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The Hidden Time Bomb Explodes: A Previously Asymptomatic and Undiagnosed Hepatocellular Carcinoma Presenting as a Tumour Rupture

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ABSTRACT

Hepatocellular carcinoma is the third leading cause of cancer-related death world-wide. Infection with hepatitis B virus is the strongest known risk factor for the development of hepatocellular carcinoma, especially in male patients. Regular surveillance is crucial for early detection of hepatocellular carcinoma as, in the absence of consistent follow-up, patients often present with advanced disease and sometimes with tumor rupture. We present here a case report of a patient from a high risk demographic—an African male infected with hepatitis B virus—whose initial presentation of hepatocellular carcinoma was that of a tumor rupture. We highlight the non-specific nature of his presentation and the importance of high clinical suspicion for hepatocellular carcinoma in patients from high-risk groups. We highlight that in the absence of timely recognition of this malignancy, especially at its advanced stage, a patient's already scarce treatment options may become even more limited.

KEYWORDS: *hepatocellular carcinoma, hepatitis B virus, tumour rupture, transarterial embolization*

INTRODUCTION

Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related mortality in the world,[1] with a specific geographic distribution and strong association with hepatitis B or C virus (HBV and HCV) carrier status.[2,3] It is especially prevalent in Sub-Saharan Africa, with Gambia specifically having the incidence of 33.1 per 100,000 males per year and 12.6 per 100,000 females per year.[4,5] The increased susceptibility of males

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> **We highlight that in the absence of timely recognition of this malignancy, especially at its advanced stage, a patient's already scarce treatment options may become even more limited.**

to HCC is observed world-wide and is thought to be due to multiple factors, including hepatitis carrier state, environmental exposures, and the effect of androgens.[4,5]

Infection with HBV was shown to be more likely to progress to HCC in patients positive for HBeAg, which is one of the viral polypeptides thought to modulate the host immune response, compared to those positive only for HBsAg, which in turn was higher than those of inactive carriers.[6] Treatment of HBV was shown to reduce the risk of progression to HCC although it does not bring it back to baseline.[7-9] Along the same lines, the risk of progression to HCC in HBV carriers was shown to be greater in patients with higher viral loads.[7]

Presentation of HCC is non-specific.[10] Patients with HCC may have no symptoms other than those related to their chronic liver disease; in other words, some patients may present with decompensation of their previously compensated cirrhosis. More advanced lesions may present with mild-moderate upper abdominal pain, night sweats, fever, diarrhea, and symptoms related to the location of metastatic spread. A dramatic presentation is usually seen with tumour rupture, which can occur in up to 15% of patients.[11] Clinical features include acute abdominal pain, distension, and hemodynamic instability; the thirty day mortality rate can be over 30%.[12] Hemodynamic stabilization followed by transarterial embolization to control bleeding are essential to minimize mortality.[11] Patients with ruptured HCC are at high risk for metastatic peritoneal seeding; however, this does not preclude an attempt at a potentially curative resection in suitable patients.[11] At least one study on a small group of patients who underwent liver resection following rupture of their HCC suggested that there was a benefit to peritoneal lavage.[13] The authors proposed that it may retard the growth of extrahepatic metastasis.

As with other malignancies, early detection is critical to maximize patient survival, and consequently, routine monitoring is recommended in patient populations at high risk. HBV carriers of African descent are of particularly high concern, with ultrasonographic surveillance advised every six to 12 months in patients over the age of 20.[14] The treatment options depend on the extent of the disease spread. Potentially curative resection offers the best chance of survival to suitable candidates. Liver transplantation may be considered as well. In patients with unresectable lesions, various types of ablation and embolization can prolong survival. Radiation therapy, as well as systemic chemotherapy, can also be offered.

We present here a case of a HBV carrier from Gambia with HCC rupture as first presentation, with discussion of his diagnosis and treatment options.

CASE REPORT

A 52-year-old African male with a remote history of infectious hepatitis presented to the Vancouver General Hospital (VGH) complaining of severe epigastric pain lasting one week. The pain had been persistent and progressive, radiated throughout his abdomen, and was graded as 10/10 in severity at presentation. The patient was also suffering from constipation and had been experiencing night sweats. There were no other associated symptoms at presentation. Several days prior he had visited another emergency department with similar symptoms and was discharged with the diagnosis of constipation. The patient reported two prior episodes of severe abdominal pain: one occurred three years previously during a trip to Gambia and another four months before presentation after consumption of contaminated water.

This patient's past medical history included insulin-dependent diabetes mellitus. His diagnosis of hepatitis infection was made 13 years ago and the patient's family history was not significant for liver disease or other gastrointestinal concerns. He immigrated to Canada from Africa 24 years ago and denied history of alcohol abuse or illicit drug use.

On presentation, the patient was alert and not distressed with vital signs within the normal limits. The exam was remarkable for scleral icterus and mild ascites but no other stigmata of chronic liver disease. The abdomen was obese, soft, and non-tender with no evidence of hepatosplenomegaly or abdominal masses. The rest of the examination was unremarkable.

Laboratory investigations revealed a mild normocytic anemia with a slightly elevated creatinine. Liver enzymes were all mildly elevated, and lipase was within normal limits. Total and direct bilirubin as well as LDH were elevated while albumin was decreased.

Abdominal ultrasound revealed active ascites and two irregularly defined hyperechoic lesions in the left hepatic lobe measuring 3.7 cm and 8.6 cm. The gallbladder contained multiple calculi and sludge. Extrahepatic or intrahepatic biliary ductal dilatation was absent. Lastly, portal vein thrombosis was present.

To follow up on these findings a triphasic CT scan of the abdomen was done. It showed multifocal HCC with rupture of the dominant 6.6 cm exophytic tumor in the lateral segment of the left liver lobe surrounded by a highly localized high-attenuation fluid consistent with blood (Figure 1A). In segment 4a, a 3.3x3.4x2.6 cm well-defined lesion was seen as well as numerous other hypervascular lesions in segments 6, 7, and 8 of the right lobe consistent with multi-focal HCC. No active bleeding was

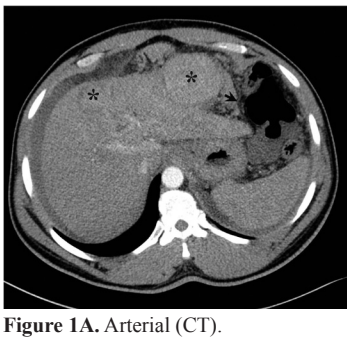

Figure 1A. Arterial (CT).

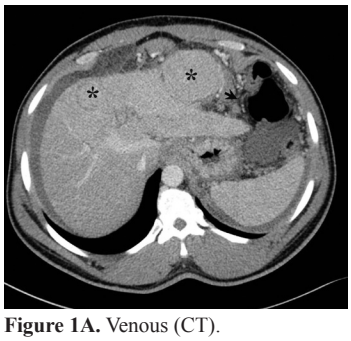

Figure 1A. Venous (CT).

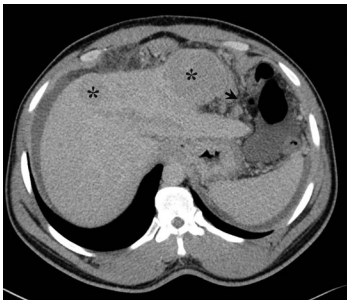

Figure 1A. Delayed (CT).

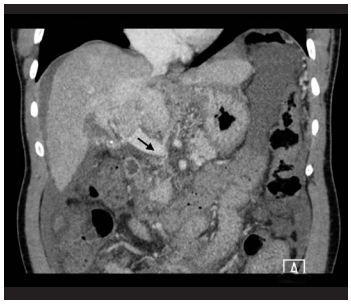

Figure 1B. Coronal view (CT).

demonstrated. Additionally, tumor thrombus was identified in the left and right portal vein branches as well as in the main portal vein (Figure 1B). Cholelithiasis and mild ascites were also noted.

The patient underwent a bland embolization of the dominant left hepatic lobe mass. He tolerated the procedure well with uneventful recovery.

HBV serologies demonstrated the presence of anti-HBc antibody, HBsAg, and an anti-HBsAg antibody level of 22.3 mIU/L. Despite the anti-HBs antibody titre, the presence of HBsAg is consistent with a chronic HBV infection. Antibodies to HCV were not detected.

Upon discharge, the patient's liver enzymes remained elevated above normal limits but were lower than on admission.

DISCUSSION

While, as mentioned previously, HCC presents with rupture in only a small percentage of patients, the potential consequences of not recognizing this event can be very severe. To avoid this potential disaster, a high index of suspicion for a previously unrecognized HCC should exist when encountering patients from high-risk demographics, such as the patient presented here.

Initially, hemodynamic control is of prime importance and can be achieved via embolization of the arteries supplying the ruptured tumor. Following stabilization of the acute presentation, appropriate follow-up care to maximize survival and quality of life becomes paramount. Unfortunately, our patient's severe abdominal pain (which we felt signified the rupture of his HCC) started several days prior to his presentation to VGH. Therefore, by the time the stabilization of the ruptured tumour was achieved, he was already outside of the window of opportunity for peritoneal lavage to minimize peritoneal seeding. Although his high disease burden and the presence of portal vein thrombosis indicated a high chance of extrahepatic metastases prior to rupture, timely peritoneal lavage could have still minimized his disease burden and improved his prognosis. This once again highlights the importance of having a high suspicion for HCC in patients from high-risk demographics, allowing for timely diagnosis and management.

Prognosis for advanced HCC with extrahepatic spread is generally poor. However, sorafenib (Nexavar®), a small molecule that inhibits tumour angiogenesis and proliferation while increasing apoptosis, has been shown recently to be effective in prolonging survival of patients with metastatic HCC for up to three months.[15] A number of other systemic therapeutic agents for HCC are currently in various stages of clinical trials.[1] These options were discussed with our patient. Unfortunately, our patient was not a candidate for either liver resection or transplantation, due to his high and multifocal hepatic tumour burden and extrahepatic spread, respectively. However, the fact that his liver enzymes were elevated at presentation and there were no signs of decompensated cirrhosis (Child-Pugh Class A) demonstrated that he still had a reasonable hepatic reserve, which is a good prognostic indicator.

In conclusion, our case of multifocal HCC presenting with rupture highlights the importance of having a high clinical suspicion in appropriate patient populations as well as the essence of timely diagnosis and treatment initiation to improve the patient's prognosis.

SOAP Note.

Subjective
Fifty-two-year-old Gambian male with remote history of infectious hepatitis presents with several days of extreme epigastric pain, constipation, and night sweats.

Objective
Several stigmata of chronic liver disease on physical exam with no palpable abdominal masses or hepatosplenomegaly. Biochemical profiling demonstrated elevated liver enzymes and bilirubin with a decreased albumin. Radiological imaging demonstrated multifocal hepatic tumours consistent with HCC, with evidence of rupture of the dominant exophytic mass. Serological work-up revealed chronic HBV infection.

Assessment
Multifocal HCC secondary to infectious hepatitis with tumour rupture as first presentation.

Plan
Bland embolization of the ruptured mass to achieve hemodynamic control; recommendations for systemic chemotherapy to maximize survival.

POST-SCRIPT

This patient returned to his native country and passed away from his HCC two months after presentation. He willingly consented to this case report in the belief that it would enhance awareness and medical education about his condition at this university. We dedicate this publication to him.

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