Serum alpha-fetoprotein level (> 10,000 U/mL) is a marker of hepatocellular carcinoma: A case study

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ABSTRACT

Hepatocellular Carcinoma (HCC) development in young adults is strongly multifactorial. Important risk factors for the same are smoking, alcohol abuse and hepatitis C virus (HCV) infection at an early age. However, suspecting HCC is enigmatic at early age in which biochemical marker may aid in identifying such patients. In this article, we describe an unusual case of a 27-years-old male who presented with complaints of vague right upper abdominal fullness, non-bilious, non-projectile vomiting, loss of appetite, and significant weight loss for the past 2 months. On examination, there was firm, non-tender hepatomegaly. Patient had normal liver enzymes with very high alpha-fetoprotein (AFP) level (> 10,000 U/mL). Ultrasound abdomen suggested hetero-echoic lesion in liver along with chronic kidney disease (CKD) changes. The triple phase CT of the abdomen showed a liver mass with arterial enhancement and delayed washout suggestive of HCC. Chronic HCV infection was confirmed with high RNA titres (> 50,000 IU/mL). Patient was diagnosed as HCC at an early stage, which allowed for timely initiation of treatment. This early age onset of HCC in a young adult may be due to multiple factors such as HCV infection, alcoholism, cirrhosis, and CKD. This single case study confirms that alcohol-induced liver injury increases the risk of developing early age HCC in persons infected with HCV and complicated with CKD. And AFP measurement helps in early identification of HCC, especially at such high level > 10,000 U/mL.

Key words: alcoholism, biomarker, chronic kidney disease, cirrhosis, hepatitis C virus

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most frequent type of malignant lesion of the liver. Liver cancer can rarely occur below the age of 40 years and reaches a peak at approximately 70 years. Rates of HCC among men are two to four times as high as the rates among women. Although not frequently, HCC can occur in a non-cirrhotic liver. In comparison with cirrhotic HCC, non-cirrhotic HCC has some characteristics, such as: (a) a lower male preponderance and a bimodal age distribution; (b) a lower prevalence of the three major risk factors (hepatitis B and C virus infections and alcohol abuse), with an increased prevalence of other etiologies, such as exposure to genotoxic substances and sex hormones, inherited diseases, genetic mutations; and (c) a more advanced tumor at the time of diagnosis, as it is usually detected due to the occurrence of cancer-related symptoms, outside any scheduled surveillance program.

Here we report a case of HCC who presented with abdominal pain, vomiting, loss of appetite, body edema, and significant weight loss.

CASE PRESENTATION

Chief complaints

A 27-year-old Indo-Aryan man, resident of North-India, a cook by profession, without co-morbidities presented
with abdominal pain, vomiting, loss of appetite, body edema, and significant weight loss of 2 months duration.

History of present illness
Abdominal pain was in right upper abdomen, mild dull aching, non-radiating, associated with non-bilious, non-projectile vomiting, loss of appetite and significant loss of weight. He also complained of swelling of both lower limbs, facial puffiness and decreased urine output. There was no history of frothy frothuria, hematuria, history of photosensitive rash, oral ulcer, or Raynauds phenomenon.

History of past illness
He had no prior illnesses.

Personal and family history
He used to smoke around 10 cigarettes per day for last 5 years. He also used to consume alcohol 20–30 g per day for last 05 years. There was no family history of cancer or any other liver disorders in the family.

Physical examination
On examination, he had bilateral pedal edema without any pallor or icterus and stigmata of chronic liver disease. No signs of hepatic failure were present. He had elevated blood pressure but his cardiovascular system examination was normal. His abdomen was distended with liver palpable 3 cm below the right costal margin without any tenderness. There was no splenomegaly or signs of ascites. Other system examinations were within normal limits.

Laboratory examinations
Laboratory examination revealed hemoglobin of 12.1 g/dL, hematocrit of 36%, white blood cell count of 13,970/L, and platelet count of 296,000/L. Other laboratory findings included normal total serum bilirubin (0.31 mg/dL), alanine transaminase (22 U/L) and aspartate transaminase (34 U/L), gamma-glutamyl transferase (GGT) (257 U/L) and alkaline phosphatase (302 U/L) levels were slightly raised. Serum albumin level and INR were also normal, 3 g/dL and 1.16, respectively. Renal function tests revealed blood urea level of 323 mg/dL and creatinine level of 09.21 mg/dL. HCV antibodies were positive with HCV RNA titre of 53309 copies per mL. Evaluation for sepsis including urine and blood cultures was negative. Serum AFP level was markedly raised 16237 ng/mL. Amoebic serology was negative.

Imaging examinations
Chest X ray was normal (Figure 1A). Ultrasound showed a thick heteroechoic subcapsular collection in segments VII & VIII of liver measuring approximately 8.6 × 8.7 cm² in size, without liquefaction & features of bilateral renal parenchymal disease prompting further investigation. Triple phase CT revealed well defined large heterogeneous mass lesion in segment VII/VIII of the liver measuring 11.3 × 9.3 × 9.7 cm³ showing arterial phase enhancement, multiple arterial channels (predominantly from right hepatic artery), and capsular enhancement in delayed phase images—LIRADS 5 lesion (Figure 1B). Further workup for metastasis by high resolution CT thorax and upper GI endoscopy were all normal.

Final diagnosis
After thorough investigations, he was diagnosed as hepatocellular carcinoma (BCLC-C), chronic hepatitis C infection and acute on CKD.

Treatment
He was started on direct-acting antivirals (sofosbuvir and velpatasvir) for HCV infection. Medical oncology review was done and the patient was unfit for any systemic chemotherapy in view of deranged renal parameters. Gastroscopy review was also done and he was planned for transarterial chemo embolization (TACE) on follow-up. The patient received 3 sessions of hemodialysis during hospital stay following which his urine output improved. He was discharged in a stable hemodynamic condition.

Outcome and follow-up
He was planned TACE for HCC. Unfortunately, he could not follow up further and report back to hospital. On contacting his family members telephonically after 2 months of last hospitalization, he had sudden cardiac arrest at his home and died.

DISCUSSION
HCC is one of the commonest primary liver cancer. HCC has an annual incidence of 600,000 newly diagnosed patients. It constitutes the sixth most frequent form of cancer worldwide and holds third place in terms of malignancy-related mortality. Eighty percent (80%) of liver cancers are found in cirrhotic livers, which themselves carry a high risk for HCC. HCC in a young patient with no cirrhosis or fibrosis is a relatively rare diagnosis. This is compatible with the case presented as the patient showed no evidence of pre-existing liver disease. Clinical presentation of the patient was similar to liver abscess in view of right upper abdominal pain and leukocytosis. Initial ultrasound abdomen done at a private center was suggestive of liver abscess and the patient was started on broad spectrum parenteral antibiotics. Interventional radiology opinion was taken for pig tail drainage of the abscess and review ultrasound revealed that the lesion is not liquefied and it is unlikely to be an abscess. Few similar cases of HCC mimicking...
Figure 1. Radiological images of the patient. A. Chest X-ray of patient with absence of any lung metastasis. B. Triple phase contrast-enhanced computed tomography of the abdomen having large space occupying lesion (arrow) in liver suggestive of hepatocellular carcinoma.

Liver abscess were also reported by Yeom et al. and Hayashi et al.[4,5]

HCC in adults is largely a disease common among 50–70 years old; however, there is a type of HCC with characteristic histological features that usually occurs in young adults known as fibrolamellar hepatocellular carcinoma (FHCC). FHCC is rich in fibrous tissue with males and females being at equal risk. It does not produce alpha-fetoprotein and it has a good prognosis.[6] The age of our patient and lack of coexisting liver disease favor the diagnosis of FHCC, but radiological findings and high alpha-fetoprotein level are against such diagnosis. Pathologically, HCC can be either single or occur as multiple nodules throughout the liver. Histologically, it consists of cells resembling hepatocytes. It can metastasize via the hepatic or portal veins to the lymph node, bones and lungs.[7] On CT and MRI, HCC typically enhances more than the adjacent liver after the intravenous contrast is administered especially if the liver is imaged within 20 seconds after contrast is given (during the hepatic arterial phase of contrast enhancement of the liver since HCC is a hypervascular cancer and is fed by hepatic artery).[8] Our patient’s metastatic workup showed no evidence of metastasis.

Patients with HCC diagnosed at an early stage are optimal candidates for resection, liver transplantation, or percutaneous ablation. Surgical resection is recommended for patients with single tumor, absence of clinically relevant portal hypertension, and normal bilirubin. Transplantation is indicated in patients with 3 nodules of < 3 cm size or with single tumor of < 5 cm size with liver function impairment precluding resection.[9] Sorafenib is indicated as the first line of treatment in patients who cannot benefit from the above therapeutic options and still have a preserved liver function.[10] It could not be given to our patient because of compromised renal function.

Finally, rare clinical presentation, multiple factors (smoking, alcohol, HCV, CKD) and relatively younger age of the patient at the time of presentation are the interesting features in this particular case.

CONCLUSION

Our experience is a piece of evidence that prompts search of HCC in a liver space occupying lesion looking like abscess. Multiple factors—HCV infection, smoking, alcohol and CKD can lead to early age onset of HCC in young adult. Serum AFP level > 10,000 U/mL can be considered diagnostic of HCC in appropriate clinical context. Serum AFP measurement is a handy aid for early identification of HCC.

DECLARATIONS

Author contributions
Gaur S and Gupta AK collected data, wrote the manuscript, analyzed the review literature, and approved the manuscript; Panda PK gave the concept, designed, critically reviewed, and approved the manuscript.

Ethics statement
The authors of this manuscript declare that this scientific work complies with reporting quality, formatting and reproducibility guidelines set forth by the EQUATOR Network. The authors also attest that this clinical investigation was determined to not require Institutional Review Board/Ethics Committee review.
Conflicts of interest
There is no conflict of interest among the authors.

Data sharing statement
No additional data is available.

REFERENCES