

CASE SERIES

Varied Treatment Responses in Liver Abscesses at a Malaysian Teaching Hospital: A Case Series

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ABSTRACT

Introduction: Pyogenic liver abscesses (PLA) are increasingly prevalent in Malaysia, with a national incidence of 1.43 cases per 100,000 people per year. Common causative organisms from the gut include *Escherichia coli*, *Enterobacteriaceae*, *Klebsiella pneumoniae* and anaerobes. Untreated PLA can be fatal, however with the development of modern diagnostic modalities, treatment approaches and antimicrobial therapies, mortality can be significantly reduced. **Case series:** We include four patients who were admitted to a tertiary teaching hospital, detailing their clinical characteristics, treatment approaches and outcomes during their hospital stay. All four patients had a common risk factor of diabetes mellitus, presenting with non-specific symptoms of anorexia with or without fevers and had a liver abscess greater than 5cm in size. Only two patients underwent percutaneous catheter drainage and the duration of antibiotics ranged from 44 to 94 days in total. **Conclusion:** Management of PLA remain challenging due to its heterogeneity in causative organisms and treatment responses which calls for a better consensus on antibiotic duration and methods for monitoring treatment response.

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PLA, henceforth reporting a case series from our tertiary academic hospital.

CASE SERIES

Case 1

A 63-year-old male presented with one week's history of anorexia, lethargy, and fevers. He had type 2 diabetes mellitus (DM), hypertension, dyslipidaemia, stroke with residual right hemiparesis, and end-stage renal failure on regular haemodialysis via a right brachiocephalic fistula. He had bilateral below knee amputations due to necrotising fasciitis complicated by ESBL-producing *Escherichia coli* infection 6 months prior to this presentation. On admission, he was afebrile, oxygen saturation on room air was 90% requiring supplementation. He was otherwise not tachycardic and normotensive. On examination of his abdomen, it was soft, non-tender and no hepatomegaly felt. Investigations showed raised neutrophils, C-reactive protein (CRP) and liver enzymes (Table I). Liver ultrasound (USS) confirmed a 6.9cm collection and was drained percutaneously. Blood and pus cultures grew ESBL-producing *E. coli* sensitive to Ertapenem, Imipenem and Meropenem.

INTRODUCTION

Pyogenic liver abscesses (PLA) are purulent collections in the liver parenchyma due to infective causes. First recognized in the year 1938 by Oschsner and colleagues (1), the incidence of PLA has risen globally in recent years, ranging from 3.6 per 100,000 cases in Northern America (2) to 17.6 per 100,000 cases in parts of Asia (3). In Malaysia, the incidence rate has increased by 5-fold from 0.18 to above 1 per 100,000 person-years in 2017 (4). PLA can be fatal if left untreated, leading to complications such as rupture, spreading of infection to adjacent tissues, sepsis and subsequent multiorgan failure. However, with the development of modern diagnostic modalities, percutaneous drainage approaches and antibiotic therapies, mortality can be reduced from 60% to 4% (5).

Despite its rarity, we have noticed an increasing number of patients diagnosed with difficult to treat

Surveillance imaging with USS followed by CT showed slow resolution of the abscess, requiring a second percutaneous drainage four weeks after the initial procedure. He was given intravenous Meropenem for a total of 81 days resulting in prolonged hospitalization. He was then discharged home later with regular outpatient follow-up. He re-presented 6 weeks later with acute delirium, raised inflammatory markers and PLA recurrence confirmed on CT, measuring 11.8cm. A percutaneous drainage catheter was inserted, and cultures confirmed ESBL-producing *E. coli*. He was given intravenous Meropenem for a total of 99 days during this second presentation and was discharged home on oral Ciprofloxacin for a further 2 weeks. Subsequent follow-up ultrasound showed complete resolution of liver abscess. The total antibiotic duration for this man was 194 days including 180 days of intravenous antibiotics

and 14 days of oral antibiotics.

Case 2

An 83-year-old male presented with 2 weeks of anorexia and fevers. He had DM, chronic kidney disease (CKD) stage 3, ischaemic heart disease and severe degenerative spine disease with L5 radiculopathy. On examination, he was afebrile, his abdomen was soft and non-tender. Investigations showed raised neutrophils and CRP (Table I). Blood cultures were positive for *Klebsiella pneumoniae* sensitive to amoxicillin-clavulanate. CT thorax, abdomen and pelvis performed to locate the source of bacteraemia confirmed a 5cm collection in segment VII of the liver. He was treated with intravenous amoxicillin-clavulanate and discharged home 5 days later. He continued oral amoxicillin-clavulanate for 90 days in total. There was no recurrence.

Table I: Summary of patient demographics, investigation and management of PLA

Patient	Case 1	Case 2	Case 3	Case 4
Age (years)	63	83	73	65
Gender	Male	Male	Female	Female
Ethnicity	Malay	Malay	Malay	Indian
Comorbidities:				
- DM	Yes	Yes	Yes	Yes
- CKD stage	ESRF on haemodialysis	Stage 3	Stage 2	No
Clinical presentation	Fevers, anorexia	Anorexia	Fevers, anorexia, vomiting	Fevers, anorexia, abdominal pain
Blood investigations				
- Hb (g/dL)	11.7	11.3	11.0	10.0
- WCC (x10 ³ u/L)	21.54	11.3	28.45	15.85
- CRP (mg/L)	179	22	272	293
- ALT (U/L)	370	38	65	54
- ALP (U/L)	504	227	326	152
- Total bilirubin (umol/L)	31.2	6.0	43.6	24.8
- Albumin (g/L)	20	38	24	22
Findings on imaging				
- Diagnostic modality	USS	CT	CT	USS
- Liver lobe(s) involved	Right	Right	Right, caudate	Right
- Size of abscess (cm)	6.9 x 6.6 x 6.6	5.0 x 1.8 x 3.2	6.7 x 10.4 x 10.9	5.6 x 5.4 x 4.8
- Number of abscesses	Single	Single	Multiple	Single
Culture results				
- Organism	ESBL <i>E. coli</i>	<i>Klebsiella pneumoniae</i>	Negative	Negative
- Antibiotic sensitivities	Ertapenem, Imipenem, Meropenem	Cefuroxime, Amoxicillin-clavulanate, Gentamicin	NA	NA
Management				
- PCD, number of days	Yes, 65	No	Yes, 9	No
- Number of days on antibiotics: IV; PO	74; 14	4; 90	21; 70	9; 35
- Total duration of antibiotics	88	94	91	44
Recurrence of PLA	Yes	No	No	No

DM: diabetes mellitus; CKD: chronic kidney disease; ESRF: end stage renal failure; Hb: haemoglobin; WCC: white cell count; CRP: C-reactive protein; ALT: alanine transferase; ALP: alkaline phosphatase; USS: ultrasound; CT: computed tomography; ESBL *E.coli*: Extended spectrum beta-lactamase *Escherichia coli*; PCD: percutaneous catheter drainage; IV: intravenous; PO: per oral.

Case 3

A 73-year-old, intellectually impaired female presented with 3 days of anorexia, fevers, and an episode of vomiting. There was no abdominal pain or diarrhoea. She had DM, CKD stage 3, and congenital blindness. On examination, she had coarse crepitations in the left middle and lower zones, but her abdomen was soft and non-tender. Investigations showed raised white cell count with predominant neutrophilia and raised CRP 272mg/L. She was treated for presumed

community acquired pneumonia. A hepatobiliary USS was performed due to abnormal liver enzymes (Table I) which showed a segment IV solid liver lesion measuring 3.8cm in size. A CT abdomen was done in view of non-resolving fever which showed a 10.9cm multiloculated liver collection in segment IV,V,VIII and the caudate lobe. A percutaneous drainage was performed. Blood and pus cultures showed no organisms. She was treated with intravenous ceftriaxone and metronidazole for 21 days followed by 70 days of oral amoxicillin-clavulanate.

There was no recurrence.

Case 4

A 65-year-old female presented with 10 days of anorexia associated with intermittent fevers despite a course of oral antibiotics and regular paracetamol. There were no other specific symptoms to suggest the source of infection. She had DM, hypertension, and congestive cardiac failure. On examination, she was febrile, her abdomen was soft and non-tender. Investigations showed raised white cell count with predominant neutrophilia, CRP and liver enzymes (Table I). USS performed showed a well-defined hypoechoic collection in segment VII measuring 4.7cm in size suggestive of a liver abscess. This was confirmed on CT, measuring 5.6cm in size. Blood cultures showed no growth. She was treated with 9 days of intravenous ceftriaxone and metronidazole. Percutaneous drainage was not performed as the interventional radiologist felt it was non-liquefied. She was discharged home with 35 days of oral cefuroxime and metronidazole. There was no recurrence.

DISCUSSION

Pyogenic liver abscess (PLA) is increasingly recognized in Malaysia, with a national incidence of 1.43 cases per 100,000 people per year (4). Risk factors for developing PLAs include immunosuppression from solid organ transplantation, splenectomy, diabetes mellitus (DM), chronic kidney disease (CKD), advanced age, and bacteraemia originating from non-liver sources (6, 7). All four of our patients had DM which is known to be the strongest risk factor for developing PLA due to its impact on immune response and neutrophil function (7). Diagnosis of PLA requires a high index of suspicion due to its conspicuous clinical presentation. Patients often present with abdominal discomfort and non-specific constitutional symptoms such as fevers and anorexia, which can lead to an initial diagnosis of occult sepsis or pyrexia of unknown origin, delaying the detection of PLA. Our patients had abnormal liver enzymes which prompted imaging of the hepatobiliary system, all of whom had findings of a liver collection. Ultrasound is the first imaging modality of choice in suspected cases of PLA due to its high sensitivity (8). Indeed, only one of our patients required CT for detection, which was performed to investigate for metastatic infection due to *Klebsiella* bacteraemia.

Treatment of PLA requires a multi-pronged approach, using targeted antibiotics based on culture results and/or drainage. The choice of antibiotics depends on the likely causative organisms, local antibiotic resistance patterns and patient-specific factors such as comorbidities and allergies. Common causative organisms originate from the gastrointestinal flora: *Escherichia coli*, *Enterobacteriaceae*, *Streptococcus spp.*, anaerobes, with *Klebsiella pneumoniae* being most prevalent in Asia (9). Another important cause is *Burkholderia*

pseudomallei, a gram-negative bacteria endemic to Malaysia. The highest incidence of melioidosis was found in agricultural-based states in Malaysia, where the infection is acquired through exposure to contaminated soil or water (10). Although pneumonia was the most common clinical presentation, other primary foci of infection sites such as subcutaneous tissue, liver and spleen were also identified (11). Thirty percent of PLA cases however had no identifiable organisms (4, 12-13). Empirical antibiotic therapy is first initiated prior to the availability of culture results, these include amoxicillin/clavulanate, ampicillin/sulbactam, third generation cephalosporins (e.g. cefoperazone, ceftriaxone, cefotaxime) which is effective against gram-negative bacteria, and may be combined with metronidazole to cover anaerobes. Other proposed broad spectrum antibiotics for severe sepsis include beta-lactam and beta-lactamase inhibitors (e.g. piperacillin-tazobactam) or carbapenems (meropenem, ertapenem) when multidrug-resistant organisms is suspected (14). For the first two patients, antibiotic therapy was guided by the results of culture sensitivity tests. However, for case 3 and 4, despite thorough investigations, culture results were negative. They were treated empirically with third generation cephalosporins, metronidazole and amoxicillin/clavulanate.

One of our patients had *Klebsiella pneumoniae* who responded well to antibiotics without the need for percutaneous drainage. There is, however, an emerging invasive syndrome caused by serotypes K1 and K2. These patients, often of Asian descent with DM, typically present with *Klebsiella pneumoniae* bacteraemia with extrahepatic complications, involving the central nervous system, musculoskeletal system, and eyes. To avoid poor outcomes, particularly with meningitis, empyema, and septic pulmonary embolism, a thorough investigation for metastatic sites of infection is essential in suspected cases of *Klebsiella* invasive syndrome (15). Drainage of PLAs is recommended when they are larger than 5cm in size for faster resolution. Drainage methods include surgical approaches and less invasive image-guided percutaneous needle aspiration (PNA) or catheter drainage (PCD), with the latter being preferred. A recent systematic review and meta-analyses have demonstrated a higher success rate and faster clinical recovery with PCD when compared with PNA (16). All our patients had liver abscesses measuring 5cm or larger. However, only two underwent PCD as the decision for PCD is often guided by interventional radiologists based on whether the abscess is liquefied.

Curran et al. reviewed a total of sixteen studies on antibiotic duration. The mean antibiotic duration across these studies varied between 8.4 to 68.9 days, with a pooled mean treatment duration of 32.7 days (17). The mean duration of antibiotics in our case series was longer, 79.25 days (range 44-94). There are several reasons for this: majority of our patients were immunocompromised

with a diagnosis of DM and CKD, all four patients had large liver abscesses, ranging from 5cm to 10.9cm in diameter, and one of them had *ESBL E. coli*, a multidrug-resistant organism. These factors have been shown to require longer antibiotics courses (4, 18).

Upon discharge from hospital, our patients would typically have an ultrasound scan every 2 to 4 weeks to monitor treatment response. We would stop antibiotics when the patients have demonstrated a complete resolution of abscess on imaging even though they have improved clinically and biochemically.

In terms of recurrence of PLA, there are several risk factors, these include the presence of multi-resistant organisms and involvement of both liver lobes (19). One patient experienced a recurrence of liver abscess, requiring readmission for repeated percutaneous drainage and antibiotics. The presence of ESBL-producing *E coli* in his case proved difficult to treat and was particularly concerning. A possible source of the ESBL-producing *E coli* was contaminated water from cattle farms near the patient's residence (20). The patient had been advised to avoid drinking water from their residence's water filter and only to consume boiled water instead. No further recurrence since.

CONCLUSION

Our case series highlights the heterogeneity in response to treatment in patients with liver abscess. There is currently no consensus on the duration of antibiotics, as it is dependent on antibiotic sensitivity, percutaneous drainage, and close monitoring of the size of liver abscess whilst on treatment.

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