Massive Liver Abscess Caused by Multidrug Resistant *Citrobacter freundii*

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Abstract

Pyogenic liver abscess is a disease entity that may follow infections of the biliary tract, blood stream and intra abdominal conditions like appendicitis, diverticulitis etc. Co- morbid conditions like diabetes mellitus, renal disease, malignancy, immune suppression etc. may contribute to the development of an abscess and affect the overall outcome of liver abscess as well. *Escherichia coli* and *Klebsiellapneumoniae* have been reported to be the most common isolations from these cases. *Citrobacter* infections usually occur in patients with some underlying co- morbidities and mostly in hospitalized patients. Recently, an increased emergence of multi- drug resistant strains is presenting a challenge to clinicians and microbiologists.

Here, we report a case of massive liver abscess in an immunocompetent patient caused due to *Citrobacterfreundii* resistant to gentamicin, ciprofloxacin, cotrimoxazole, amikacin, ceftriaxone and piperacillin-tazobactam. It showed in vitro sensitivity to meropenem and aztreonam only.

Keywords: **Citrobacter, pyogenic liver abscess, drug resistance.**

Introduction

Liver abscess is a pathological condition, which is common in the Indian subcontinent and usually results from bacterial, amoebic, fungal or traumatic aetiologies. Pyogenic abscess of the liver is not that common and may follow infections of the biliary tract, blood stream and intra- abdominal conditions like appendicitis, diverticulitis etc.[1, 2] Penetrating trauma can also inoculate organisms directly into the liver parenchyma resulting in pyogenic liver abscess. Co-morbid conditions like diabetes mellitus, renal disease, malignancy, immune suppression etc. may incite the development of an abscess and affect the overall outcome of liver abscess as well. *Escherichia coli* and *Klebsiellapneumoniae* have been reported to be the most common isolations from cases of pyogenic liver abscess, other less common organisms include *Staphylococcus, Enterococcus, Pseudomonas spp.*, Anaerobes *etc*.[2]

Citrobacter infections usually occur in patients with some underlying co-morbidities and immunosuppression and mostly in the hospital settings.[3] Recently, an increased isolation of this pathogen has been observed among indoor cases and emergence of multi- drug resistant strains is presenting a challenge to the hospital infection control microbiologists and therapeutic dilemma to the clinicians.

Here we report a case of pyogenic liver abscess in an immunocompetent adult male infected with multidrug resistant *Citrobacterfreundii*.

Case Report

A 58 years old male patient, farmer by occupation, presented to the medical emergency of our hospital with chief complaints of low-grade intermittent fever for 1 week, right upper quadrant abdominal pain for 5 days, right- sided chest pain for 3 days and productive cough since 2 days. He was a chronic alcoholic. On examination, the patient was febrile with a temperature of 101^{o}F and pulse rate 108/min. There was no pallor, icterus, clubbing or pedal oedema. On abdominal examination, tender hepatomegaly could be appreciated. Respiratory examination revealed reduced movement of the diaphragm on the right side. Cardiovascular and central nervous system examinations were within normal limits.

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Investigations

Laboratory investigations revealed a total leucocyte count (TLC) of 26,400/mm^3 with a differential leucocyte count (DLC) of 84% polymorphs and 15% lymphocytes. Random blood sugar, kidney function tests (KFT), liver function tests (LFT) and serum electrolytes (SE) were within reference ranges except serum alkaline phosphatise (ALP) which was markedly raised at 927 IU/l. HBsAg, Anti- HCV and HIV were non reactive in ELISA serology. The Chest X-ray (CXR) was suggestive of minimal right- sided pleural effusion. The ultrasound of abdomen showed a large hypo echoic area in the right lobe of the liver, suggestive of an abscess. The patient was managed empirically with intravenous injections of ceftriaxone and metronidazole considering liver abscess to be the diagnosis. However, even after 48 h of intravenous antibiotics, the clinical condition of the patient deteriorated and then a clinical decision for CECT abdomen was taken to rule out any possible peri-hepatic or other abdominal pathologies. The contrast- enhanced CT (CECT) of the abdomen revealed a large sub- capsular liver abscess with a mild pleural effusion. A CT-guided percutaneous liver abscess drainage was performed with a pigtail insertion under all aseptic precautions and approximately 300 ml of pus was aspirated. The aspirated pus was forwarded to the microbiology department for culture and sensitivity. The sample was processed using standard microbiological procedures including Grams staining and Acid Fast staining. No micro- organisms were visualised in grams stain and Ziehl- Neelsen stain was negative for Acid fast bacilli. On Blood Agar, a pure growth of 1-2mm, non- hemolytic, convex, opaque, moist colonies was obtained after overnight incubation. On MacConkey Agar, a pure growth of 1-2mm, lactose fermenting, moist, convex colonies was obtained after overnight incubation. The organism was catalase positive, oxidase negative and fermented glucose and mannitol. Indole was not produced. H_2S production was evidenced on Triple sugar Iron Agar while urease test was negative. The isolate was provisionally identified as *Citrobacter spp.* and confirmed as *Citrobacterfreundii* in the Automated Microscan 3D ID system. Antibiotic sensitivity testing was done using Modified Kirby-Baeurdisc diffusion method and a screen for ESBL production was also put up by Double disk synergy method. The isolate was an ESBL producer and also resistant to gentamicin, ciprofloxacin, cotrimoxazole, amikacin, ceftriaxone and piperacillin + tazobactam. It showed invitro sensitivity to meropenem and aztreonam only.

A pleural tap was also undertaken in this case and fluid was received for culture. This pleural fluid also grew *Citrobacterfreundii* with an antibiogram pattern compatible with the isolate recovered from liver abscess. The other tests done were Ziehl-Neelsen staining on pleural fluid and sputum, both of which were reported to be negative.

Management

Based on the culture sensitivity report, the patient was started on meropenem. The clinical improvement was fast and remarkable. A repeat ultrasound after one week of starting meropenem revealed significant reduction in the size of the abscess. The laboratory parameters returned to reference ranges and pleural effusion cleared at the time of discharge. The patient has been keeping well on follow up visits.

Discussion

Abscess of liver has been recognized since the time of Hippocrates who based the prognosis on the basis of the fluid recovered from the abscess. The incidence of PLA ranges from 8 to 20 cases per 1,00,000 hospital admissions in the western population.[1] Even today, PLA is still a serious illness and a diagnostic challenge. This is reflected in significant mortality rates and is a result of lack of specificity of clinical signs and symptoms.

PLA may be of biliary, portal, arterial or traumatic origin. However, in approximately 15-55% patients, no identifiable cause or source can be identified, i.e. cryptogenic liver abscess.[1, 4]

Escherichia coli and *Klebsiellapneumoniae* have been reported as the dominant species in liver abscesses. Genus *Citrobacter* belonging to family Enterobacteriaceae includes organisms commonly found in association with environmental sources like soil, water and intestinal tract of humans and animals. *Citrobacter* is usually associated with hospital acquired infections in patients with existing co- morbid conditions like diabetes mellitus, renal disease, immunodeficiency etc. and rarely cause disease in general population.[3] Isolation of *Citrobacter spp*. has been reported from a variety of clinical specimens like urine, pus, blood, CSF etc.[5]

Organisms of genus *Citrobacter* are Gram-negative straight rods, found singly or in pairs, and are motile by peritrichous flagellae. They are facultative anaerobes, oxidase-negative, and typically utilize citrate as the sole source of carbon. The genus *Citrobacter* comprises of 11

different species. Among these, *Citrobacterkoseri* (previously known as *C. diversus*) and *C. freundii* are the commonest species implicated in infections. *Citrobacter* species can cause variety of infections like, respiratory tract infections, urinary tract infection, blood stream infections, wound and burns infections, meningitis, endocarditis, and peritonitis.[5]Neonates and immunocompromised hosts are highly susceptible to *Citrobacter* infections, which are mainly caused by *Citrobacterfreundii* and *Citrobacterkoseri*. *C. Freundii* is usually associated with infections of the hepatobiliary tract, while *C. Koseri* is associated with neonatal meningitis and brain abscess with high mortality rates.[3]

Recently, the isolation of this pathogen in the hospital settings is increasing across the globe and emergence of multidrug resistant strains present a challenge for the clinician and the clinical microbiologists because of their enhanced appearance on the nosocomial front. *Citrobacter* species have been reported to be resistant to extended- spectrum cephalosporins. Chromosomal, inducible AmpC β-lactamases in these have been well described and have been found to be an important mechanism of resistance to β-lactams. SHV- and TEM- derived extended-spectrum β-lactamases (ESBLs) have also been described for *Citrobacter* species in the context of outbreaks of clonal strains and/or plasmids.[6]Increasing resistance to quinolones and aminoglycosides, in addition to β-lactams, has been found in a series of *C. Freundii* isolates collected in Taiwan between 1987 and 1998. A majority of these isolates were resistant to extended-spectrum cephalosporins and antipseudomonalpenicillins.[7]

Citrobacter may be spread by direct contact with hospital staff members or through environmental sources but person to person transmission is more prevalent. In this particular case, it appears that involvement of liver with this organism could have followed some insult in the gall bladder or intestinal tract since the patient was a chronic alcoholic and alcoholics are prone to have some mucosal injuries in the gastrointestinal tract and gall bladder, offering an advantageous situation to organisms like *Citrobacter*. The massive size of the abscess and its sub-capsular location could have resulted in the involvement of the pleural cavity probably through formation of some kind ofmicro-fistulous tract.Since the isolate was an ESBL producer, it did not respond to initial first line treatment of ceftriaxone and metronidazole but responded to meropenem.

The present case highlights *Citrobacter* as a rare cause of PLA. This report also highlights the fact that we need to be vigilant to the possibility of organisms like *Citrobacter* even when underlying co- morbidities like diabetes or immunodeficiency are grossly absent. Cases of liver abscess responding unsatisfactorily to conventional treatments must be investigated for drug resistant organisms so that appropriate therapy can be instituted.

Pyogenic liver abscess can be managed with much better outcome if Ultrasound or CT guided aspirations are undertaken early and examined for microbial pathologies. There should always be high degree of suspicion in all patients presenting with right upper abdominal pain, tenderness, fever and leucocytosis. Clinical signs may not always support the diagnosis, therefore, an appropriate therapy with the real time antibiogram pattern of the organism may help in early recoveryof the patient and reduce the chances of surgical intervention. This will also definitely go a long way in reducing the mortality associated with this clinical condition.

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