Pleural Empyema as a Complication of Pyogenic Liver Abscess: Can the Minimum Achieve the Optimal? A Comparison of 3 Approaches

Zeead M. AlGhamdi
Dhuha N. Boumarah
Shadi Alshammary
Hatem Elbawab

Case series

Patients: Male, 29-year-old • Male, 42-year-old • Male, 26-year-old
Final Diagnosis: Empyema
Symptoms: Abdominal pain • dyspnea
Medication: —
Clinical Procedure: —
Specialty: Surgery
Objective: Rare coexistence of disease or pathology
Background: Pyogenic liver abscess is an uncommon entity that is potentially lethal. Pleural empyema and mediastinal collection are 2 rare complications of hepatic abscess that negatively impact the prognosis.

Case Reports:
Herein, we report 3 cases of pyogenic liver abscesses complicated by pleural empyema, each approached differently, along with a succinct review of the literature. Case 1: A 29-year-old man diagnosed with Crohn's disease presented with Crohn's disease-associated hepatic abscess complicated by pleural empyema and concurrent mediastinal collection. The patient demonstrated significant improvement after administration of intrapleural fibrinolytic therapy. Case 2: A 42-year-old man with unremarkable past medical history presented with abdominal pain and dyspnea. Upon investigation, he was found to have massive pleural empyema secondary to liver abscess. In contrast to case 1, case 2 required pleural debridement via video-assisted thoracoscopic surgery followed by formal decortication through a posterolateral thoracotomy. Thereafter, a dramatic clinical improvement was observed. Case 3: A 26-year-old man with history of brucellosis 6 months before was transferred to our facility as a case of pleural empyema secondary to transdiaphragmatic extension of liver abscess. Unlike case 1 and 2, this patient was managed by drainage of hepatic and pleural collections under radiological guidance only, without the need for intrapleural fibrinolytic therapy or surgical intervention.

Conclusions: The current paper sheds light on one of the uncommon complications of hepatic abscess and contributes to this scant literature by summarizing pertinent publications. Adequate drainage remains the cornerstone of any pus collection management despite the complexity of some encountered cases.

Keywords: Crohn Disease • Empyema, Pleural • Liver Abscess, Pyogenic
Abbreviations: PLA – pyogenic liver abscess; CD – Crohn’s disease; ER – Emergency Room; IV – intravenous; RUQ – right upper quadrant; WBC – white blood cell; ALP – alkaline phosphatase; GGT – gamma-glutamyl transferase; PT – prothrombin time; CXR – chest X-ray; CT – computed tomography; HIV – human immunodeficiency virus; IR – interventional radiology; PTC – percutaneous transhepatic cholangiogram; ERCP – endoscopic retrograde cholangiopancreatography; CBD – common bile duct; tPA – tissue plasminogen activator; CRP – C-reactive protein; ESR – erythrocyte sedimentation rate; BUN – blood urea nitrogen; VATS – video-assisted thoracoscopic surgery; DM – diabetes mellitus

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Pyogenic liver abscess (PLA) is recognized as an uncommon entity, with an estimated incidence ranging between 0.5% and 0.8% [1]. Although mortality and morbidity rates have decreased tremendously with recent advances in diagnostic and therapeutic modalities, PLA remains a potentially life-threatening condition, with an overall mortality rate reaching up to 30% [2]. This is mainly attributed to the associated broad spectrum of sequelae, including sepsis, hepatic failure, and extension to adjacent structures [3]. Pleural empyema and mediastinal collection, in particular, are 2 of the rare complications of liver abscesses [4]. Surprisingly, it has been reported that PLA-related empyema has a fatality rate of 100% when left untreated, leading to inevitable death [5]. Therefore, when similar rare complications present, they significantly worsen the prognosis and represent a significant challenge for physicians [4]. Herein, we report 3 cases of pyogenic liver abscess complicated by pleural empyema and present a succinct review of the literature.

Case Reports

Case 1

A 29-year-old man diagnosed with Crohn’s disease (CD) 2 months prior presented to the emergency room (ER) with a 1-week history of right upper quadrant (RUQ) abdominal pain. The pain was associated with subjective fever, constipation, abdominal distension, and exertional dyspnea. He also reported a history of unintentional weight loss of 9 kg within the previous 2 months. When the CD diagnosis was established, the patient was started on immunosuppressive medications, namely, prednisolone and mesalamine. Furthermore, he was an occasional alcohol consumer and tobacco smoker for 11 years. The patient also gave a history of daily cannabis consumption, but he had no history of recent travel or contact with sick patients, and he was not an intravenous (i.v.) drug user. Upon examination, the patient was noted to be slightly tachycardic and tachypneic. Diminished air entry over the right lung base with stony dullness note on percussion were evident on chest examination. An abdominal examination showed mild RUQ tenderness and hepatomegaly, with a liver span of approximately 20 cm.

Laboratory results revealed microcytic anemia, leukocytosis (21 800/μL), hyperbilirubinemia, elevated alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT). Prothrombin time (PT) was found to be prolonged and all inflammatory markers were high. To further investigate his symptoms, chest X-ray (CXR) and contrast-enhanced computed tomography (CT) scan of the chest and abdomen were performed. As demonstrated...
A 42-year-old man with unremarkable past medical history presented to the ER with abdominal pain and dyspnea of 1-day duration. At presentation, the patient was severely tachycardic, tachypneic, febrile, and hypertensive, necessitating immediate admission to the Intensive Care Unit (ICU) to restore his hemodynamic stability. Absence of air entry along with stony dullness all over the right side of the chest were present on physical examination. Laboratory investigations revealed leukocytosis with WBCs exceeding 29,000/μL and lactate level of 9.67 mmol/L, indicating severe tissue hypoperfusion. Inflammatory markers were markedly elevated, with C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) of 19.22 mg/dl and 106 mm/h, respectively. Additionally, a liver function test showed increased levels of direct bilirubin (1.3 mg/dl), ALP (612 U/L) and GGT (265 U/L). Acute renal failure was evident, with elevated serum creatinine and blood urea nitrogen (BUN) approaching 1.70 and 30 mg/dL, respectively. Furthermore, his random blood glucose was 452 mg/dL.

CXR was performed and showed massive right-sided pleural effusion, with contralateral mediastinal shift, as shown in Figure 4. To explore the characteristics and etiology of pleural effusion, CT of the chest (Figure 5) was obtained, wherein the massive pleural effusion was found communicating with multiple multiloculated hepatic abscesses and causing complete collapse of the right lung. CT of the abdomen during week 3 of admission was performed, obtaining immediate admission to the Intensive Care Unit (ICU) to restore his hemodynamic stability. Absence of air entry along with stony dullness all over the right side of the chest were present on physical examination. Laboratory investigations revealed leukocytosis with WBCs exceeding 29,000/μL and lactate level of 9.67 mmol/L, indicating severe tissue hypoperfusion. Inflammatory markers were markedly elevated, with C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) of 19.22 mg/dl and 106 mm/h, respectively. Additionally, a liver function test showed increased levels of direct bilirubin (1.3 mg/dl), ALP (612 U/L) and GGT (265 U/L). Acute renal failure was evident, with elevated serum creatinine and blood urea nitrogen (BUN) approaching 1.70 and 30 mg/dL, respectively. Furthermore, his random blood glucose was 452 mg/dL.

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pneumoniae on culture, thus confirming the diagnosis of PLA. Hydatidosis, amebiasis, hepatitis, HIV, and tuberculosis were all ruled out. Further investigations regarding his persistent hyperglycemia confirmed the diagnosis of diabetes mellitus (DM), with a glycosylated hemoglobin of 11%.

Similarly, pleural collection and liver abscess were drained under radiological guidance. Pleural pigtail drained around 1 L of suppurative material on a daily basis within the first 10 days.

Attempts to drain the pleural empyema via tube thoracostomy failed due to the presence of loculations. Therefore, the decision was made to perform surgical debridement via video-assisted thoracoscopic surgery (VATS). Upon exploration of the pleural cavity, extensive blood clots were found mixed with fresh blood. Complete drainage and debridement were performed and 2 chest tubes were inserted apically and basally. Fortunately, the patient demonstrated clinical improvement and was extubated 3 days postoperatively and was shifted to the general ward. However, his respiratory function did not return to baseline due to the presence of a fibrotic layer limiting maximum expansion of the right lung. Therefore, formal decortication through a posterolateral thoracotomy was carried out to free the lung. The patient improved dramatically thereafter and was discharged on postoperative day 5. Several days after discharge, he developed cholecystitis and underwent cholecystectomy.

Case 3

A 26-year-old man with a history of brucellosis 6 months before was transferred to our facility as a case of pleural empyema secondary to transdiaphragmatic extension of liver abscess. He initially presented with a 1-month history of progressive right-flank and RUQ pain associated with fever, chest pain, and shortness of breath. The patient also reported a history of unintentional weight loss of more than 20 kg since being...
diagnosed with brucellosis, which was treated with a full course of antibiotics. Moreover, his past medical history was significant for type 2 DM, hypertension, and dyslipidemia. A subcapsular hepatic collection was detected on CT and drained through a pigtail by the referring team. Following drainage, the patient developed hydro pneumothorax and was managed via chest tube insertion. His clinical status failed to improve despite multiple antibiotic regimens and several drainage attempts; therefore, he was transferred to our facility to be managed by a specialized multidisciplinary team. Upon presentation, the patient was vitally stable apart from slight tachycardia and tachypnea. A physical examination revealed mild RUQ tenderness and a stoney dullness note of percussion over the right side of the chest.

His laboratory investigations revealed microcytic anemia and thrombocytosis along with elevated hepatic parameters and mild hypoaBloodinemia. Inflammatory markers were significantly high, with CRP of 7.32 mg/dl and ESR of 114 mm/h. Some electrolyte abnormalities were also present, including hyperkalemia (5.6 mmol/L) and hyponatremia (125 mmol/L). As similarly encountered with case 2, the patient had uncontrolled DM with random blood glucose exceeding 430 and glycosylated hemoglobin of more than 11%.

A right hemithorax opacification was evident on a CXR performed upon admission. Furthermore, a contrast-enhanced CT of the abdomen showed a multiloculated hepatic lesion located along the posterior surface of the liver, measuring around 7.2×8.6 cm with thickening of the diaphragm and extension to the right pleural space. As shown in Figure 7, a contrast-enhanced CT of the chest confirmed the presence of a massive right-sided pleural effusion with multiple septations and subsequent atelectasis of the right lung, supporting the diagnosis of right-sided pleural empyema secondary to transdiaphragmatic extension of hepatic abscess. *Echinococcus granulosus* and *Entamoeba histolytica* titers were both low. A brucella-related collection was initially suspected based on elevated serological parameters, but the culture result did not support the diagnosis. Additionally, cultures of other bacterial pathogens were negative, probably due to initiation of empirical antimicrobial therapy before obtaining the sample.

After administering a broad-spectrum antibiotic and correcting electrolytes and blood glucose abnormalities, hepatic and pleural collection were performed. Unlike case 1 and 2, the management plan consisted of drainage of hepatic and pleural collections under radiological guidance only, without the need for intrapleural fibrinolytic therapy or surgical intervention. His condition significantly improved 3 days after drainage. A follow-up CT of the chest demonstrated marked regression in size of both hepatic and pleural collections. He was discharged in satisfactory condition after 10 days of admission, having the shortest hospital stay among the 3 discussed patients.

### Discussion

Liver abscess is defined as a localized collection of suppurative material within the hepatic parenchyma [6]. As exemplified in the present cases, a clear male predominance exists among hepatic abscess patients, with males accounting for 72% of cases [7]. Based on the causative organism, hepatic abscess can be broadly classified into pyogenic and amebic entities. Although the 2 categories have some overlapping features, it is crucial to differentiate between them as the management and prognosis markedly differ [8]. Pyogenic forms, for example, tend to present as multiple lesions and have a polymicrobial origin [2,8]. *Escherichia coli*, *Streptococcus* species and *Klebsiella pneumoniae* are among the predominant causative pathogens of PLA, with the latter being the most aggressive agent [5,9]. Amebic liver abscess, on the other hand, can be suspected when a solitary cyst presents, especially among residents of endemic areas [8,10]. In fact, the clinical manifestations of PLA are usually a combination of non-specific systemic and local symptoms that often include fever, anorexia, RUQ abdominal pain, nausea and vomiting. A recent retrospective study by Yin et al on 1572 Chinese patients with hepatic abscess reported that fever and abdominal pain are the most common presenting features of PLA, accounting for 88.9% and 51.3% of cases, respectively [11].

Anatomically, hepatic abscess has a right lobar preference, with 65% of cases involving the right lobe of the liver [12]. This observed preponderance can be simply explained by the rich blood supply delivered to the right hepatic lobe. The close

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*Figure 7.* Contrast-enhanced CT of the chest illustrating the presence of a massive right-sided pleural effusion with multiple septations (white arrows).
proximity of hepatic lesions to diaphragmatic muscle makes extension of liver abscess and subsequent development of pleural empyema a possible complication, as demonstrated in the presented cases. Interestingly, an extensive review of the English literature revealed a total of 23 cases of pleural empyema secondary to transthoracic extension of liver abscess; only 1 of them was documented to be in a Crohn’s disease patient and none had concurrent mediastinal collection, highlighting the uniqueness of our first case. Table 1 compares the included cases in terms of patient presentation, causative agent, management approach, and outcome after intervention [4-6,13-23]. Another rare yet devastating complication of liver abscess was reported by Cho et al, where a 65-year-old man was diagnosed with pericarditis secondary to intrathoracic extension of left lobe hepatic abscess. Endophthalmitis, manifesting in a form of blindness and eye inflammation, has also been reported as one of the metastatic complications of PLA, with an incidence of 0.84-1.92% [24].

The etiology of pleural empyema varies widely and includes a range of benign and malignant conditions. Parapneumonic pleural effusion constitutes about 60% of all causations, followed by iatrogenic and traumatic cases [25]. Transdiaphragmatic extension of hepatic abscess is an extremely rare causative factor [20]. The evolving pattern of empyema has been represented in 3 distinctive stages to facilitate the decision regarding extent of intervention. The exudative stage is the first to appear and is characterized by the presence of fluid with low cellular content. This is followed by a fibrinopurulent phase which, as the name indicates, consists of fibrin deposits with apparent loculations. Last is the organized stage, where a pleural cortex presents, resulting in lung entrapment that subsequently jeopardizes the respiratory process, as encountered with our second case [26]. It is worth noting that pleural empyema was found to exert a negative impact on the prognosis of hepatic abscess; therefore, early detection and management are of paramount importance [4].

Several factors have been identified as predictors of development of metastatic infections secondary to liver abscess, including chronic alcoholism and DM, all of which were present among the 3 cases reported here [4]. Diabetes mellitus, in particular, was not only recognized as a significant predictor but also as a poor prognostic factor [22]. This might be attributed to the fact that diabetic patients are more prone to develop K. pneumoniae-related infections, which in turn is considered as a major predisposing factor for metastatic infections of liver abscess [5,27]. Notably, knowledge about this well-established association between DM and K. pneumoniae facilitated detection and diagnosis of DM in our second patient. Furthermore, in 2019, Yi and colleagues investigated the potential risk factors of pleural empyema development, concluding that bilateral pleural effusion and the presence of concurrent biliary tract diseases, such as cholangitis or cholecystitis, are highly predictive of transdiaphragmatic extension of liver abscesses, with resultant pleural empyema [4].

It is not uncommon for Crohn’s disease to manifest with hepatobiliary-related complications [28]. The fistulizing, abscess-forming nature of CD, along with the induced immunocompromised status, make CD patients 10-15 times more likely to develop hepatic abscess compared to the general population [29]. Translocation of the intestinal flora and subsequent dissemination through portal circulation is one of the hypothesized mechanisms of infection [30]. One of our cases was diagnosed with CD 2 months prior to the manifestation of liver abscess and had a classical picture of CD-associated hepatic abscess. Streptococcus species, specifically Streptococcus milleri, was reported as the most common isolated organism among patients with CD [31].

Antimicrobial therapy and adequate drainage are the cornerstones of any pus collection treatment. The last decade has witnessed a paradigm shift in the management of hepatic abscess and pleural empyema, with surgery currently being the last resort. Studies addressing the management of pleural empyema as a transdiaphragmatic extension of liver abscess, in particular, are lacking. Based on our experience, we suggest percutaneous drainage with the help of interventional radiology, whenever feasible, as the initial method to manage thoracic empyema, combined with targeted antimicrobial therapy whenever applicable. Interventional radiology plays a pivotal role in managing similar cases, with valuable diagnostic and therapeutic applications. Pigtail catheter drainage is a safe, less invasive, alternative to the use of large-bore chest tubes [32]. A study by Jain et al showed comparable efficacy of pigtail catheter drainage to large-bore chest tube, with lower rates of morbidity [33]. Additionally, to achieve excellent prognosis, drainage of both hepatic and pleural collections is recommended. Despite the fact that both pus cavities might have direct communication, it is essential to drain thoracic empyema and hepatic abscess separately. Lee et al reported that empyema drainage alone was not sufficient to attain complete resolution [22]. When loculations are present, administration of intrapleural fibrinolytics can be an option. Growing evidence suggests the use of intrapleural fibrinolytic agents to reduce the requirement of surgical intervention, as in our first case. However, findings regarding the effectiveness of each substance remain controversial [34]. Generally, failure of standard therapy validates the decision of surgical intervention; therefore, management should be individualized based on the patient and treating physician [26]. When surgery is indicated, according to the American Association of Thoracic Surgery, VATS is preferred over open thoracotomy. The superiority of VATS stems from the associated lower rates of mortality and morbidity along with its cost-effectiveness compared to...
### Table 1. A brief summary of all pleural empyema cases developing secondary to liver abscess.

| Author(s) (year) | Age/Sex | Clinical presentation | Comorbidities | Liver abscess microbial agent | Management of empyema (other than Abx) | Follow-up and outcomes |
|------------------|---------|-----------------------|---------------|-------------------------------|----------------------------------------|------------------------|
| Valero et al (1985) | 28/M | Dyspnea and chest pain | CD | Enterobacter aerogenes | Chest tube drainage followed by surgical drainage | Complete resolution after 1 month |
| Luthariana et al (2005) | 24/M | Abdominal pain, nausea, vomiting and anorexia after history of fever and weight loss | None | Negative culture | Chest tube drainage | LOS was 1 month |
| Loulergue et al (2009) | 57/M | Chest pain, anorexia, watery diarrhea and weight loss | None | Entamoeba histolytica | Pleural drainage for 10 days | Uneventful and no recurrence until 6 months |
| Chang et al (2011) | 27/M | Dyspnea and abdominal pain | None | Entamoeba histolytica | Chest tube drainage | LOS was 1 month. No recurrence until 1 year |
| Sano et al (2015) | 64/M | Dyspnea and fever | None | Klebsiella pneumoniae | Chest tube drainage followed by thoracotomy for decortication and drainage | Uneventful |
| Ahmed et al (2015) | 21/M | Fever, abdominal pain, diarrhea and weight loss followed by respiratory distress | None | Fusobacterium | Chest tube drainage followed by VATS for partial decortication and drainage | Developed intra-abdominal abscesses managed with IV Ertapenem and complete resolution was achieved after 9 weeks of treatment |
| Pandhi et al (2017) | 20/M | Chest pain, abdominal pain, fever, dyspnea and cough | HIV | Entamoeba histolytica | Chest tube drainage | Uneventful |
| Nasrullah et al (2017) | 42/M | Dyspnea, fever, chest pain and cough | IHD and HTN | Entamoeba histolytica | Chest tube drainage followed by VATS for decortication and drainage | The patient’s symptoms failed to resolve initially, necessitating laparotomy to drain the liver abscess |
| Doh Kim (2018) | 47/M | Dyspnea, fever, chest pain, and abdominal pain | None | Streptococcus constellatus | Percutaneous drainage through a pig-tail catheter | Symptoms improved after management, with no evidence of recurrence until 6 months |
| Sheih et al (2018) | 49/F | Abdominal pain and fever | DM | Klebsiella pneumoniae | Thoracentesis followed by VATS for decortication and drainage | LOS was 49 days |
Table 1 continued. A brief summary of all pleural empyema cases developing secondary to liver abscess.

| Author(s) (year) | Age/Sex | Clinical presentation | Comorbidities | Liver abscess microbial agent | Management of empyema (other than Abx) | Follow-up and outcomes |
|------------------|---------|-----------------------|---------------|-------------------------------|--------------------------------------|-----------------------|
| Cho et al (2018) | 65/M    | Dyspnea, fever and abdominal pain | None | Klebsiella pneumoniae | Pigtail catheter drainage | Pt had also pericardial effusion, progressed, necessitating surgical pericardiostomy and was discharged 25 days of surgery |
| Lee et al (2019) | 81/F    | Dyspnea and fever | HTN | Klebsiella pneumoniae (pleural fluid only) | Chest tube drainage for 28 days | Improvement was observed after hepatic abscess drainage |
| Gohar et al (2019) | 54/M | Dyspnea, fever, chest pain, night sweats, weight loss and abdominal pain | Non | Fusobacterium | Chest tube drainage for 7 days | LOS was 7 days. No recurrence until weeks of follow-up |
| Yi et al (2019) | 10 out of 234 developed empyema (median age was 60.2±14.5) 4 of these cases were males | – | DM, HTN, CKD, heart disease and 1 pt was smoker | Klebsiella pneumoniae in 3 pts. Gram-positive organisms in 3 pts, mixed culture in 3 pts and 1 pt had a negative culture | Chest tube drainage in 5 pts; 5 pts required VATS for surgical decortication (3 patients underwent initial chest tube drainage, and 2 patients underwent initial VATS drainage without chest tube insertion) | Median LOS was 38.5±12.7 days |

M – male; F – female; RUQ – right upper quadrant; Abx – antibiotics; LOS – length of stay; Pt – patient; IHD – ischemic heart disease; HTN – hypertension; IV – intravenous; VATS – video-assisted thoracoscopic surgery; CKD – chronic kidney disease; DM – diabetes mellitus; HIV – human immunodeficiency virus; CD – Crohn’s disease.

the open approach [35]. Future research should explore long-term outcomes related to the suggested approach to further assess its effectiveness.

Conclusions

Pleural empyema secondary to transdiaphragmatic extension of pyogenic liver abscess is a rare yet potentially lethal complication. The current report sheds light on one of the uncommon complications of liver abscess and contributes to this scarce field by summarizing pertinent literature. Early detection of thoracic empyema is essential to reduce rates of associated mortality and morbidity. Effective treatment requires a multidisciplinary, patient-tailored approach in which combined therapeutic modalities are utilized. Significantly, adequate drainage remains the cornerstone of any pus collection management despite the complexity of some encountered cases.

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