



Case report

Septic shock caused by emphysematous hepatitis complicated with intracranial infection

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ABSTRACT

Purpose: Emphysematous hepatitis is an uncommon and life-threatening hepatic infection, characterized by the presence of gas within the liver and high mortality. There are few reports of this condition.

Method: We report a case of septic shock caused by emphysematous hepatitis complicated with intracranial infection, and review the current literature on emphysematous hepatitis.

Results: A 57-year-old male with uncontrolled diabetes mellitus developed emphysematous hepatitis complicated with intracranial infection, which progressed to septic shock. The patient was treated with antibiotics and received percutaneous liver puncture drainage early and was discharged preferably in remission. From the literature review, we found 16 previously published cases of emphysematous hepatitis.

Conclusion: Given our experience and the literature review, percutaneous liver puncture drainage or surgical treatment in the early stage may be beneficial to patients with emphysematous hepatitis.

Introduction

Emphysematous hepatitis is an uncommon and life-threatening hepatic infection, characterized by the presence of gas within the liver. This condition predominantly affects patients with impaired immunity, such as diabetics or transplant recipients. The literature on emphysematous hepatitis is scarce, and most of them have poor prognosis despite aggressive treatment. Since Blachar et al. described the first case of emphysematous hepatitis in 2001 [1], only a few cases have been reported, with most of the lesions limited to the abdomen [2–16]. Here, we report a rare case of septic shock caused by emphysematous hepatitis complicated with intracranial infection, who recovered after aggressive therapy. Subsequently, we conducted a literature review and attempted to describe this rare disease.

Case report

A 57-year-old male patient with a history of uncontrolled diabetes was admitted to the intensive care unit due to fever, epilepsy seizure,

and disturbance of consciousness. The patient developed fever up to 40°C five days ago and visited our emergency department for anti-infection treatment two days prior to admission. However, the fever persisted, and he was transferred to our hospital after developed generalized seizure and disturbance of consciousness.

On physical examination, the patient presented with a Glasgow Coma Scale (GCS) of 8 (E4V1M3), and exhibited the following positive signs: cervical rigidity, Kernig sign and the right upper quadrant of the abdomen was tender to palpation.

Laboratory tests (Table 1) indicated an elevated white blood cell count and neutrophils ratio, coupled with a marked decrease in platelet. Concurrently, there was a significant elevation in C-reactive protein (CRP), Interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), and procalcitonin (PCT), suggesting the presence of a severe infection. Additionally, both blood glucose and glycosylated hemoglobin levels were elevated, indicative of suboptimal blood glucose regulation in the patient. Furthermore, both bilirubin and hepatic enzyme levels were increased. An abdominal computed tomographic (CT) scan showed an 86 mm by 65 mm area of gas in the right hepatic lobe (Fig. 1).

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Table 1
Laboratory tests.

Specimen	Value	Reference (Unit)
Blood		
WBC	21.27	4–10 ($\times 10^9/L$)
NEUT%	97.1	34–71.1 (%)
PLT	40	100–400 ($\times 10^9/L$)
CRP	> 200.00	0–10 (mg/L)
PCT	72.1	0–0.5 (ng/ml)
IL-6	1081	0–7 (pg/ml)
TNF- α	86.5	≤ 8.1 (pg/ml)
Blood glucose	30.06	3.9–6.1 (mmol/L)
Glycosylated hemoglobin	11.1	
Total bilirubin	69.1	3–21 ($\mu\text{mol/L}$)
Direct bilirubin	64.3	0–6.8 ($\mu\text{mol/L}$)
Indirect bilirubin	4.8	1.7–15.5 ($\mu\text{mol/L}$)
ALT	584	5–40 (U/L)
AST	595	13–40 (U/L)
Lactate	2.9	0.5–1.6 (mmol/L)
Pathogen(s)	Klebsiella pneumoniae	None
CSF		
WBC	7420	0–8 ($\times 10^6/L$)
Protein	5546.3	80–430 (mg/L)
Glucose	13.03	2.5–4.4 (mmol/L)*
Chloride ion	101.9	120–130 (mmol/L)
Pathogen(s)	None	None
Drainage pus		
Pathogen(s)	Klebsiella pneumoniae, CRE	None

* Glucose levels in cerebrospinal fluid are influenced by blood glucose levels and are approximately 60 % of blood glucose levels

Furthermore, the scan indicated the presence of pneumoperitoneum, and a multitude of air bubbles were discernible beneath the skin and within the muscular structure of the left gluteal region (Fig. 1). Following the acquisition of familial consent, a lumbar puncture was performed, yielding cerebrospinal fluid for subsequent examination and culture. The ensuing results indicated an elevation in both leukocyte and protein, coupled with a decline in chloride ion and glucose. These findings suggest the presence of a concurrent intracranial infection in the patient. Consequently, considering the patient's diagnosis of emphysematous hepatitis complicated by an intracranial infection, culminating in sepsis (as indicated by a Sequential Organ Failure Assessment (SOFA) score of 10 points), we initiated an anti-infective regimen of ceftriaxone in combination with metronidazole. Prior to the commencement of the therapeutic intervention, a blood sample was procured for the purpose of conducting a culture. However, a mere 10 hours subsequent to admission, the patient experienced another episode of epilepsy seizure, accompanied by dyspnea and respiratory distress. Consequently, we administered medication to manage the epileptic symptoms and proceeded with endotracheal intubation, supplemented by mechanical ventilation. By the following day, a decline in the patient's blood pressure was observed. Despite aggressive fluid resuscitation efforts, hypotension persisted. Given the deterioration in

the patient's condition (as indicated by a SOFA score of 17 points) and the onset of septic shock, we initiated norepinephrine administration to maintain blood pressure levels. Concurrently, we intensified our anti-infective regimen to include meropenem in combination with metronidazole. Additionally, ultrasound-guided percutaneous catheter drainage was performed; however, only a minimal amount of pus was drained. Subsequent blood culture indicated a result of *Klebsiella pneumoniae*, and the culture of the drainage pus suggested an infection with *Klebsiella pneumoniae* and carbapenem-resistant Enterobacteriaceae (CRE). Based on the results of the drug susceptibility test of pathogens and the decrease in infection markers (such as PCT), we adjusted the antibiotic to ceftriaxone combined with levofloxacin according to the principle of antimicrobial de-escalation. After rigorous therapeutic intervention, the patient exhibited a gradual improvement in condition. Consciousness levels progressively normalized, and a follow-up abdominal computed tomography scan revealed a reduction in the size of the lesion and resolution of the pneumoperitoneum. On the 18th day post-admission, endotracheal intubation was discontinued. Ultimately, the patient was discharged from the hospital in a significantly improved state of health.

Discussion

Emphysematous hepatitis is an exceedingly rare and life-threatening condition characterized by the presence of gas within the liver radiologically[17]. Currently, literature on emphysematous hepatitis is sparse, with its epidemiology, risk factors, and pathogenesis remaining largely elusive. We present a case involving a 57-year-old patient afflicted with emphysematous hepatitis complicated by an intracranial infection culminating in septic shock. Furthermore, we provide a comprehensive review of all existing literature pertaining to emphysematous hepatitis to enhance clinicians' understanding of this rare condition.

To our knowledge, excluding this case, there have been 16 cases of emphysematous hepatitis to date, with 10 resulting in death. This equates to a mortality rate of 62.5 %. However, we believe this figure may be underestimated due to survivorship bias, where some fatal cases may not have been reported due to poor prognosis. In these cases, the age of patients ranged from 38 to 82 years, with no reports of younger patients to date. Additionally, most patients had a history of past illness. In our case, the patient had a history of diabetes, with a glycosylated hemoglobin level of 11.1 mmol/L upon admission, indicating suboptimal blood glucose regulation. Consistent with other case reports[2,5,7,8,11–16], we also believe that diabetes may be one of the risk factors for emphysematous hepatitis. On the one hand, high blood glucose levels in circulation may provide an environment for microbial fermentation. On the other hand, diabetes may slow the transport of metabolite, leading to gas accumulation and thus increasing the likelihood of emphysematous hepatitis. However, it is evident from all reported cases that diabetes does not increase the mortality rate of patients. In addition,

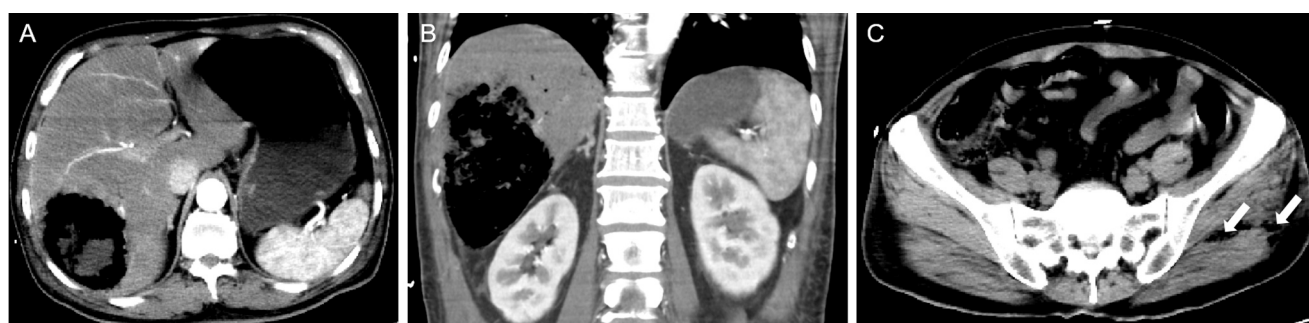


Fig. 1. Abdominal CT. A and B: Axial (A) and coronal (B) computed tomography scans of emphysematous hepatitis, showing an 86 mm by 65 mm area of gas in the right hepatic lobe. C: Axial (A) computed tomography scans of hypogastrium, showing a multitude of air bubbles beneath the skin and within the muscular structure of the left gluteal region.

Table 2
Baseline characteristics of emphysematous hepatitis.

	All (n = 16)	Survival (n = 6)	Non-Survival (n = 10)
Age	72.5 (54.5,78.5)	63 (45.5,72.25)	74.5 (67.25,80)
Sex (female)	9 (56.3 %)	3 (50.0 %)	6 (60.0 %)
History			
Diabetes mellitus	10 (62.5 %)	5 (83.3 %)	5 (50.0 %)
Hypertension	6 (37.5 %)	3 (50 %)	3 (30.0 %)
Hyperlipidemia	2 (12.5 %)	1 (16.7 %)	1 (10.0 %)
Hilar cholangiocarcinoma	3 (18.8 %)	0	3 (30.0 %)
Pancreatic adenocarcinoma	1 (6.3 %)	0	1 (10.0 %)
ERCP	2 (12.5 %)	0	2 (20.0 %)
Other liver diseases (hepatitis C)	1 (6.3 %)	0	1 (10.0 %)
Clinical symptoms			
Abdominal pain	11 (68.8 %)	3 (50.0 %)	8 (80.0 %)
Fever	9 (56.3 %)	3 (50.0 %)	6 (60.0 %)
Vomit	3 (18.8 %)	3 (50.0 %)	0 (00.0 %)
Altered consciousness	5 (31.3 %)	2 (33.3 %)	3 (30.0 %)
Pathogen (n = 15)			
Klebsiella spp.	7 (46.7 %)	3 (50.0 %)	4 (44.4 %)
Klebsiella pneumoniae	4 (26.7 %)	1 (16.7 %)	3 (33.3 %)
Klebsiella oxytoca	3 (20.0 %)	2 (33.3 %)	1 (11.1 %)
Enterobacter spp.	7 (46.7 %)	3 (50 %)	4 (44.4 %)
Escherichia coli	6 (40.0 %)	3 (50.0 %)	3 (33.3 %)
Enterobacter cloacae	1 (6.7 %)	0	1 (11.1 %)
Clostridium perfringens	5 (33.3 %)	1 (16.7 %)	4 (44.4 %)
Enterococcus spp.	4 (26.7 %)	2 (33.3 %)	2 (22.2 %)
Enterococcus faecium	2 (13.3 %)	2 (33.3 %)	0 (00.0 %)
Enterococcus faecalis	2 (13.3 %)	0	2 (22.2 %)
Streptococcus	2 (13.3 %)	1 (16.7 %)	1 (11.1 %)
Treatments (n = 14)			
Antibiotics	14 (100.0 %)	6 (100.0 %)	8 (100.0 %)
Puncture drainage	6 (42.9 %)	3 (50.0 %)	3 (37.5 %)
Surgical	5 (35.7 %)	4 (66.7 %)	1 (12.5 %)

cholangiocarcinoma may also be a risk factor, but this requires further validation through additional studies.

Abdominal pain and fever are the most common clinical symptoms of emphysematous hepatitis. In addition, some patients may have mental symptoms such as altered consciousness. We hypothesize that this may be related to septic shock in the patients. In this case, the patient presented with epilepsy seizure and disturbance of consciousness as the main clinical manifestations, besides fever. However, unlike other cases, the patient did not have signs of septic shock at the onset of the illness. The epilepsy seizure and disturbance of consciousness might be caused by intracranial infection, which was supported by the examination of cerebrospinal fluid (CSF). Unfortunately, no pathogen was obtained from the CSF, so it could not be confirmed whether the intracranial infection was related to the hepatic infection or not.

Emphysematous hepatitis is an infectious disease, whose pathogens include *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Escherichia coli*, *Clostridium perfringens*, *Enterococcus* spp. and *Streptococcus* spp. Among them, *Escherichia coli* is the most common. In the reported pathogens, except for *Enterococcus faecalis* and *Enterobacter cloacae*, the rest have successful treatment cases[13]. In this case, *Klebsiella pneumoniae* was cultured from both blood and drainage pus, and carbapenem-resistant *Enterobacteriaceae* (CRE) was also cultured from drainage pus. The diversity and resistance of microorganisms suggest that the patient may have a severe mixed infection, which also increases the difficulty of choosing the antibiotic.

The current treatment for emphysematous hepatitis mainly includes antibiotics, percutaneous liver puncture or surgical treatment. Considering that emphysematous hepatitis is an infectious disease, all cases have used antibiotics, and most patients (69 %) have also undergone percutaneous liver puncture or surgical treatment. A few patients may not have undergone these procedures due to the rapid progression or severity of the disease, and only received antibiotic treatment. These

patients eventually end up with a poor prognosis. Although this may be affected by the severity of the patient's condition, it may also suggest the importance of puncture drainage and surgical treatment in emphysematous hepatitis. In our case, antibiotics were administered after diagnosing emphysematous hepatitis, and percutaneous catheter drainage were performed in the early stage, which may also provide a guarantee for the patient's good prognosis.

Conclusion

Emphysematous hepatitis is a fatal disease with a high mortality rate. Its diagnosis relies on imaging examinations, especially computed tomography, which has high sensitivity and specificity. In addition to antibiotics, we believe that it is necessary to perform percutaneous liver puncture drainage or surgical treatment in the early stage, which may improve the prognosis of the patients.

Ethical approval

The study was conducted by complying with the declaration of Helsinki 1964. Informed written consent was taken to publish the case report.

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Author agreement

We the undersigned declare that this manuscript entitled "Septic shock caused by emphysematous hepatitis complicated with intracranial infection" is original, has not been published before and is not currently being considered for publication elsewhere.

We would like to draw the attention of the Editor to the following publications of one or more of us that refer to aspects of the manuscript presently being submitted. Where relevant copies of such publications are attached.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We understand that the Corresponding Author is the sole contact for the Editorial process. He is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs.

CRediT authorship contribution statement

Miao Chen: Conceptualization, Project administration, Supervision, Validation, Writing – review & editing. **Jianbo Chen:** Data curation, Investigation, Methodology. **Zhengzhi Zhuang:** Data curation, Investigation, Methodology. **Xiaojun He:** Data curation, Investigation, Methodology. **Yue Wang:** Formal analysis. **Junwen Liang:** Formal analysis. **Runpei Lin:** Conceptualization. **Gengxin Cai:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

All authors disclosed no relevant relationships.

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