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Case Report: Death due to Overwhelming Shock following Bland Embolization of Liver Metastases

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Liver infection; Clostridium perfringens; Hemolysis; Hepatic Artery Embolization (HAE); Liver Abscess

1. Abstract

Liver abscess formation is a potential major complication following ablation or embolization of liver tumors and metastases. Infection with Clostridium perfringens following such a procedure is a rarely documented event with high mortality (70-100) %. We present a case where a 63-year-old man underwent bland Hepatic Artery Embolization (HAE) of liver metastases from esophageal adenocarcinoma, and died of fulminant septic shock, accompanied by intravascular hemolysis, within 30 hours of the procedure despite aggressive operative source control and maximal medical care including pressors and CRRT. Intraoperative cultures later returned with *Clostridium perfringens*. This appears to be the first recorded case of death due to clostridium perfringens sepsis after HAE of liver metastases. The clinical presentation, risk factors, and possible prevention of Clostridium perfringens sepsis after embolization or ablation will be discussed in this case study.

2. Introduction

Clostridium perfringens is a gram-positive, anaerobic bacterium normally found in the gastrointestinal and genital tracts that can become pathogenic, causing everything from asymptomatic bacteremia to septic shock and death, in the context of ischemia, immune compromise, or trauma. In cancer patients in whom surgical resection is not an option, many patients receive Radiofrequency Ablation (RFA), Transcatheter Arterial Chemoembolization (TACE), Microwave Ablation (MWA) cryoablation, irreversible electroporation, radioembolization, or bland Hepatic Artery Embolization (HAE) for both primary liver tumors and liver metastases [1-4]. A rare, but documented complication of these procedures is Clostridium Perfringens sepsis, which can also lead to massive intravascular hemolysis. This report presents a case of *Clostridium perfringens* sepsis with massive intravascular hemolysis, resulting in death within 30 hours of undergoing transcutaneous biopsy and bland embolization of liver metastases.

3. Case Report

A 63-year-old man with a history of metastatic esophageal cancer which progressed after Ivor Lewis esophagectomy and chemotherapy, presented to the emergency department with abdominal pain and tenderness less than 24 hours after percutaneous ultrasound guided biopsy, replaced right Hepatic Artery Angiogram, and HAE of right hepatic metastases by IR.

On the day of the patient's liver directed therapy, a biopsy was initially performed given the need for further histologic and molecular characterization of the metastatic disease. An ultrasound guided percutaneous biopsy was accomplished using a coaxial 18 G core needle. Four core biopsy samples were obtained with online cytopathologic review to confirm adequate samples. The largest deposit of metastatic disease in the inferior aspect of the right hepatic lobe was targeted. There were no imaging findings of complications on ultrasound following the immediate procedure.

Following this, preparations were made for HAE. Arterial access was obtained *via* the patients right common femoral artery. From

this access, a visceral arteriogram was performed showing a replaced right hepatic artery arising from the SMA supplying the majority of the hypervascular metastasis in the right hepatic lobe (adjunctive Figure A). The artery was subselected to the level of the supply to the metastatic disease and HAE was performed using 100-300 um microspheres. Following HAE, there was no evidence of nontarget embolization with preservation of the hepatic artery divisions that were supplying normal parenchyma. No residual tumor was noted on the completion angiogram. 1 G of ceftriaxone was given prior to initiation of the biopsy and HAE procedures. The patient was recovered as per standard same day angiography protocol and was discharged home.

Approximately 10 hours following the biopsy and HAE procedures, the patient presented to the emergency department complaining of severe abdominal pain and chills. His vitals were notable for tachycardia, with heart rate in the 120's, though he was normotensive and afebrile. His laboratory values were notable for a WBC count of 22 $x10^3/\mu L$, creatinine of 1.8 mg/dL, lactate of 5.5 mmol/L, and indirect hyperbilirubinemia with direct bilirubin of 0.4 mg/dL and total bilirubin of 3.2 mg/dL. The remainder of his liver and coagulation profile was unreportable due to hemolysis. Of note, his labs continued to repeatedly hemolyse throughout the remainder of his hospital course.

Computed tomography, as demonstrated in Figures 1-3, revealed "extensive cavitary necrosis of right hepatic metastases post-treatment, moderate pneumoperitoneum, and no evidence of bowel injury or ischemia." Along with free air in the abdomen, air was also present within the substance of the tumor as well as the bile ducts. CT scan did not reveal any evidence of coexisting hepatic infarct. The hepatic arteries and portal vein remained patent on the CT scan.

Initial intervention included aggressive volume resuscitation and IV piperacillin tazobactam (Zosyn). Both surgery and IR were consulted. He was evaluated by the surgery team, and immediately booked for an exploratory laparotomy, with the intent of ruling out a missed enterotomy, and obtaining source control of the necrotic liver metastases.

Within an hour he was in the operating room, where he underwent excision and debridement of multiple necrotic hepatic lesions. On entering the abdomen, the surgical team noted a foul odor and dark blood throughout the abdomen. No enteric injury was identified. Necrotic liver tissue was debrided in segments 6 and 8 utilizing suction irrigation and digital dissection. Two blake drains were laid and the abdomen was closed. At the time the case concluded, the patient was profoundly acidotic (ABG pH <6.8, base excess -28) and requiring levophed to maintain MAP. His intraoperative resuscitation included one unit of packed red blood cells, one unit of fresh frozen plasma, and 1.5 L crystalloid. He also received zosyn, cefepime, flagyl, and micafungin perioperatively.

The patient was transferred to the Surgical and Trauma ICU where he was started on vasopressin and epinephrine, as well as a bicarbonate drip, and an amiodarone drip for atrial fibrillation. He was emergently started on CVVHD. Unfortunately, his condition continued to deteriorate despite all available interventions and he expired 6 hours after leaving the OR, approximately 30 hours after his initial IR procedure.

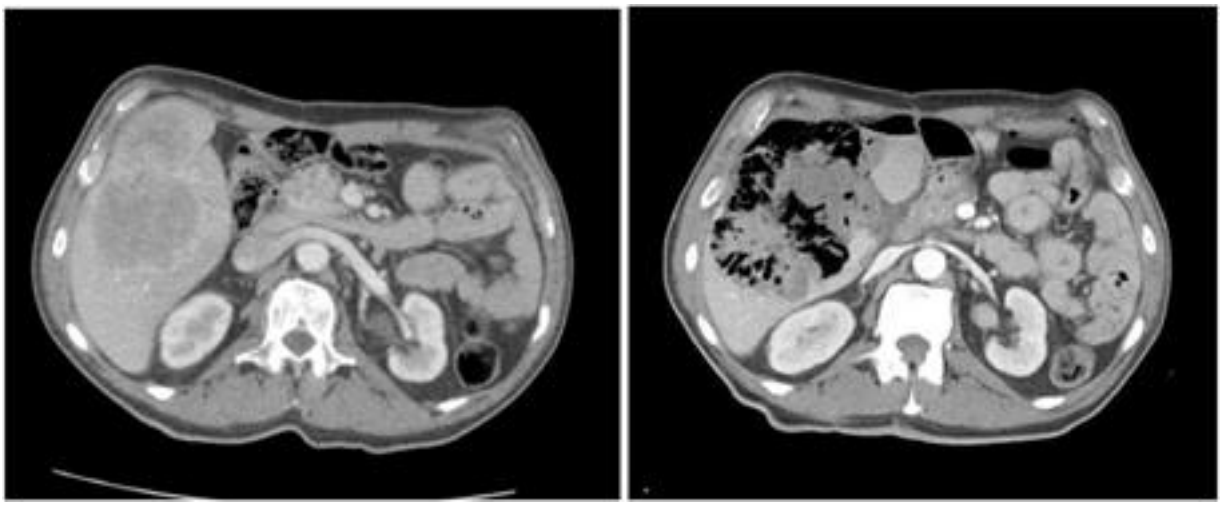


Figure 1: Pre-procedure CT completed one month prior to embolization (left), compared to CT on presentation to the emergency department post-embolization (right), axial view, showing a gas-forming liver abscess in the right lobe of the liver.

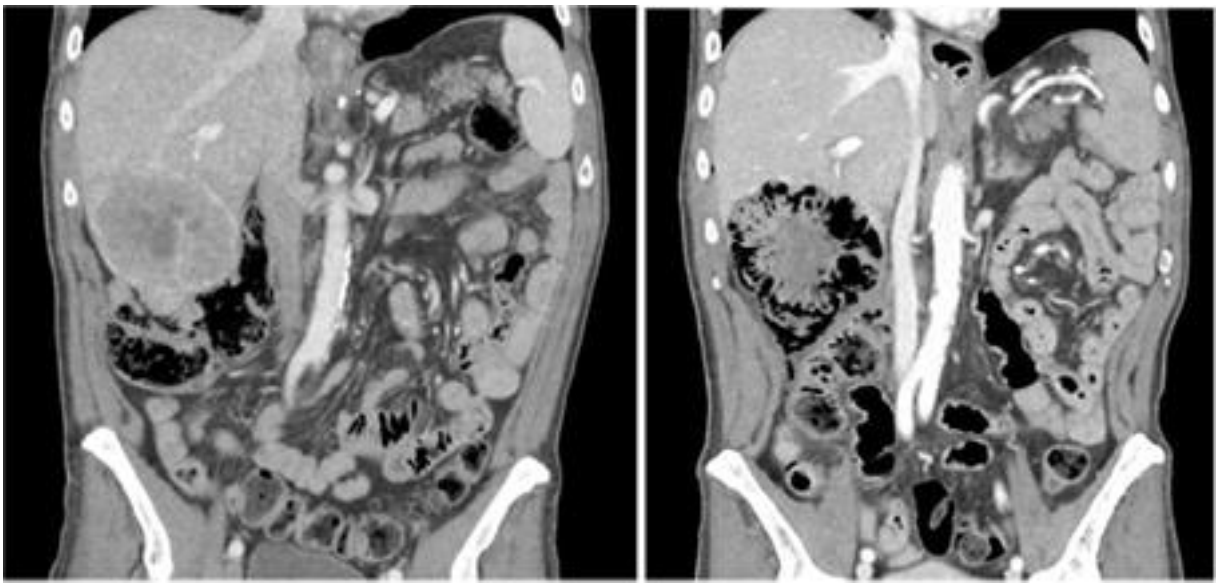


Figure 2: Pre-procedure CT completed one month prior to embolization (left), compared to CT on presentation to the emergency department post-embolization (right), coronal view, showing a gas-forming liver abscess in the right lobe of the liver.

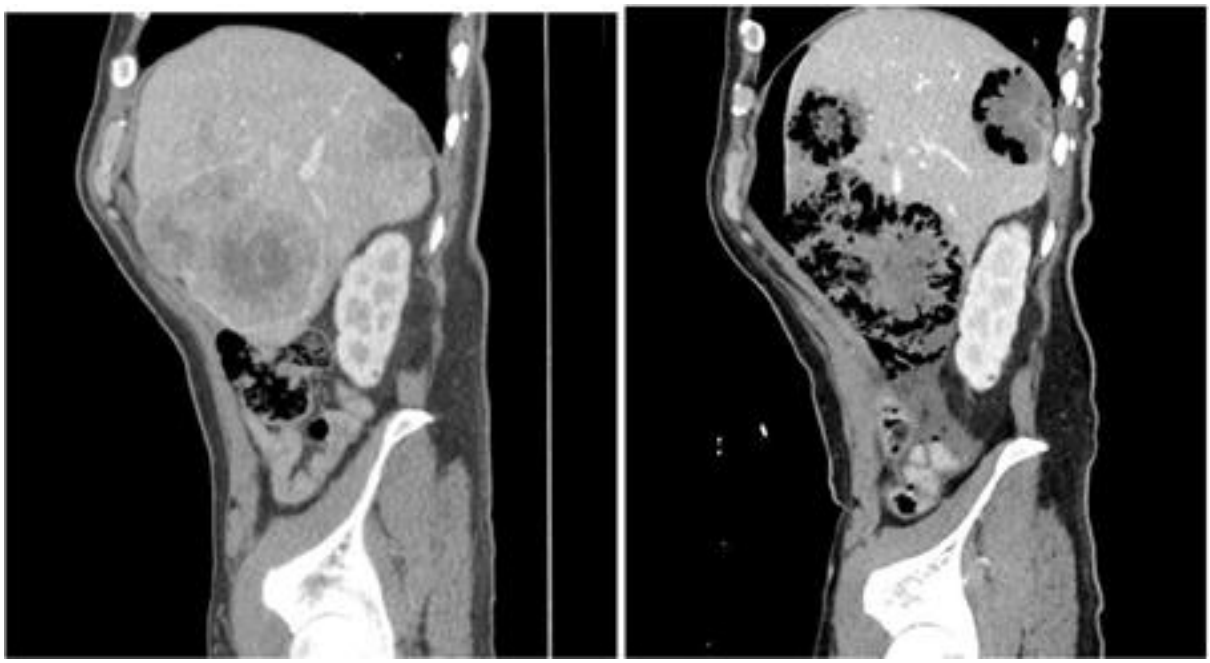
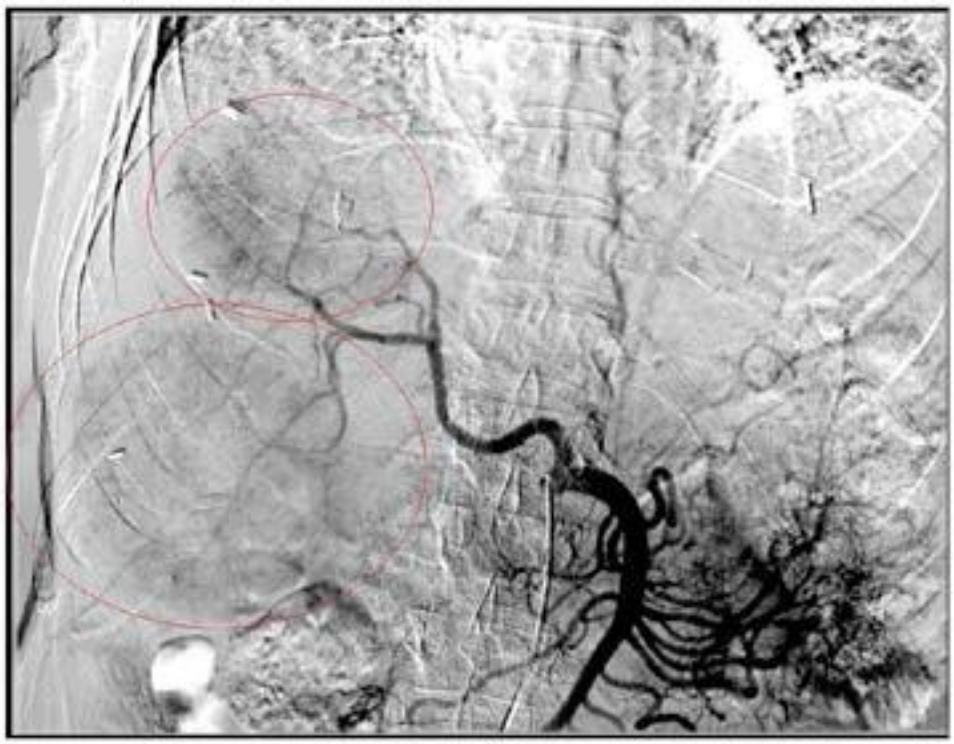
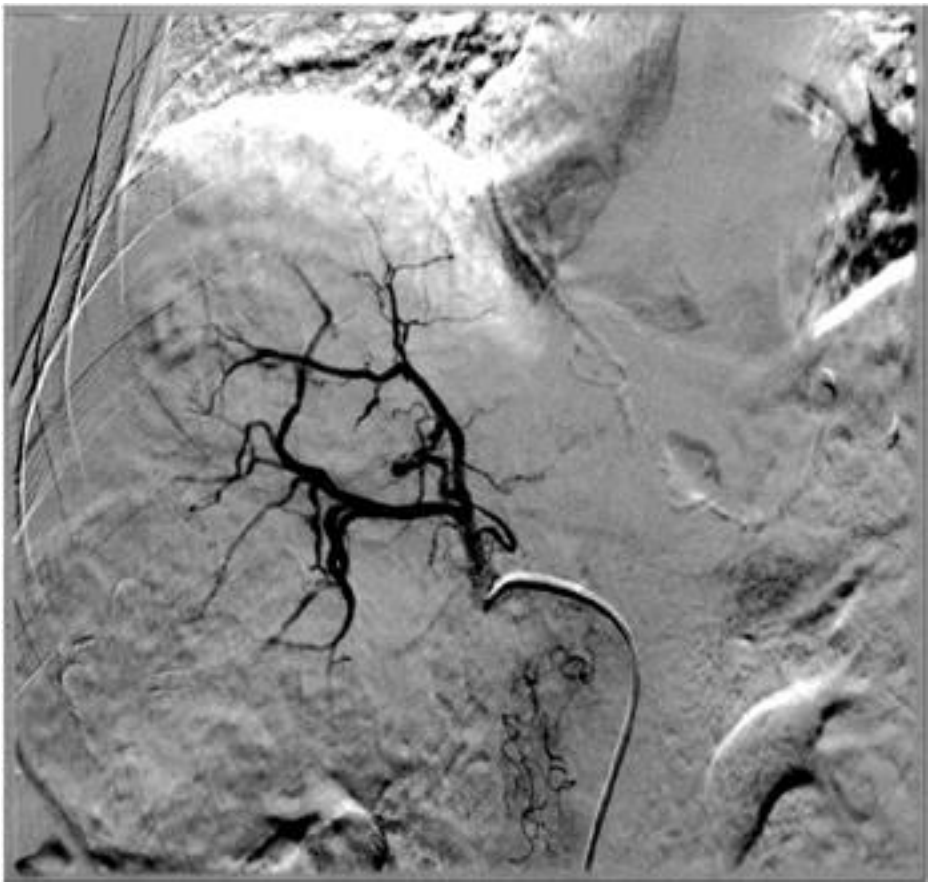


Figure 3: Pre-procedure CT completed one month prior to embolization (left), compared to CT on presentation to the emergency department post-embolization (right), sagittal view, showing a gas-forming liver abscess in the right lobe of the liver.



Adunctive Figure A: SMA arteriogram demonstrating a replaced right hepatic artery feeding two large hypervascular foci in the right lobe of the liver.



Adjunctive Figure B: Post embolization angiogram demonstrating no evidence of persistent hypervascular tumor and preservation of the normal forward flow in the remainder of the segments 5-8 hepatic arteries.

4. Discussion

Here we present a fatal case of *Clostridium perfringens* sepsis with massive intravascular hemolysis in a 63-year-old male with metastatic gastroesophageal cancer within 30 hours following a transcutaneous image guided liver biopsy and HAE metastatic adenocarcinoma in the liver. C. *perfringens* sepsis is a devastating condition with a reported mortality rate ranging from 70-100% with a rare, but known association with massive intravascular hemolysis as the

result of secreted alpha-toxin [1,2]. This disease process is a rare finding with the only several case reports and reviews existing within the literature. In the context of liver directed therapy such as HAE, the available literature becomes even more scarce.

A thorough literature review reveals that this is the first report of C. *perfringens* sepsis with intravascular hemolysis following image guided biopsy and HAE. Prior literature reviews of TACE/TAE have identified only 5 prior cases of C. *perfringens* sepsis with intravascular hemolysis [5]. There has been one prior case report of C. *perfringens* sepsis following transcutaneous liver biopsy. It is reported that the patient in that report had a rapid clinical decline the day following the imaging guided biopsy, a time course which is similar to this case [6].

The available literature identifies immunocompromised patients as a primary risk factor for C. *perfringens* septicemia including gastric or pancreatic malignancy, diabetes, or hematologic disorders, as well as focal infection following hepatobiliary or gynecologic interventions [7]. Additional case reports also identify other malignancies such as esophageal, colon, and hepatic cancers as notable risk factors.

The general consensus for treatment of this condition is centered around early identification with initiation of broad-spectrum antibiotics. Source control involving image guided drainage procedures or surgical debridement also being a prognostic indicator for survival [7].

No guidelines regarding the prevention of this complication currently exist. However, antimicrobial prophylaxis at the time of the initial procedure, as is standard in most surgical procedures, could possibly have utility in infection prevention. There is no consensus on antimicrobial prophylaxis in transarterial embolization. Overall complication rates after TACE/TAE are approximately 10%. Of this, 4.6%, is postembolization syndrome that requires extended stay or readmission, liver failure (2.3%), abscess (0-15%, dependent on presence and functionality of sphincter of oddi), and <1% experience gastrointestinal hemorrhage or ulceration, pulmonary arterial oil embolus, biloma requiring percutaneous drainage, and surgical cholecystitis [8]. Lastly, death within 30 days occurs in 2-4% of patients [8]. A prospective review by Chinmaya S. et al. analyzed 59 patients with hepatocellular carcinoma who underwent either bland, TAE, or Yttrium-90 embolization. Overall, it was found that the use of antibiotics in both pre- and post-procedure was variable with no supporting evidence for any antimicrobial use [9,10].

5. Conclusions

Infection with *Clostridium perfringens* following biopsy or embolization of liver tumors and metastases is a rarely documented event with extremely high mortality (70-100) %. In this case report, we have presented the first recorded case of death due to clostridium perfringens sepsis after HAE of liver metastases, though deaths have previously occurred after TACE/TAE and percutaneous liver biopsy. While uncommon, we propose that in medically frail patients at greatest risk for infection after such procedures, clinicians should consider periprocedural prophylactic antibiosis and post-procedure observation. Additional investigation, and generation of evidence-based guidelines regarding the prevention of this rare but severe complication is warranted.

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