

# Gas-forming pyogenic liver abscess

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## ABSTRACT

**Gas-forming pyogenic liver abscess (GPLA) is rare and is associated with a high mortality rate. It is commonly associated with underlying diabetes mellitus (DM). Gas formation occurs as a result of mixed acid fermentation within the abscess by formic hydrogenlyase, an enzyme produced by certain bacteria. Presentations can be nonspecific leading to a delay in diagnosis. Management includes urgent drainage of the abscess. We report three cases of GPLA as a result of *Klebsiella* spp. and *Escherichia coli* infections. All three patients had DM and were very sick at presentation. Diagnosis was delayed in one patient and this likely contributed to his death. Hospitalisations were prolonged. These cases highlight the need to consider GPLA in diabetic patients presenting with fever, abdominal pain, nonspecific symptoms or septic shock.**

**Keywords:** diabetes mellitus, formic hydrogenlyase, gas-forming liver abscess, hepatic abscess, liver abscess, pyogenic liver abscess

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## INTRODUCTION

Pyogenic liver abscess (PLA) is uncommon and is associated with significant morbidities and mortality.<sup>(1)</sup> Gas-forming PLA (GPLA) is even less common, accounting for 7%–24% of all PLA.<sup>(2)</sup> Patients with GPLA are often sicker and have higher mortality rates. Most reports on GPLA have come from the East where the organism most commonly associated with both PLA and GPLA is the *Klebsiella* spp.<sup>(2-5)</sup> We report three cases of GPLA and discuss the mechanisms of gas formation.

## CASE REPORTS

### Case 1

A 34-year-old woman, with poorly-controlled diabetes mellitus (DM) (HbA1c 12.7%) and hyperlipidaemia, was admitted with a one-week history of epigastric pain, fever and loss of appetite (LOA). On examination, she was unwell, dehydrated and had a non-tender hepatomegaly. Blood investigations showed mild anaemia (10.0 g/dL), leucocytosis ( $23.3 \times 10^9$ /dL), thrombocytosis ( $508 \times 10^9$ /dL), severe hypoalbuminaemia (18 g/dL), hyperglycaemia

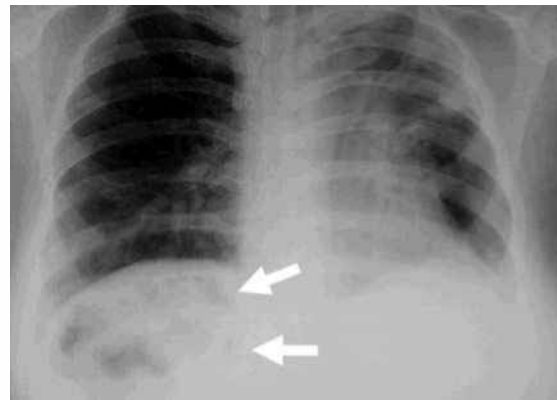


Fig. 1 Case 1. Frontal chest radiograph shows gas pockets (arrows) within the hepatic parenchyma.



Fig. 2 Case 1. Axial CT image shows a gas-forming liver abscess.

(18.8 mmol/L), C-reactive protein (33.9 mg/dL) and erythrocyte sedimentation rate of > 140 mm/hr. Chest radiography showed left upper lobe collapse and also gas within the liver parenchyma (Fig. 1). Computed tomography (CT) confirmed the presence of a large gas-forming liver abscess measuring 10 cm × 8 cm × 11 cm in the right lobe (Fig. 2).

She was resuscitated with intravenous fluid, started on intravenous insulin and broad spectrum intravenous antibiotics (amoxicillin/clavulanic acid and ceftazidime). She was later transferred to the intensive care unit (ICU) for further management. A drainage catheter was inserted, and this resulted in a rapid improvement of her condition. The catheter was removed ten days later. Both blood and pus cultures grew *Escherichia coli* (*E. coli*). Repeat CT showed resolution of the gas collection. She completed five weeks of intravenous antibiotics and continued with another two weeks of oral amoxicillin/clavulanic acid. She

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**Fig. 3** Case 3. Reformatted coronal CT image shows a gas-forming liver abscess.

was discharged 38 days after admission. Follow-up scans showed the formation of an inflammatory pseudotumour at the site of liver abscess, confirmed with liver biopsy. Serial tumour and inflammatory markers, liver function test were normal and the latest imaging done ten months after presentation showed regression of the pseudotumour.

### Case 2

A 59-year-old woman, who was previously well, was admitted with a one-week history of fever, LOA, nausea and diarrhoea. There was no abdominal pain. On examination, she was febrile, dehydrated, had bilateral lower pulmonary crackles and hepatomegaly. There was no tenderness or guarding. Blood investigations showed leucocytosis ( $17.8 \times 10^9/\text{dL}$ ), hypoalbuminaemia (25 gm/dL) and hyperglycaemia (30 mmol/L). She was later diagnosed with DM. Ultrasonography (US) showed a hyperechogenic focus in the right lobe. CT showed a large abscess with gas and fluid level measuring 8 cm  $\times$  9 cm  $\times$  9 cm in the right lobe. She was started on broad spectrum intravenous antibiotic (amoxicillin/clavulanic acid and ceftazidime) and insulin.

However, her condition deteriorated rapidly and was complicated by septic shock, disseminated intravascular coagulopathy and acute renal failure, requiring admission to the ICU. Her blood pressure stabilised with intensive fluid support. She underwent aspiration of the liver abscess twice but eventually required insertion of a drainage catheter. Blood culture was positive for *Klebsiella terrigena*. Pus culture did not yield any organism. Colonoscopy done to evaluate bleeding per rectum revealed only haemorrhoids. She recovered slowly and was discharged 34 days after admission. She completed

four weeks of intravenous antibiotics and continued with another two weeks of oral antibiotics. She remained well on follow-up.

### Case 3

A 45-year-old man was admitted with a one-week history of fever, LOA and feeling generally unwell. He only had a day's history of right upper quadrant pain. His background history included poorly-controlled DM (HbA1c 11.7%), hypertension, hyperlipidaemia and ischaemic heart disease that was complicated with myocardial infarction requiring percutaneous coronary angioplasty. On admission, the patient was in septic shock with tenderness in the epigastrium. He was admitted directly to the ICU and commenced on inotropes (dopamine and dobutamine) and broad spectrum intravenous antibiotics (amoxicillin/clavulanic acid and ceftazidime). He was treated for acute cholecystitis or liver abscess. Blood culture was positive for *Klebsiella pneumoniae*. His condition deteriorated rapidly with the development of acute respiratory distress syndrome and acute renal failure requiring intubation and renal supports. His condition remained unstable and unfortunately a US was done only 18 days later. This showed multiple hepatic heterogenic echotexture lesions and subhepatic free fluid.

CT showed a GPLA in the right lobe (Fig. 3). There were few additional smaller abscesses in the liver, a 1-cm gallstone, fluid collections within the bowel loop at the hepatic flexure area and small ascites. A drainage catheter was inserted and thick maroon-coloured mucoid pus, which yielded the same organism, was drained. His recovery was protracted and was complicated by prolonged intubation and few episodes of nosocomial infections. He required a tracheotomy and was later discharged to the medical ward. Unfortunately, he had a cardiorespiratory arrest and required readmission to the ICU. He sustained hypoxic brain damage and was deemed too ill for any surgical intervention. His condition deteriorated rapidly and subsequently passed away 59 days after admission.

### DISCUSSION

GPLA is rare, and in our local setting, it accounts for less than 4% (out of 84 cases) of all PLA diagnosed and treated over an eight-year period. This is less than what was reported by Lee et al.<sup>(2)</sup> Apart from the *Klebsiella* spp, other organisms reported to cause GPLA include *E. coli*, *Salmonella* and *Clostridial* infections.<sup>(6-9)</sup> Common presentations include fever and abdominal pain, but can be nonspecific, resulting in a delay of diagnosis. In fact, one of our patients did not have any abdominal pain throughout her illness. Diagnosis can easily be made with radiological imaging. Radiographs may show pockets of gas within the liver parenchyma, but this has been reported to be visible in only up to 36% of patients with GPLA.<sup>(2)</sup> It is dependent

on the amount of gas accumulated, and unless suspected, this may be mistaken as bowel gas. In our series, only the first case had gas pockets seen on plain radiography. US is also useful, but CT is the most sensitive test. The remaining two cases had gas collection detected on CT.

Patients with GPLA are sicker and progression can be very rapid. Two large case series studies from Taiwan which involved 28 and 83 patients with GPLA, respectively, showed significant differences between GPLA and non-GPLA.<sup>(3,4)</sup> These studies showed a statistically higher incidence of septic shock, bacteraemia and mortality in patients with GPLA compared to non-GPLA patients.<sup>(3,4)</sup> Symptoms duration was also shorter with more abnormal blood parameters: higher serum glucose, urea, serum aspartate aminotransferase and alkaline phosphatase.<sup>(4)</sup> All our patients had multiorgan failures requiring admission to the ICU, and all had positive blood cultures done on admission. Management of GPLA includes haemodynamic support, broad spectrum intravenous antibiotics and urgent drainage that can be either percutaneous or surgical, as the risk for rupture is high.<sup>(10)</sup> The mortality rate remains high at up to 37.1%.<sup>(2)</sup> The mortality in our report (33.3%) was likely contributed by a combination of delayed diagnosis, rapid deterioration and multiple nosocomial infections.<sup>(4)</sup> Surgical drainage was not initially considered as the patient was slowly responding to treatment and he was also deemed high risk for surgical intervention. Surgical drainage has been shown to be very effective particularly for large abscesses.<sup>(11)</sup> Surgery has also been shown to be associated with lower mortality compared to medical treatment and/or aspiration of the liver abscess.<sup>(4)</sup> However, surgery requires expertise and also depends on the practice of the surgical department.<sup>(11)</sup> In our institution, liver abscesses have traditionally been managed by physicians in close collaboration with the radiologists. Our earlier results have been comparable to the published data.<sup>(12)</sup> Surgical referrals are only considered if responses are slow or if our standard treatment is expected to fail. However, it is very important to consider this option earlier and liaise closely with the surgical department.

The production of gas occurs as a result of mixed acid fermentation within the abscess. The mechanism involves fermentation by formic hydrogenlyase, an enzyme that is only produced in an acidic environment when the local pH reaches 6 or less as a result of acid accumulation. Formic acid accumulated within the abscess is converted to carbon dioxide and hydrogen gas by formic hydrogenlyase.<sup>(2)</sup> The organisms reported to produce this enzyme include *Klebsiella* spp. and *E. coli*. These were isolated in our patients. Hyperglycaemia is an important factor and poor DM control leads to compromised immunity, neutrophil dysfunction and chemotaxis dysfunction. This provides a favourable microenvironment for rapid growth and vigorous metabolism of the organisms, leading to gas

formation.<sup>(13-15)</sup> Poor microcirculation in the affected areas has also been postulated to contribute to gas accumulation. This may explain the reason for higher incidence of GPLA in patients with DM.<sup>(4)</sup> All of our patients had poorly-controlled DM and only one had additional biliary pathology. Biliary pathologies are important causes of PLA especially in the West and associations with colonic neoplasm have also been reported.<sup>(16)</sup>

In conclusion, our three cases highlight the importance to consider GPLA in patients with poorly-controlled DM presenting with fever, abdominal pain, nonspecific symptoms or septic shock. These patients are often sicker and require urgent drainage of the abscess. It is very important to perform imaging studies early to reach a diagnosis, as GPLA is still associated with a high mortality.

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