OPEN ACCESS

Saudi Journal of Medical and Pharmaceutical Sciences
Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) | ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Case Report **Gastro Enterology**

Case Report: Budd-Chiari Syndrome (BCS) on Hepatocellular Carcinoma (HCC): Primary or Secondary Cause?

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DOI: 10.36348/sjmps.2024.v10i02.013 | **Received:** 06.01.2024 | **Accepted:** 15.02.2024 | **Published:** 26.02.2024

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Abstract

This is the case of a 63-year-old female patient admitted for management of a liver mass discovered incidentally on imaging. The patient presented with weight loss and prutitus, and on clinical examination had collateral venous circulation and scraping lesions. Abdominal ultrasound coupled with Doppler showed a hepatic tissue mass with left-sided portal thrombosis. Hepatic MRI confirmed the diagnosis and also revealed SBC with infiltration of the left and median hepatic veins. Liver biopsy confirmed diagnosis of hepatocellular carcinoma (HCC)in cirrhotic liver. Etiological work-up for prothrombotic factors and cirrhosis was negative. The patient was a candidate for palliative treatment. But our dilemma: is this a case of primary or secondary BCS?

Keywords: BCS, hepatocellular carcinoma, palliative care, cirrhosis.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the fifth most common cancer worldwide and the second cause of cancer-related death. Currently, the HCC is a known and proven complication of the primary BCS, but sometimes it's hard to identify if the HCC is a complication or a cause of BCS. The management of BCS-HCC is not well codified in all the guidelines because the rarity of this situation

CASE REPORT

A 63-year-old female patient who has a past medical history of type 2 diabetes treated with oral antidiabetics and hypertension with amlodipine.

The patient was admitted for management of a hepatic mass discovered incidentally on imaging. Clinically, the patient presented with pruritus and weight loss.

Initial clinical examination revealed collateral venous circulation (CVC), a straight liver with a firm anterior border and regular surface area, scraping lesions without other signs of portal hypertension.

Abdominal ultrasound was suggestive of heterogeneous liver with a nodular hypoechoic lesion in the segment VIII measuring 4 cm with posterior echo enhancement and left portal thrombosis on Doppler.

Hepatic MRI confirmed the diagnosis and showed a dysmorphic liver with lesional processes of the hepatic dome (VIII and IV) heterogeneously enhanced in arterial time and late wash out, measuring 45x64mm.

In addition, MRI showed the infiltration of the left portal branch with perfusion disorder, confirmed the diagnosis of BCS with infiltration of the median and left hepatic veins with a suspicious-looking hilar adenopathy and grade I ascites

Biologically, the patient had cytolysis dependent on aspartate aminotransferase at 520UI/L (normal value 25IU/L), anicteric cholestasis with gamma-glutamyl transferase at 264IU/L (normal value 44UI/L), and alkaline phosphatase at 169.5UI/L (normal value 150UI/L) and no hepatocellular insufficiency.

The blood count showed no anemia, with hemoglobin at 14.2g/dl, iron levels at 97ng/ml (normal range 7-140ng/ml) and thrombocytopenia at106,000/

mm³ (normal range 150,000/). White blood cell count was normal at 5490.

Alpha-feto protein was 30ng/ml (normal value less than 10ng/ml). A liver biopsy was performed on the tumor process and on healthy liver and showed a well-differentiated HCC with active liver cirrhosis classified as A3F4 in the metavir score system.

A complete etiological work-up for prothrombotic factors was carried out, but the results were negative. An etiological work-up for hepatic cirrhosis was also carried out, but the results were also negative.

Hence our dilemma: is it primary SBC due to portal vein compression by HCC or SBC due to a tumor thrombus formation in advanced HCC?

Therapeutically, the patient was considered for palliative treatment and put on a cardio selective beta blocker. Prognostically, the Child Pugh score was B7, MELD 17 and stage C of Barcelona classification liver cancer (BcLc)

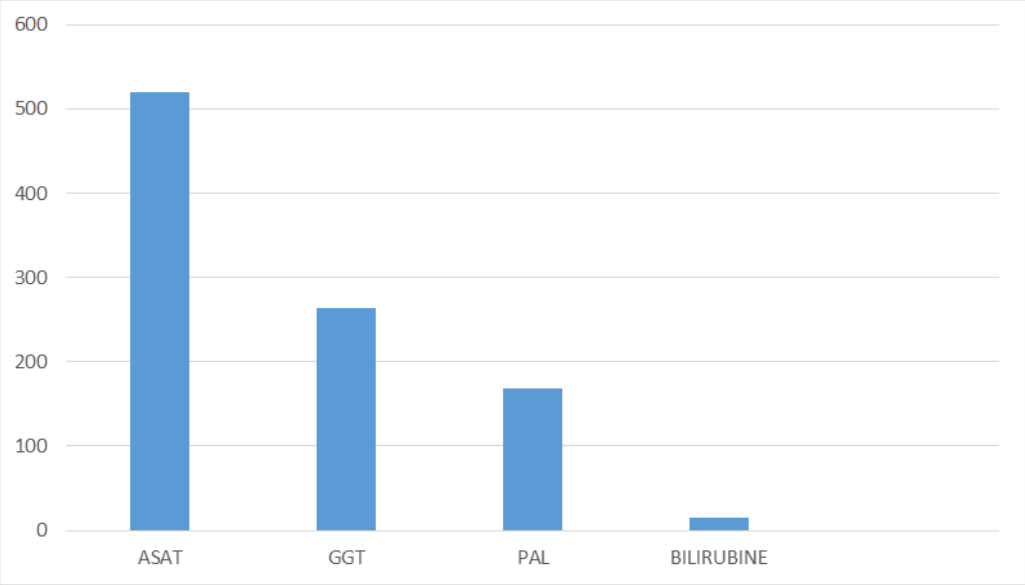
The table below shows the clinical features of our case:

Clinical characteristic of BCS/HCC	**Results**
AGE	63 yo
GENDER	female
CLINICAL MANIFESTATIONS	Weight loss and pruritus
CLINICAL EXAMINATION	CVC and liver overload

The table below shows the results of the blood count and alpha foeto protein (AFP) of our case:

Parameters	**Results**
Hemoglobin	14,2g/dl
white blood cells	5490 elements
blood platelets	106.000/mm³
AFP	30ng/ml

The histogram below shows the results of the liver tests of our case:



DISCUSSION

INTRODUCTION [1, 2]**:**

Hepatocellular carcinoma (HCC) is the fifth most common cancer worldwide and the second cause of cancer-related death. The primary BCS represented an anecdotal cause of HCC; a few data in the form of case-reports or retrospective series were available, providing limited information about this association.

Currently, the HCC is a known and proven complication of the primary BCS, since many authors have objectively evaluated this risk by prospective studies. Therapeutic management of BCS-associated HCC (BCS HCC) is not well codified, because of the rarity of this condition.

Epidemiology [3, 4, 5]:

In a French study including 97 patients, the prevalence of HCC was 11.3% and the cumulative incidence during a median follow-up of 5 years was 4%.

In India, a recent study published in 2015, including 421 BCS patients, the prevalence of HCC was 1.9%, and the cumulative incidence was 3.5% at 10 years. The mean age of the development of HCC in patients with BCS varies between 30 and 50 years.

In BCS-HCC patients, this male predominance is not constant. Sixteen BCS-HCC patients were compared to 405 BCS patients without HCC in a case-control study; females were predominant (62.5%), with a mean age of 36.2 years, significantly higher than control cases: 36.2 ± 11.4 years vs 29.0 ± 10.3 years (p=0.001). Moreover, female sex was considered as a risk factor for HCC in Asian countries which is the case for our patient.

Diagnostic [6-10]:

Diagnosis of both HCC and BCS may be concomitant, making the differential diagnosis with a secondary BCS quite difficult.

The diagnosis is generally based on characteristic imaging findings in combination with alpha-fetoprotein (AFP) level and/or histological examination of the tumor.

This is consistent with our case. Some authors, with a high expertise in BCS, recommend for the diagnosis of HCC, to perform a biopsy if the nodule is heterogeneous, ≥3 cm in diameter, or increases in size at successive determinations, with an AFP level >15 ng/ml, as the classical imaging modality has little accuracy.

The location and extent of venous obstruction, although not shared by all authors, seems to be a risk factor of HCC in BCS [23]. In the systematic review published by Ren et al., the pooled prevalence of HCC was 4.2% (95% CI: 1.6–7.8%) and 26.5% (95% CI: 14.4–40.7%) in HV-obstruction and IVC obstruction studies, respectively. The odds-ratio of IVC obstruction for HCC was 7.73 (95% CI: 0.82–73.19%) [11]. In Asia and South Africa where BCS related to inferior *vena cava* (IVC) membrane (MOVC) predominates, HCC prevalence can reach 40–50%. These patients have latent or poorly symptomatic clinical form of BCS, lately diagnosed at the cirrhotic stage with HCC; in contrast, hepatic veins (HV) thrombosis often has an acute or subacute course, which facilitates the diagnosis. However, in these countries, other demonstrated carcinogens, particularly HBV and aflatoxin, may explain this overestimated prevalence of HCC. In more recent studies excluding other liver carcinogens, long segment IVC obstruction, and moreover combined IVC-HV obstruction remain predictor factors of HCC in patients with BCS.

In Western countries, it is very rare to see HCC without cirrhosis, but it has been observed with patients with large cell dysplasia or iron overload. Injuries to the portal venous system have also been found to cause PVTT [11].

In our case, despite the dilemma of whether it was primary or secondary BCS, the involvement was in the hepatic veins which is not the case for many studies.

When a biopsy of a liver nodule is performed, it should also interest the non-tumorous liver. On histological examination, BCS-HCC is often nodular, well differentiated, with a low biliary and vascular invasiveness, which might be relative to an extensive hepatic fibrosis.

Management [12-14]:

The modified Barcelona Clinic Liver Cancer (BCLC) staging system and treatment strategy clearly stated that “preserved liver function” refers to Child-Pugh class A without any ascites. However, in BCS, ascites may occur in a patient with well-preserved liver function, and with almost normal prothrombin time and platelet count. In this case, a surgical resection or another treatment could be performed after removal of the ascites by a transjugular intrahepatic porto-systemic shunt (TIPS) placement. In the same way, if a BCS patient had multiple hypervascular nodules with no characteristic washout in the portal phases, and a high AFP level, even if only one lesion is an HCC, we will consider that this patient is at an intermediate-stage (BCLC-B: multinodular asymptomatic tumors without vascular invasion or extrahepatic spread), and thus the first-line choice therapy should be transarterial chemoembolization (TACE), while the patient is in fact BCLC-A and should rather benefit from a liver transplantation. Many questions remain about therapeutic management, mainly because of the small sample size of published studies, and a lack of evidence.

Since there is no generally accepted treatment recommendation, the management of BCS-associated HCC should be discussed in a multidisciplinary meeting.

Screening and Prognosis [15]**:**

Routine screening for early-stage detection of HCC in patients with BCS should be actively recommended. The follow-up interval for HCC screening can be maintained at 6 months, as for other cirrhosis, since the incidence of HCC in patients with BCS is quite similar to that reported for other cirrhosis. A closer monitoring can be suggested for patients with risk factors for HCC, patients with no possibility for hepatic venous outflow restoration, and those with multiple benign nodules.

A clinical and biochemical examination including AFP level associated with US Doppler should be performed to detect the HCC recurrence and control HV/IVC patency. Multiphasic CT or MRI must be realized at a 6-month interval

CONCLUSION

The BCS-HCC association is very rare, and the diagnosis is based on a range of arguments, but sometimes, as in the case of our patient, it represents a diagnostic challenge because we can't decide whether it's primary BCS on CHC or secondary to HCC thrombosis.

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