Pyogenic Liver Abscess Caused by Burkholderia pseudomallei in Taiwan

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Pyogenic liver abscess in Taiwan is a well-known disease entity, commonly associated with a single pathogen, Klebsiella pneumoniae. Melioidosis is an endemic disease in Taiwan that can manifest as multiple abscesses in sites including the liver. We report three cases of liver abscesses caused by Burkholderia pseudomallei. The first patient was a 54-year-old diabetic woman, who presented with liver abscess and a left subphrenic abscess resulting from a ruptured splenic abscess, co-infected with K. pneumoniae and B. pseudomallei. The second patient, a 58-year-old diabetic man, developed bacteremic pneumonia over the left lower lung due to B. pseudomallei with acute respiratory distress syndrome, and relapsed 5 months later with bacteremic abscesses of the liver, spleen, prostate and osteomyelitis, due to lack of compliance with prescribed antibiotic therapy. The third patient was a 61-year-old diabetic man with a history of travel to Thailand, who presented with jaundice and fever of unknown origin. Liver and splenic abscesses due to B. pseudomallei were diagnosed. However, in Taiwan, liver abscess caused by Klebsiella pneumoniae is a frequently described entity, especially in diabetic patients. Melioidosis is a systemic infection caused by Burkholderia pseudomallei, contracted mainly by inoculation or inhalation. This disease is endemic in Southeast Asia and northern Australia, especially during the rainy season. Taiwan is geographically located in similar latitudes, but was not regarded as an endemic area until indigenous cases were reported in 1992. Melioidosis is known for its propensity to cause abscesses, and may cause liver abscesses, with concomitant splenic abscesses in up to 56% of patients. It often develops in diabetic patients in whom it is associated with a higher mortality and relapse rate. We report three cases of liver abscess caused by B. pseudomallei as a reminder that melioidosis should be included in the differential diagnosis of patients with liver abscess in Taiwan.

Key Words: Burkholderia pseudomallei, Klebsiella pneumoniae, liver abscess, melioidosis, spleen abscess
Case Reports

Case 1
A 54-year-old diabetic woman presented with fever and chills for 10 days. She reported no travel history to China. Physical examination showed an acutely ill appearance and knocking tenderness was elicited over the left upper quadrant of the abdomen.

Sonogram and computed tomography (CT) scan of the abdomen showed multifocal hypodensities in the left lobe (S4) of the liver and splenic abscess with rupture to the left subphrenic space. Culture of the aspirated pus isolated <i>K. pneumoniae</i> and <i>B. pseudomallei</i>. Blood culture showed no growth. Ceftazidime 2 g was given every 8 hours for 30 days, followed by oral minocycline with amoxicillin-clavulanate for 28 days. Antibiotics treatment was then switched to trimethoprim/sulfamethoxazole (TMP/SMX) for a total of 8 months at the outpatient clinic. She was well at follow-up 2 months later, and there was no relapse over the next 2 years.

Case 2
A 58-year-old diabetic man presented with fever, vomiting and diarrhea for 3 days. He also had hypertension and chronic hepatitis B. He had worked as a fisherman in the sea around Indonesia and the Philippines.

Five months before this admission, bacteremic <i>B. pseudomallei</i> pneumonia over the left lower lung complicated with acute respiratory distress syndrome (ARDS) was diagnosed and he was treated with ceftazidime 2 g every 8 hours for 3 weeks and oral TMP/SMX (TMP 80 mg; SMX 400 mg) two tablets every 6 hours for 6 weeks. He was lost to follow-up thereafter.

During presentation, he appeared acutely ill with impaired liver and renal function. Physical examination elicited local tenderness over the right upper quadrant of the abdomen. CT of the abdomen disclosed multiple abscesses over both lobes of the liver, spleen, and prostate (Figure). Two sets of blood culture grew <i>B. pseudomallei</i>. Osteomyelitis scan showed increased uptake over the right shoulder, proximal humerus, proximal femur and left femoral head. Relapse of septicemic <i>B. pseudomallei</i> with multiple organ (liver, spleen, prostate, bone) involvement due to incomplete maintenance treatment was diagnosed. Ceftazidime 2 g every 8 hours was given for a total of 18 days and then changed to amoxicillin-clavulanate two tablets every 8 hours for 4 months. He was well at follow-up at the outpatient clinic 1 year later.

Case 3
A 61-year-old diabetic man presented with epigastralgia, fever and progressive jaundice for 1 week. Asymptomatic gallstone had been found during a routine health check up 1 year previously. He had traveled to Thailand 2 years previously and suffered from fever of unknown cause upon return to Taiwan.

He visited a regional hospital initially, where gallstone with acute cholecystitis was diagnosed. Laparoscopic cholecystectomy was performed, but jaundice and fever persisted. He was then admitted to our hospital.

CT of the abdomen disclosed at least three low-density areas over the right lobe of the liver with peripheral enhancement, and one low-density area within the spleen. The pus from the postoperative drainage tube grew <i>B. pseudomallei</i>. Four sets of blood culture were negative. Cefazolin, gentamicin and metronidazole were given initially for the treatment of intra-abdominal infection, but
his fever persisted. Ceftazidime 2 g every 8 hours
was given for a total of 14 days, and then it was
switched to oral amoxicillin-clavulanate (375 mg;
amoxicillin trihydrate 250 mg + clavulanic acid
125 mg) two tablets every 8 hours for a total of 6
months. He was well without relapse at follow-up
1 year later.

Discussion

Pyogenic liver abscess is an uncommon complica-
tion of intra-abdominal infection, usually arising
from a biliary source in around 30–35% of
cases.7 The etiology is often polymicrobial, with
Escherichia coli, the most often cultured bacteria,
accounting for about 35–40% of the cases.8

In Taiwan, liver abscess is most often caused by
a single pathogen, K. pneumoniae. This pathogen
accounted for 30% of liver abscesses in the 1980s
to 80% in the 1990s.9 The estimated incidence is
over 200 cases annually in Taiwan. Melioidosis is
a systemic infection due to B. pseudomallei, which
often causes multiple abscesses. Taiwan was not
considered an endemic area until 2001, after
publication of the first two indigenous cases in
1996.10 Liver abscess is not an infrequent manifesta-
tion of melioidosis; however, only two cases of
this condition have been previously reported in
Taiwan.10,11 Both K. pneumoniae liver abscess and
melioidosis are associated with diabetes mellitus.
Other reported risk factors of melioidosis are
renal disease, liver cirrhosis, thalassemia, alco-
holism, use of immunosuppressive agents, cystic
fibrosis and kava consumption.12

K. pneumoniae liver abscess has a good progno-
sis when treated with adequate drainage and com-
bination antimicrobial therapy for 2–3 weeks.
Poorer outcome is associated with the occurrence
of metastatic infections, rupture of abscess or
severe sepsis, with a mortality rate of 18% and
relapse rate of 7%.13 In contrast, melioidosis is
difficult to treat, with a slow clinical response to
high dose parenteral antibiotics. The median time
for resolution of fever was 9 days, and may be
even longer in the presence of a large abscess or
empyema.13 The response is so slow that physi-
cians who have no clinical experience with this
disease often tend to change antibiotic regimens
due to fear of drug resistance and treatment fail-
ure. The mortality rate is about 37% in acute septicemia, but only 4% in nonsepticemic cases.14
The relapse rate is about 10%, and rises to 30% if
maintenance antimicrobial agents are not given
for at least 5 months.15 Both mortality and relapse
rates of melioidosis are higher than K. pneumoniae
liver abscess. Therefore, in cases of liver abscess
not due to K. pneumoniae, it is important to keep
in mind the possibility of melioidosis as a cause
of liver abscess in Taiwan. Concurrent infection
with K. pneumoniae and B. pseudomallei has not
been reported previously and is of uncertain signifi-
cance. However, diabetes mellitus is a predispos-
ing factor for both pathogens. The clinical course
and outcome of Case 1 in this report are typical.

K. pneumoniae causing liver abscess in Taiwan
is usually susceptible to many antibiotics (most
β-lactams, sulfamethoxazole-trimethoprim and
aminoglycosides) except ampicillin and ticarcillin.14 However, B. pseudomallei is intrinsically
resistant to penicillins other than ureidopenicillins,
first- and second-generation cephalosporins, mac-
rolides, rifampins and aminoglycosides,15 and is
only susceptible to chloramphenicol, tetracyclines,
trimethoprim-sulfamethoxazole, ureidopenicillins,
third-generation cephalosporins, carbapenems and
amoxicillin-clavulanate. This difference in anti-
microbial susceptibility will result in treatment
failure when melioidosis is empirically treated as
K. pneumoniae or other community-acquired,
enteric Gram-negative bacteria. Resistance to
aminoglycosides in an oxidase-positive, Gram-
negative rod is a useful clue, since B. pseudomallei
is frequently misidentified as Pseudomonas spp.
other than Pseudomonas aeruginosa.16

Ceftazidime (40 mg/kg every 8 hours) is the
antibiotic of choice for melioidosis17 and other
third-generation cephalosporins should not be
used despite evidence of good in vitro susceptibil-
due to increased mortality rate.18 Imipenem
(20 mg/kg every 8 hours) or intravenous amoxi-
cillin-clavulanate are also alternative choices.19–21
Parenteral antibiotics should be continued for at least 10–14 days, until clear improvement is noted and the patient is able to take oral medications. Oral maintenance therapy with amoxicillin-clavulanate (amoxicillin 27 mg/kg day divided into three doses) or trimethoprim-sulfamethoxazole (trimethoprim 8 mg/kg/day and sulfamethoxazole 40 mg/kg/day) should be given for at least 20 weeks.22

The characteristic features of melioidotic liver abscess on ultrasound or CT are the presence of multiple, small cavities, appearing like Swiss cheese, and the involvement of other visceral organs. The spleen is the most common site.23,24 The gold standard for diagnosis is culture of sputum, blood or aspirated pus, which takes several days. B. pseudomallei can be cultured aerobically in most agar media within 24 hours at 37°C.15 Throat swab has 90% sensitivity compared to sputum, especially in a child or patient whose sputum is not available. Rapid diagnosis may be achieved by methods including Gram or Wright stain of the sputum or pus, which will disclose Gram-negative rods with bipolar staining, shaped like safety pins. Direct immunofluorescence microscopy is 98% specific and 70% sensitive compared to culture. Other rapid diagnostic methods include serology tests, such as indirect hemaglutination assay.12

In conclusion, K. pneumoniae is the most common cause of liver abscess in Taiwan in patients without biliary tract abnormalities. However, in cases not due to K. pneumoniae, B. pseudomallei should be kept in mind as a possible pathogen, since misdiagnosis results in treatment failure and a high mortality rate. Distinguishing clinical characteristics include travel history to endemic areas (in imported cases), bipolar staining on a Wright stain, slow response to treatment, multiple small abscesses on imaging, concomitant involvement of other visceral organs, especially the spleen, unusual resistance to aminoglycosides and a higher mortality and relapse rate. Taiwan is now considered an endemic area for melioidosis, and physicians should include melioidosis in the differential diagnosis of pyogenic liver abscess in Taiwan.

References

Melioidosis presenting as liver abscess


