at risk for osteoporosis-related fractures. Although bisphosphonates remain the most commonly used class of drugs for managing osteoporosis, the effectiveness of oral bisphosphonates in patients with IBD may be diminished due to distressing gastrointestinal side effects, which hinder compliance, and also due to poor absorption by diseased intestine.

While intravenous bisphosphonate therapy remains an option for these patients, denosumab has emerged in recent years as an alternative bone-modifying agent. Denosumab received FDA approval for treatment of postmenopausal osteoporosis in 2010 and clinical trials have demonstrated that this medication is both efficacious and well tolerated. Hypocalcemia is a known adverse effect of this medication, although in clinical trials, denosumab has been well tolerated, and numerous trials, most notably the FREEDOM trial (and its two-year extension trial), have failed to demonstrate a significant risk of hypocalcemia while receiving denosumab \[1\]. However, there have been no formal studies assessing for the risk of hypocalcemia while receiving denosumab in patients who have gastrointestinal disorders such as IBD. This report details a patient with a history of corticosteroid-treated Crohn’s disease, who developed severe, symptomatic hypocalcemia shortly after beginning denosumab therapy.