

# Rare complications of pyogenic liver abscess

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## ABSTRACT

**Pyogenic liver abscess (PLA) is still associated with significant morbidity and mortality. With advances in imaging, most cases are now diagnosed early and effectively treated. However, complications, although considered rare, may still occur. We report three cases of PLA that were associated with rare and significant complications. Two patients had an abscess rupture that resulted in pyopericardium in one patient and sub-diaphragmatic abscess in the other. Another patient with *Klebsiella pneumoniae* PLA had bilateral endophthalmitis that resulted in blindness. Death secondary to overwhelming sepsis occurred in the patient with *Escherichia coli*-related pyopericardium. Delay in diagnosis contributed to the complications in two of the patients.**

**Keywords: endophthalmitis, pyogenic liver abscess, spontaneous rupture, subphrenic abscess**

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## INTRODUCTION

Pyogenic liver abscess (PLA) is a condition that is considered rare in the West (1.0–2.3/100,000 population). However, it is still common in countries such as Taiwan, with an increasing estimated incidence reported from 11.15/100,000 population in 1996 to 17.59/100,000 in 2004.<sup>(1,2)</sup> With advances in imaging and effective antimicrobial therapy, most cases are now diagnosed at early stages and are being effectively treated. As a result, complications rarely occur. These rare complications include abscess rupture and endophthalmitis.<sup>(3-7)</sup> We report three cases of PLA with rare complications: two cases of abscess rupture and one associated with bilateral endophthalmitis.

## CASE REPORT

A 62-year-old Malay woman with a history of hypertension and ischaemic heart disease was referred for the evaluation

of a hepatic mass. The examination was unremarkable at the time of referral, and there was no history of fever. Abdominal ultrasonography (US) revealed a large left hepatic mass (7.1 cm × 5.8 cm) that raised suspicion of an underlying neoplasm, which was confirmed on computed tomography (CT) imaging. Inflammatory, viral (hepatitis B surface antigen [HBsAg] and hepatitis C virus immunoglobulin G [HCV IgG]) and tumour (carcinoembryonic antigen [CEA], carbohydrate antigen 19-9 [CA 19-9] and alpha-fetoprotein [AFP]) markers were normal. Prior to a scheduled biopsy, the patient was admitted to the hospital with a chest infection and was started on penicillin. This was later changed to intravenous (IV) penicillin. The patient's condition initially improved but deteriorated a few days later, with distended jugular veins, dyspnoea and orthopnoea consistent with cardiac tamponade. Chest radiography (CXR) revealed a large globular heart and a left-sided pleural effusion. Repeat CT imaging showed a large pericardial effusion (Fig. 1) in addition to the hepatic mass and lymphadenopathies in the para-aortic and lower mediastinal regions. Under suspicion of malignant effusion, the patient underwent an emergency subxiphoid pericardial window and drainage of the effusion. The pericardium was opened and a large amount of pus was evacuated, with more pus exuding from the diaphragm. The pus culture isolated *Escherichia (E.) coli*. The patient's condition deteriorated despite appropriate antibiotic coverage, aggressive inotropic and intra-aortic balloon pump supports. She died of multiple organ failure five days later. The underlying diagnosis was that of a ruptured PLA resulting in pyopericardium and septicaemia.

## CASE 2

A 40-year-old Malay woman with a background history of diabetes mellitus (DM) was admitted with a one-month history of right upper quadrant pain, weight loss, intermittent fever and rigors. She also experienced night sweats, headache and intermittent non-productive cough. On examination, she was found to be mildly anaemic and afebrile, but had no significant abdominal findings. Chest examination showed findings consistent with a small right

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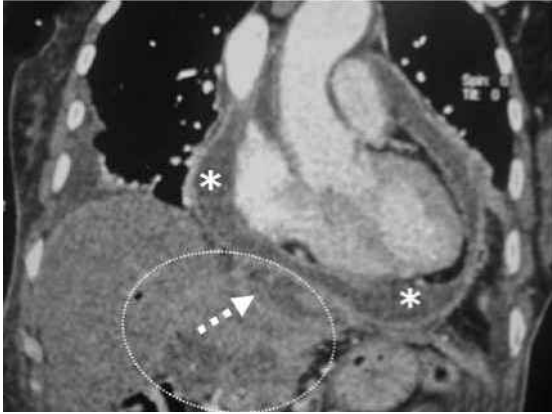
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**Fig. 1** Coronal CT image shows the pyopericardium (stars), pyogenic liver abscess (dotted circle) and rupture site (broken arrow).



**Fig. 3** Photograph shows bilateral endophthalmitis in Case 3.

effusion confirmed on CXR. She was empirically started on IV amoxicillin-clavulanic acid (1.2 gm t.i.d). US showed a segment 7 PLA (5.4 cm × 4.3 cm) that had ruptured into the sub-diaphragmatic space, with the tract clearly visualised on US. A small right pleural effusion was also observed. CT imaging likewise confirmed these findings (Fig. 2). Both US and CT imaging did not show any other intra-abdominal pathologies such as gallstones or diverticulitis. Pus was aspirated from the sub-diaphragmatic collection. IV metronidazole (500 mg t.i.d) was added to the antibiotic regime. Both blood and pus aspirate cultures failed to isolate any organism despite the aspirate showing neutrophilic inflammatory cells. However, the pleural aspirate was positive for acid-fast bacilli. Standard antituberculous therapy was started. The patient responded well and completed a six-week course of antibiotic and a six-month course of antituberculous therapy. Repeat US two months later showed a complete resolution of the abscess and collection.

### CASE 3

An 84-year-old Malay man was admitted with a three-day history of cough that was productive of white sputum,



**Fig. 2** Coronal CT image shows a ruptured pyogenic liver abscess with extension into the sub-diaphragmatic space.

intermittent fever and lethargy. On examination, apart from mild fever, the patient was stable without any abdominal tenderness. His background history included hypertension and evaluation of abnormal cholestatic liver profiles a year earlier. The evaluation for underlying aetiologies (HBsAg, HCV IgG and autoimmune markers, anti-nuclear antibody, smooth muscle antibody, anti-mitochondrial antibody) was negative. A liver biopsy was reported as consistent with resolving abscess and nonspecific hepatitis. Blood investigations showed neutrophilia, dehydration and mild abnormal liver function test (LFT). CXR was normal. The patient was started on IV fluid replacement. Two days after admission, he reported sudden atraumatic loss of vision in both eyes on waking up. The initial evaluations by the ward ophthalmologist revealed bilateral cataracts, right conjunctivitis, shallow anterior chambers and non-reactive pupils. This was later confirmed to be bilateral endogenous endophthalmitis. The patient was immediately started on topical and IV antibiotics. Blood culture isolated *Klebsiella (K.) pneumoniae*. In view of the abnormal LFT, US of the abdomen was conducted, which showed a PLA. 'B' scans of the patient's eyes showed exudates in both the eyes and exudative choroidal detachment in the right eye. Involvement of all the layers and periocular tissues consistent with right pan-ophthalmitis was also observed. The left eye had endophthalmitis. An urgent vitrectomy with intra-vitreous antibiotic injections into both the eyes was performed on the same day. The vitreous culture also

isolated *K. pneumoniae*. Overall, the patient remained well except for his vision (Fig. 3). Unfortunately, despite surgery and completion of the six-week course of antibiotics, his vision continued to deteriorate, with eventual complete loss of vision in both the eyes.

## DISCUSSION

PLA is still associated with significant mortality, with the reported rate at 6.0%–19.6%.<sup>(8)</sup> Septic shock with or without other complications remain the most significant risk factors for mortality. Other complications include abscess rupture and septic emboli that can lead to various manifestations. These include meningitis, endophthalmitis, brain abscesses, lumbar or cervical spondylitis or discitis, septic pulmonary emboli, lung abscess, psoas abscess, splenic abscess, necrotising fasciitis, neck abscess and osteomyelitis.<sup>(9)</sup>

Liver abscess rupture is rare and is more commonly reported with amoebic liver abscesses, at a rate of 5%–20%.<sup>(10)</sup> PLA rupture is much less common. Recent studies from Taiwan showed the PLA rupture rate as 1.2%–5.7%.<sup>(11,12)</sup> The higher rate was associated with *Klebsiella*-associated PLA.<sup>(12)</sup> Spontaneous rupture of *Klebsiella*-associated PLA was shown to be significantly associated with a larger abscess size, DM, gas formation and involvement of the left hepatic lobe.<sup>(12)</sup> Therefore, organisms that are associated with gas formation are likely to be associated with a higher risk for abscess rupture.<sup>(12,13)</sup> The presence of gas in the abscess increases tension within the abscess cavity and therefore, the risk for abscess rupture. As DM is associated with gas-forming PLA, it is also found to be associated with an increased risk for abscess rupture.<sup>(14)</sup> The significance of left hepatic location may be related to the relatively smaller size of the left lobe. Both Case 1 and 2 had large abscesses; one was located subcapsular and the other, in the left hepatic lobe. Subcapsular location increases the risk.

Our first case with abscess rupture into the pericardium was due to *E. coli*, which is still a common cause of PLA in the West.<sup>(15)</sup> However, in the Asia Pacific region, the *Klebsiella* species is a predominant organism. *E. coli* is usually associated with underlying gastrointestinal pathology such as diverticulitis, appendicitis and biliary tract disease.<sup>(15)</sup> It has also been shown to be associated with gas formation.<sup>(14)</sup> Our patient did not have any evidence of intra-abdominal pathology or gas formation. The close proximity of the abscess to the heart, compounded by the delay in appropriate treatment was probably the most important

factor. In our second case, we did not isolate any organism from the aspirate or blood culture. However, acid fast bacilli were isolated from the pleural aspirate. The failure to isolate any organism in cases confirmed to be PLA is not uncommon. Tuberculosis (TB) may not have been the actual cause of the abscess in this patient. Interestingly, TB liver abscess is uncommon, even in endemic countries. The presentations range from multiple small microabscesses to the more common large solitary lesion.<sup>(16)</sup> A literature search did not yield any report of TB liver abscess complicated by rupture.

Generally, abscess ruptures are considered as surgical emergencies. However, as shown in two of our cases, the outcomes are also dependent on other factors such as the location of rupture. Depending on the site of rupture, it can lead to the formation of sub-phrenic, peri-hepatic or sub-hepatic abscesses, peritonitis, empyema, mediastinitis and pyopericardium. Rupture into the bowel or the retroperitoneal space is rare. Ruptures resulting in peritonitis would require urgent surgical interventions, whereas localised ruptures can be managed with drainage, either percutaneous or surgical, in addition to appropriate antimicrobial treatment.

Metastatic infection, usually to the brain and eyes, has been most commonly reported with *K. pneumoniae*-associated PLA, occurring in 3.5%–20.0% of cases.<sup>(4,6,9)</sup> This condition has been categorised as a distinctive syndrome. The serotype K1 that is genetically determined by the *magA* (mucoviscosity-associated gene-A) gene is the most common important virulent factor associated with this syndrome. This virulent factor enables the organism to be more resistant to phagocytosis. K2 has also been shown to be important, although not consistently. The presence of poor glycaemic control is believed to contribute to the susceptibility to metastatic manifestations.<sup>(17)</sup>

Endophthalmitis refers to bacterial or fungal infection of the vitreous or aqueous humour of the eyes.<sup>(18)</sup> Although not life-threatening, it is frequently associated with significant visual loss. It is most commonly associated with ophthalmic procedures or trauma, and is referred to as exogenous endophthalmitis. Endophthalmitis in association with PLA, also known as endogenous endophthalmitis, is rare, and the most commonly associated organism reported is *K. pneumoniae* with K1 serotype. This infection is particularly common in Taiwan, and is reflected by the number of reports from the

country.<sup>(19,22)</sup> A retrospective study from Taiwan reported that endophthalmitis occurred in 23.5% of patients with *K. pneumoniae*-associated PLA.<sup>(49)</sup> This is far higher compared to PLA associated with other organisms. Another study found that 23% of patients with underlying DM and *K. pneumoniae*-related PLA developed bilateral endophthalmitis.<sup>(21)</sup> Successful management of endophthalmitis requires early diagnosis and the institution of intra-vitreous and systemic antibiotic. Surgical vitrectomy is usually required. Despite aggressive therapies and surgical interventions, *K. pneumoniae* endophthalmitis commonly results in poor visual outcome due to its rapid progression.

In conclusion, PLA is still associated with significant complications. However, most are related to the delay in diagnosis, either due to late presentations, lack of the typical symptoms of PLA, or unawareness of the possible complications. It is important to reach a diagnosis early so that appropriate treatments can be implemented to avoid associated complications.

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