Scientific Research Publishing

Open Journal of Emergency Medicine, 2024, 12, 77-84
https://www.scirp.org/journal/ojem
ISSN Online: 2332-1814
ISSN Print: 2332-1806

Hemoperitonium: Atypical Presentation Caused by Spontaneous Rupture of Hepatocellular Carcinoma in an Undiagnosed Patient

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How to cite this paper: Abboud, Y., Burki, L. and Abdalkarim, D. (2024) Hemoperitonium: Atypical Presentation Caused by Spontaneous Rupture of Hepatocellular Carcinoma in an Undiagnosed Patient. *Open Journal of Emergency Medicine*, **12**, 77-84.
https://doi.org/10.4236/ojem.2024.123010

Received: June 24, 2024
Accepted: September 10, 2024
Published: September 13, 2024

Abstract

Introduction: Acute hemoperitoneum due to the spontaneous rupture of hepatocellular carcinoma (HCC) is a rare case of non-traumatic intra-abdomen bleeding that requires a high index of suspicion to approach, especially if no known history of HCC. It can mislead the physicians when the patient presents in an atypical way. **Case Presentation**: In this case report, we describe a fortuitous rupture of hepatocellular carcinoma in a 58-year-old male who was not previously diagnosed as having HCC and who came with atypical symptoms and signs of hemoperitoneum. He was then treated by trans-arterial embolectomy. **Discussion**: Diagnosis of hemoperitoneum in a case with bradycardia and hypotension is uncommon, as it goes more towards cardiogenic shock than hypovolemic shock, especially in a patient who is previously not symptomatic and has no risk factor for hepatocellular carcinoma. **Conclusion**: physicians should be alert to the possibility of encountering a hemorrhagic shock, although no trauma injury in any hypotensive patient with no clear reason for his condition.

Keywords

Hepatocellular Carcinoma, Rupture of HCC, Trans-Arterial Embolectomy, Hemoperitoneum, Liver Cancer

1. Introduction

According to the World Health Organization GLOBOCAN database, Hepatocellular carcinoma (HCC) is the fourth leading cause of cancer-related deaths in the world. It is a primary tumor of the liver that usually develops in the setting of

chronic liver disease, particularly in patients with cirrhosis due to heavy alcohol use, cirrhosis due to chronic hepatitis B or C, Aflatoxin exposure, metabolic disorders such as diabetes, obesity and non-alcoholic fatty liver disease (NAFLD). [1] [2] Spontaneous rupture of HCC is an uncommon and sometimes fatal complication with an incidence rate of 3 - 15%. In recent years, the screening of the patients who are at high risk for HCC has improved as a result the incidence has decreased steadily. Mortality due to spontaneous rupture is the third most common cause of HCC-related death after tumor progression and liver failure [3]. Previous studies have shown that the risk factors for HCC rupture are tumor location on the hepatic surface and/or protrusion of the tumor diameter > 5 cm, portal hypertension, liver cirrhosis, inappropriate anti-aggregating or anticoagulant therapy, the presence of coagulopathy and thrombocytopenia associated with liver cirrhosis and metastatic tumor. [3] [4] Patients with the rupture of hepatocellular carcinoma (RHCC) generally present to the emergency department with the following common clinical manifestations 1) Peritonitis: Sudden severe epigastric pain, tenderness, rebound tenderness and muscle tension, 2) Different degrees of hemorrhagic shock: dizziness, fainting, restlessness, palpitation, shortness of breath, thirst and fatigue, increased heart rate, oliguria, "anemia appearance" and so on. 3) Hemoperitoneum: abdominal distension, extraction of non-coagulated blood through the diagnostic abdominal puncture, etc. 4) Liver cirrhosis and HCC: jaundice, palmer erythema and spider nevi [5]. The diagnosis of rupture in patients without a history of cirrhosis or HCC may be difficult. The most common symptom of ruptured HCC is abdominal pain seen in 66 - 100% of the cases, shock at the time of presentation can be seen in 33 - 90%, and abdominal distension is reported in 33% of the cases. The diagnoses can be confirmed by computed tomography scan or ultrasonography or both in 75% of the cases. Careful pre-treatment evaluation is essential to decide the best treatment option. Management of ruptured HCC involves multi-disciplinary care where achieving hemostasis remains a primary objective [6]. We report a case of hemoperitoneum caused by spontaneous rupture of previously undiagnosed HCC.

2. Case Presentation

We report a 58 years old male, known case of hypertension, chronic atrial fibrillation on anticoagulant medication (rivaroxaban), and benign prostatic hyperplasia, non-alcoholic, non-smoker brought by the Ambulance to the emergency room with hypotension (65/40 mmHg), bradycardia (52 beats/min) (**Figure 1**), dizziness and epigastric pain, associated with constipation for past two days, no vomiting, fever, jaundice or abdominal distention. On the initial physical examination, he was conscious GCS 15/15, respiratory rate 13 breaths/min, oxygen saturation 98%, the chest was clear, heart sounds audible, the abdomen was soft and lax, not distended with mild right upper quadrant tenderness and normal bowel sound. ECG done showed slow rate atrial fibrillation, IV fluids were started along with one dose of atropine, and his heart rate picked up, but he remained hypotensive,

noradrenaline was started immediately his BP increased to 105/80 mmHg. Following were his laboratory values: Troponin T quantitative 0.01 ng/mL, VBG showed no acidosis PH 7.38, normal serum electrolytes K 3.9 mmol/L, Na 140 mmol/L, Hb: 14 g/dl (**Figure 2**), WBC 13.3 × 10^9/L, PLT 181 × 10^9/L, AST 20 U/L, ALT 8.3 U/L, ALP 61 IU/L, and Lipase 25.3 U/L. X-ray of the chest and abdomen were done and were unremarkable. The Cardiologist was involved and echocardiogram was done in the ED, which ruled-out cardiac tamponade, during the last minutes of the echocardiogram, his BP started to deteriorate and reached 90/70, which made him severely dizzy and diaphoretic, unstable to reach the radiology department for CT abdomen. The decision was taken to transfer him to the ICU for further investigations and observation. After 2 hours, his Hb dropped to reach 9 g/dl, INR 2.85, PT 36.6 sec, APTT 37.9 sec, and his abdomen started to distend with increasing pain and generalized tenderness, rigidity and guarding, despite the low BP emergency CT abdomen was performed, it showed: shrunken liver, mild cirrhosis with multiple masses, at least 8 were identified, some were hypervascular on arterial phase suggestive of HCC, extensive fluid was seen around the liver and spleen suggestive of acute venous hemorrhage (**Figures 3(A)-(B)**). He was given 8 units of FFP and 8 units of packed RBC, then he was shifted to the operation room for emergency exploratory laparotomy. Massive blood collection, 3400 ml of blood was collected in the cell saver, blood clots of around 1 - 1.5 liter were removed and 6 packs were placed in the abdomen with drains. Extensive blood transfusion was started, still after 2 hours of surgery patient did not improve hemodynamically, his BP was 100/50 mmHg and HR was 150 b/min still showing atrial fibrillation, even though he was receiving noradrenaline and vasopressin. In the VBG lactic acid was 9 mmol/L. His PLT was 52 × 10^9/L and nonstop blood was coming in the drain bag, so it was decided to do a re-exploration. The surgeon found active bleeding from a hyper-vascular tumor within the right lobe of the liver, 2300 ml of blood was collected in cell savor, blood clots of around 700 ml were removed, abdomen was packed with gauze pieces, NovoSeven 1 mg was given, after achieving hemostasis abdomen was closed. The patient was then shifted for emergency angiography and embolization of the branch of the right hepatic artery was done. Post procedural angiograms demonstrated complete devascularization of the hyper-vascular tumor. Immediately the BP started to improve. Post-operative patient remained intubated, an episode of fast atrial fibrillation was managed by amiodarone, his BP remained stable without inotropes. After 2 days, with the multidisciplinary team's decision, the abdomen was reopened and 12 packs were removed, gall bladder was necrotic, so cholecystectomy was done. Till after 10 days patient did not have any postoperative complication. Abdominal drain was taken out on the 14th postoperative day. Histopathology (**Figure 4**) was performed in our hospital, which revealed features of an atypical hepatocyte epithelial proliferation, favoring the diagnosis of well-differentiated hepatocellular carcinoma. His Ca 19 - 9 was normal, Hepatitis C antibody and hepatitis B surface antigen were negative, CEA was normal, AFP was mildly elevated.

Following the surgery, the patient had an uncomplicated hospital stay of 15 days, including 14 days in the ICU. He was discharged in good medical condition. On the follow-up in the clinic, his blood tests showed Hb 11.3 g/dL, WBC 9.87 × 10^9/L, PLT 301 × 10^9/L, AST 42 U/L, ALT 14.9 U/L, ALP 337 IU/L, the patient was doing well, gaining weight and had resumed his basic life activities.

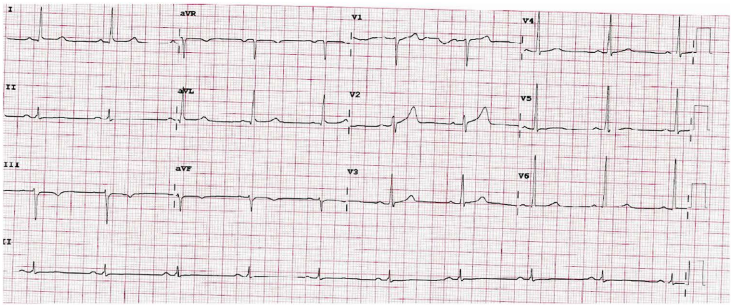
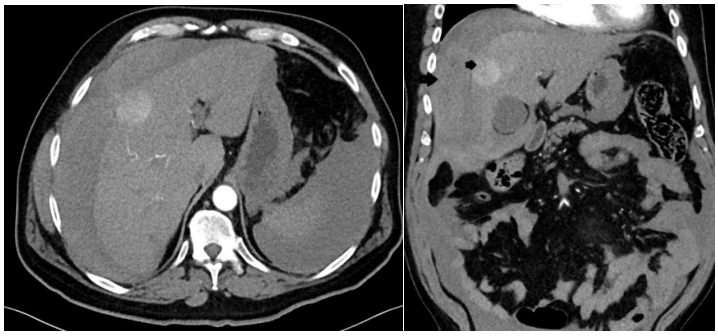


Figure 1. ECG.

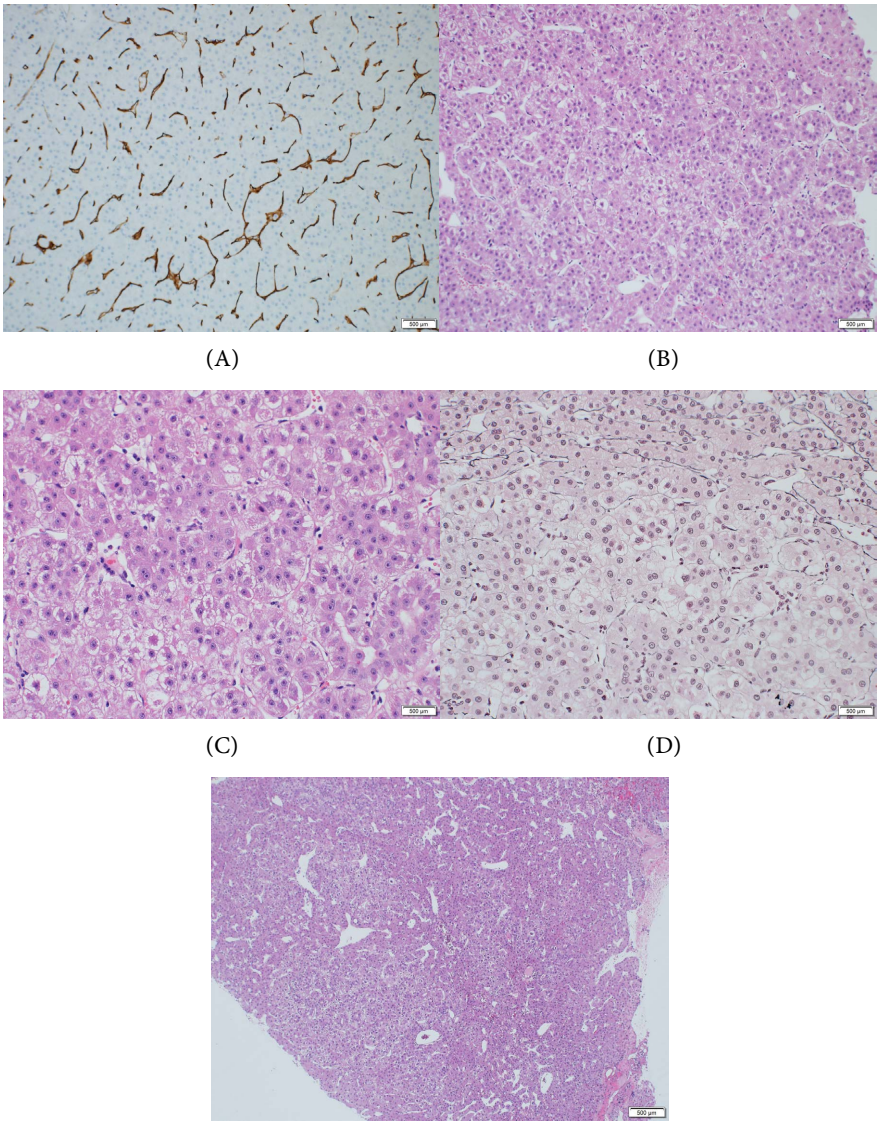
pH	7.435	[	7.350 -	7.450]	
PCO_2	32.9 mmHg	[	32.0 -	48.0]	
PO_2	35.1 mmHg	[	83.0 -	108.0]	↓
Hct	40.6 %	[	36.0 -	53.0]	
Na^+	135.7 mmol/L	[	136.0 -	145.0]	↓
K^+	3.87 mmol/L	[	3.50 -	5.10]	
Ca^{2+}	0.896 mmol/L	[	1.150 -	1.330]	↓
Cl^-	107.5 mmol/L	[	98.0 -	107.0]	↑
Glu	7.0 mmol/L	[	4.1 -	5.6]	↑
Lac	2.9 mmol/L	[	1.0 -	1.8]	↑
tHb	13.4 g/dL	[	11.5 -	17.8]	
SO_2	73.2 %	[	94.0 -	98.0]	↓
O_2Hb	71.4 %	[	94.0 -	98.0]	↓
COHb	1.8 %	[	0.0 -	3.0]	
MetHb	0.7 %	[	0.0 -	1.5]	
HHb	26.1 %	[	0.0 -	2.9]	↑
Bili	Value below 3.0 mg/dL				⇊ ×
$cHCO_3^-$	21.6 mmol/L				
BE	-1.84 mmol/L				
$cHCO_{3\,st}^-$	22.8 mmol/L				
nCa^{2+}	0.91 mmol/L				
AG	10.5 mmol/L				
PF index	167.19 mmHg				

Figure 2. POCT VBG.



(A) (B)

Figure 3. Transverse and Coronal sections of CT scan abdomen, arterial view angiogram?, shows extensive hypo-attenuation within the liver involving left hepatic lobe, caudate lobe and hepatic dome (Right hepatic lobe?) demonstrates subcapsular hematoma and multiple hypo-dense lesions of varying size.



(A) (B)

(C) (D)

(E)

Figure 4. Histopathology.

3. Discussion

Accurate diagnosis is the first step in optimal cancer care. However, because HCC often presents atypically, patients might be misdiagnosed and not receive appropriate treatment in a timely manner. Risk factors for HCC include chronic hepatitis B and hepatitis C, alcohol addiction, metabolic liver disease (particularly non-alcoholic fatty liver disease) and exposure to dietary toxins such as aflatoxins and aristolochic acid [7] Cirrhosis is the most important risk factor for developing HCC since up to 80% of these tumors arise from cirrhotic livers. It is rare in non-cirrhotic liver with a different clinical, treatment and prognosis spectrum [3]. Regarding the clinical presentation and past medical history of our patient, he didn't have any risk factors for developing hepatocellular carcinoma and no symptoms or signs of liver cirrhosis. Even today, the mechanisms of spontaneously ruptured

HCC (SRHCC) are still unclear and several hypotheses have been made: rapid tumor growth with intra-lesional necrosis, separation between tumor and normal parenchyma, vascular erosion, and increased intra-tumoral pressure due to venous occlusion and coagulopathy. Hemoperitoneum due to non-traumatic liver injury can be caused by several different neoplastic and non-neoplastic diseases. Previous studies have shown that the risk factors for HCC rupture are tumor location on the hepatic surface, tumor diameter > 5 cm, portal hypertension and liver cirrhosis. One of the most relevant factors is the peripheral surface location and/or protrusion of the tumor. The most common symptom of HCC rupture is acute abdominal pain, that occurs in 66.4% of patients. Hemoperitoneum is a possible scenario resulting from spontaneous HCC rupture and it occurs more frequently in cirrhotic liver. Some conditions may increase the risk of intra-abdominal hemorrhage, for e.g. inappropriate anti-aggregating or anticoagulant therapy, the presence of coagulopathy and thrombocytopenia associated with liver cirrhosis, or in the case of metastases and tumors with a diameter greater than 5 cm. This case highlights many atypical findings of HCC and it was challenging and difficult to suspect hemoperitoneum in this patient as he had no risk factor or symptom of HCC and normal liver function. This patient with a history of hypertension and chronic atrial fibrillation presented with bradycardia and hypotension, so cardiogenic shock due to cardiac tamponade was the most probable diagnosis that was ruled out by the FAST scan and echocardiogram. The initial blood workup was done and showed no abnormality including the liver function tests. When the Hb started to decrease and BP became unstable, then internal bleeding was suspected and emergency CT scan of the abdomen was done and it showed liver masses and free fluid in the abdomen. Treatment goals primarily focus on achieving hemostasis, which is often done through conservative therapy or trans-arterial band embolization. For instance, in a case report by Mascagni et al., bleeding due to right hepatic capsule rupture and hemoperitoneum was successfully stopped by initial trans-arterial embolization followed by right hemihepatectomy. In our case, emergency laparotomy was done twice and at first, more than 3400 ml of blood and then more than 2300 ml of blood were drained respectively, and perihepatic packing was done, but the patient remained unstable despite massive blood transfusion (including 38 unit of blood transfused included Packed RBCs, platelet and FFP), so he was rushed to an emergency angiography for right hepatic artery embolization. The patient started to stabilize and his BP and biomarkers started to improve, his overall condition improved dramatically. He was successfully extubated after 2 days, he recovered well, started to eat and walk till he was discharged in a very good condition. He was discharged to follow up in the clinic for the workup and treatment of the newly discovered HCC.

4. Conclusions

Diagnosis and prediction of hemoperitoneum in the setting of bradycardia and hypotension in a patient who previously had no risk factor or symptom of hepato -

cellular carcinoma made it difficult for the physician to think about hypovolemic shock caused by the spontaneous rupture of the HCC. It is challenging and can mislead the physician towards another diagnosis especially when the patient presents with atypical symptoms. Like in our patient he was complaining of sweating, had bradycardia and hypotension, there was no abdominal pain, that made the cardiac cause as the first suspected reason for his instability. In summary, although a ruptured HCC diagnosis with no relevant history or symptoms can be challenging, physicians should be alert to the possibility of encountering this and should consider it in their differential diagnosis. It makes managing the patients presented with unjustified shock to consider it hemorrhagic until proven otherwise, (in our patient, his Hb was normal initially, dropped in 2 hours).

Having said that, the decision to take an unstable non-traumatic patient to CT scan is advisable, especially if no other reason can be found to justify shock and clinical deterioration. In most cases of HCC hemorrhage a blunt trauma was the common reason for the rupture, in our patient, when he did prolonged Echocardiography having different views and multiple windows for imaging, then he deteriorated with the need to increase the dose of noradrenaline, we can suspect that the bleeding increased due to frequent pressure on the right upper quadrant of his abdomen. It is still a point of debate if this was the reason that increased the hemorrhage. In conclusion, hemorrhagic shock should be the first cause to be considered in an unstable patient. If no clear reason is detected during the history and physical examination then the use of FAST scan, as in the ATLS protocol, to rule out cardiac tamponade, free fluid in the abdomen, haemo or pneumothorax is the best practice to find out any cause of shock. On the other hand, in the absence of trauma, free fluid detected in the abdomen could be simple ascites, but if hypotension or shock is present, we should also consider hemoperitoneum due to hepatic disease and HCC, so that early detection, treatment and action can have a better outcome.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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