

Spontaneous regression of Hepatocellular Carcinoma

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Abstract

Objective: To uncover the etiology of spontaneous regression of Hepatocellular Cancer (HCC) in a patient with HBV, HCV, and alcoholic cirrhosis.

Materials/Subjects and Methods: We present a case report about a 58-year-old African American male patient with incurable HCC, a 40-year history of alcohol abuse, infected with HCV and HBV who experienced spontaneous regression of lesions after several months.

Results: After a period of about 8 months the lesions in his liver had subsided almost completely with some areas showing evolutionary changes of post ablation therapy despite lack of any interventional therapy.

Conclusion: This is the first report of a patient with HBV, HCV, and alcoholic cirrhosis that experienced spontaneous regression of HCC without any surgical interventional or medical therapy. Regression of the malignant lesions is likely secondary to tumor ischemia due to the new onset portal vein as well as the withdrawal of alcohol.

Keywords

HCC; HBV; HCV; spontaneous regression

Abbreviations

HCC: hepatocellular carcinoma; HBV: Hepatitis B Virus; HCV: Hepatitis C Virus

Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver cancer and is the second leading cause of cancer death worldwide in men. The major known risk factors associated with HCC include hepatitis C virus (HCV), hepatitis B virus (HBV), and alcohol-induced liver disease [1]. These three risk factors when present simultaneously interact synergistically to increase one's risk of developing HCC [1].

The prognosis of HCC is unfavorable partly due to the fact that it is usually diagnosed late in the disease course. Because HCC has such a high mortality, it is remarkable that it is one of a few cancers known to spontaneously regress. Cole and Everson first defined spontaneous regression of cancer in 1956 as a complete or partial disappearance of malignant cells in the absence of treatment or in the

presence of therapy known to be inadequate for resolution [2]. They went on to clarify that spontaneous regression does not indicate complete disappearance of the malignancy nor does it mean that the patient is cured [2]. Spontaneous regression of malignancy is a rare phenomenon occurring in approximately 1 per 60,000-100,000 cancer patients [3]. The total number of reported cases, with pathological proven spontaneous regression of HCC, is 13 cases until 2012 [4]. We present a rare case of patient with HCC and a past medical history of HBV, HCV, and alcohol induced cirrhosis who experienced regression of multiple tumors within his liver without undergoing any treatment.

Case Report

We present the case of a 58-year old African American male, who had a long history of alcohol abuse that presented to the emergency department with acute abdominal pain and icterus. The pain was located mainly in the lower abdomen; the abdomen was soft and without tenderness on palpation. He was afebrile with a heart rate 73, blood pressure 155/95 mm/Hg, respiratory rate 16/minute, and O₂ saturation 100% on air. Furthermore, he had dyspnea, a feeling of abdominal distention diarrhea, nausea and one episode of vomiting. On physical examination he had clear breath sound bilaterally, a distended abdomen with diffuse dullness on percussion, compatible with ascites. He denied any fever, loss of weight, appetite changes or weakness. His past medical history was positive for arthritis, hypertension and a history of 40 years alcohol consumption. The past surgical history, the family history and the rest of the social history was not significant. Hepatitis serologies suggested HBV-HCV co-infection. Laboratories studies showed a white blood cell count 5.9 x1000/uL, serum hemoglobin 13.4 g/dL, serum platelet count 151 Thousand/uL, serum aspartate aminotransferase 207 U/L, serum alanine aminotransferase 29 U/L, serum alkaline phosphatase 165 U/L, total serum bilirubin 1.9 mg/dl, serum albumin 2.4 g/dl, APTT 30.8 seconds and INR 1.3. The day after admission, he underwent a diagnostic and therapeutic paracentesis, yielded took out 1500mL of ascetic fluid consistent with spontaneous bacterial peritonitis, which was treated with antibiotics.

He also underwent an abdominal ultrasound that showed the liver was mildly enlarged at 17.3 cm along the mid-clavicular line. The parenchyma was nodular and heterogenous in echotexture. Multiple heterogeneous masses were identified in the right and left hepatic lobes with the largest measuring 10.2 x 8.3 x 8.4 cm. There was an additional well-defined predominantly hyperechoic mass in the right lobe of the liver measuring 3.5 x 3.5 x 3.5 cm. The central hepatic and main portal veins were patent with normal directional flow. The main portal vein was 0.8 cm at the porta hepatitis.

Later the patient underwent a triphasic abdominal CT-scan, which showed multiple exophytic lesions compatible with malignancy. One lesion was located on the left lobe extending from the anterior surface to the posterior surface of the liver (solid arrow) and another one in segment VI next to right kidney (interrupted arrow)(figure1). His alpha fetoprotein (AFP) drawn the same day showed very high levels (>30,000 ng/mL). All these findings were compatible with the diagnosis of HCC. Unfortunately, he was not considered a candidate for local ablation, chemo-embolization, radio-embolization or liver transplantation due to extent of disease. Moreover he was not considered suitable to use Sorafenib due to Childs Pugh B liver disease.

He continued to follow up with Hepatology clinic for supportive care of his decompensated liver cirrhosis. Six months later, he underwent a new abdominal CT-scan with very interesting findings. Both

the lesions had subsided almost completely (figure 2), the updated AFP measurement was 554. His clinical status also improved with not accumulation of ascites.

Discussion

The proposed mechanism of spontaneous regression of HCC include tumor ischemia due to hepatic artery or portal vein thrombosis, ischemia due to rapid tumor growth, withdrawal of toxic agents such as alcohol, immunologic reactions, and herbal remedies [5,6]. Though the exact etiology of tumor regression in our case is not known, evidence points towards the culmination of multiple factors leading to the final outcome.

Although there was no pathological diagnosis of HCC made in this case, the radiologic findings on CT scan combined with the elevated AFP were highly suggestive of HCC. The initial CT scan showing multiple exophytic lesions along with a large heterogeneous region of the central left hepatic lobe suggests the presence of infiltration. Over a period of six months, the tumors were noted to have shrunk significantly in size. One main change that occurred over the six months was that the main portal vein and portal venous branches distal to the portal confluence were not well visualized on CT scan. The lack of visualization of portal venous branches was worrisome for thrombus formation with the presence of collateral formations, likely reflecting cavernous transformation.

It is estimated that 10-40% of patients with HCC have portal vein thrombosis when diagnosis occurs [7]. Patients with portal vein thrombosis are found to have a worse prognosis due to their increased likelihood of metastasis and fewer treatment options. The median survival of such patients with portal vein thrombosis treated only with supportive care is only 2.7 months versus 24.4 months in those patients without thrombosis, ($P=0.00001$) [7]. In a meta-analysis of the survival rates of untreated patients with HCC Cabibbo et al. found that portal vein thrombosis was an independent risk factor for shorter survival in patients [8].

Despite documented evidence that portal vein thrombosis is a poor prognostic factor in HCC, it has also been reported in the literature as a potential cause of spontaneous regression of HCC [4]. In a meta-analysis looking at 59 case reports of spontaneous regression of HCC Oquinena et al. found that 31% of patients had tumor regression due to ischemia [3]. Additionally, 13% of those patients had tumor regression secondary to rapid tumor growth. It is possible that regression of HCC in our present case could also be due to rapid tumor growth as noted by the highly elevated AFP of 30,000, which drastically decreased to 500. Suzuki et al. reported a similar case whereby a sudden drop was observed in AFP following with no specific treatment for cancer in a patient with a prior significantly elevated AFP [9].

The patient presented in our case had a great deal of risk factors that increased his susceptibility to HCC. One such risk factor was a 40-year history of alcohol abuse. Alcohol abuse is a known risk factor for HCC, with a relative risk of 4.6 (2.7-78) in those patients who have a history of more than 80g of ethanol per day for at least 5 years [1]. Possible causative factors are the oxidative stress and the decreased immune surveillance, which can contribute to the development of HCC. Approximately 8 months prior to the regression of tumor noted by CT scan, the patient reported that he quit drinking alcohol. Withdrawal of the causative agent of HCC was documented as the cause of tumor regression in 9.4% of patients in Oquinena et al.'s meta- analysis [3]. It is unclear as to whether this factor alone is the

reason why his tumors regressed though it could be potentially a contributing factor towards the improvement in his condition.

Out of the 85 case reports of spontaneous regression of HCC listed on PubMed (both pathological and imaging proved), there have been none that document a case in a patient that has a combination of the risk factors present in the patient presented here. The patient had hepatitis B, hepatitis C, and alcoholic cirrhosis, without any treatment. Even with the multitude of risk factors, the patient experienced spontaneous regression of his tumors in the liver likely secondary to portal vein thrombosis and withdrawal of alcohol.

Conclusion

In conclusion, HCC spontaneous regression is a very interesting phenomenon, which should be investigated in more depth. Discovering the hidden pathophysiological pathways in the cancer regression process can offer the medical society discovery of new cancer treatments.

Figures

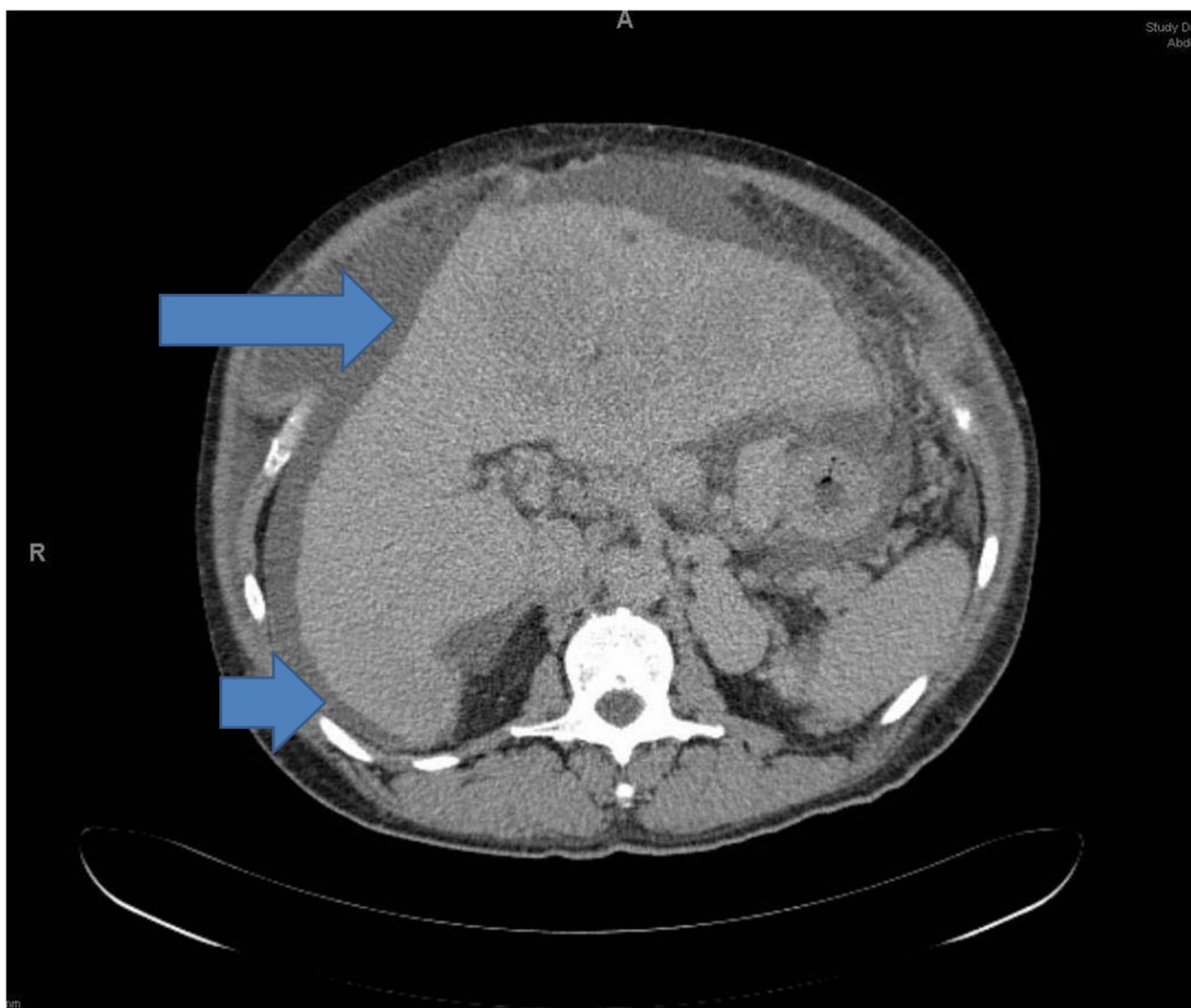


Figure 1

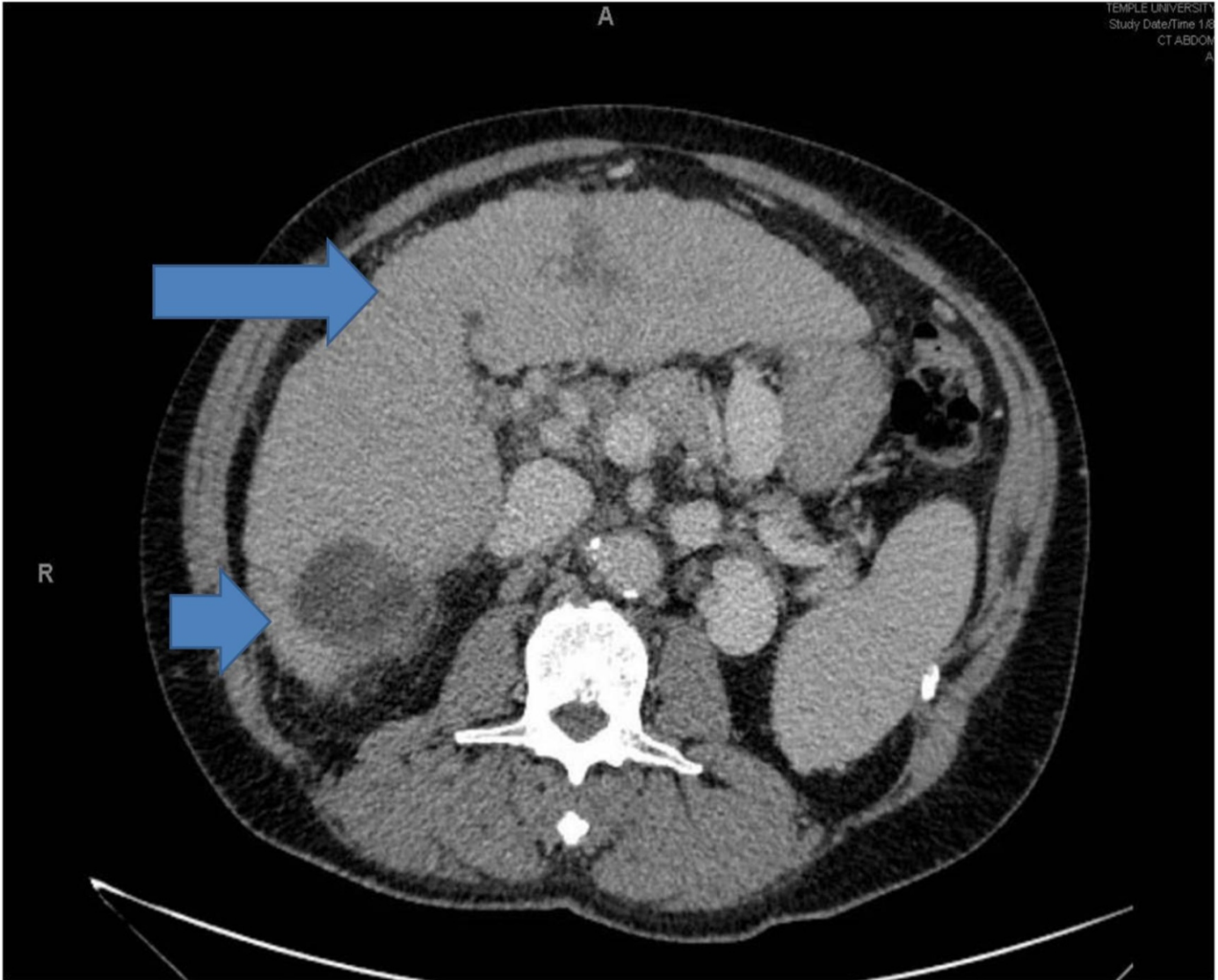


Figure 2

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