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CRYPTOGENIC DECOMPENSATED CHRONIC LIVER DISEASE COMPLICATED BY HEPATOCELLULAR CARCINOMA: A CHALLENGING CASE REPORT

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ABSTRACT

Background: Cryptogenic cirrhosis represents a form of chronic liver disease (CLD) in which no definite etiology can be identified despite comprehensive clinical, serological, and histopathological evaluation. It is increasingly recognized as a potential risk factor for hepatocellular carcinoma (HCC), posing diagnostic and management challenges.

Case Presentation: We report the case of a 70-year-old non-alcoholic male with a known history of chronic liver disease complicated by portal vein thrombosis. The patient presented with progressive abdominal distension, right hypochondrial pain, and anorexia. Clinical examination revealed icterus, hepatosplenomegaly, and bilateral pitting edema. Laboratory investigations demonstrated elevated liver enzymes, hyperbilirubinemia, hypoalbuminemia, prolonged prothrombin time, and markedly raised alpha-fetoprotein (>1000 ng/mL). Imaging findings were suggestive of chronic liver disease with multiple hepatic lesions consistent with hepatocellular carcinoma. Liver biopsy confirmed micronodular cirrhosis without identifiable etiology, establishing a diagnosis of cryptogenic cirrhosis.

Conclusion: Cryptogenic cirrhosis complicated by hepatocellular carcinoma represents a complex clinical entity requiring thorough evaluation and multidisciplinary management. Early recognition and appropriate surveillance are essential to improve patient outcomes.

Keywords: Alpha-Fetoprotein, Cryptogenic Cirrhosis, Chronic Liver Disease, Hepatocellular Carcinoma, Portal Vein Thrombosis

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INTRODUCTION

Cryptogenic cirrhosis represents a subset of chronic liver disease (CLD) in which no definitive etiology can be identified despite comprehensive clinical, serological, and histopathological evaluation [(1)]. Cirrhosis itself is a major cause of morbidity and mortality worldwide and results from progressive hepatic fibrosis leading to distortion of normal liver architecture and impaired hepatic function [(2)]. Common underlying causes include alcohol-related liver disease, chronic viral hepatitis, and non-alcoholic fatty liver disease (NAFLD), although a proportion of cases remain unexplained and are classified as cryptogenic [(3)].

Historically, cryptogenic cirrhosis was estimated to account for 5–30% of cirrhosis cases; however, with advancements in diagnostic modalities, its prevalence has

decreased to approximately 5% [4, 5]. Increasing evidence suggests that many cases previously labeled as cryptogenic may represent advanced or "burnt-out" non-alcoholic steatohepatitis (NASH), although the absence of definitive biomarkers and histological features makes this association difficult to confirm [6].

Importantly, patients with cryptogenic cirrhosis are at risk of developing complications similar to other forms of cirrhosis, including portal hypertension, portal vein thrombosis, and hepatocellular carcinoma (HCC) [7, 8]. The risk of HCC in this population is increasingly recognized but often underestimated due to the lack of clearly defined etiological factors and surveillance strategies.

This case report describes a patient with cryptogenic decompensated chronic liver disease complicated by hepatocellular carcinoma and portal vein thrombosis, highlighting the diagnostic challenges and clinical implications associated with this condition.

CASE PRESENTATION

A 70-year-old male with a known history of chronic liver disease presented to the emergency department with complaints of progressive abdominal distension, right hypochondrial pain, and anorexia. He had no history of hematemesis, fever, clay-colored stools, dark urine, drug abuse, or significant weight loss. There was no history of blood transfusion, herbal medication use, or family history of liver disease.

On clinical examination, the patient was icteric and appeared chronically ill. Bilateral pitting edema was present, along with hepatomegaly and splenomegaly. The abdomen was mildly distended with diffuse tenderness, while bowel sounds were normal. No signs of hepatic encephalopathy were observed at presentation.

Laboratory investigations revealed markedly deranged liver function tests, including elevated serum bilirubin, transaminases, and prolonged prothrombin time, along with hypoalbuminemia, indicating impaired hepatic synthetic function. Renal parameters were also elevated, with increased serum creatinine and urea levels. Notably, alpha-fetoprotein (AFP) levels were significantly raised (>1000 ng/mL), raising suspicion for hepatocellular carcinoma. A comprehensive panel for infectious and metabolic causes of liver disease, including viral serology and autoimmune markers, was negative. Detailed biochemical and serological findings are summarized in Table 1**.**

Table 1: Results from Biochemical and Serological Investigations

Investigations	Results	Normal Values
Aspartate aminotransferase	222 U/L	5–35 U/L
Alanine aminotransferase	195 U/L	10–50 U/L
Alkaline phosphatase	330 U/L	4–390 U/L
Serum bilirubin	6.73 mg/dL	0.1–1 mg/dL
Albumin	2.8 g/Dl	3.5–5.5 g/dL
Prothrombin time	28.6 sec	10–13 seconds
Alpha-fetoprotein	>1000ng/mL	<20ng/mL
HIV serology, HBsAg, Anti-HCV	NEGATIVE	NEGATIVE
Creatinie	1.78 mg/L	0.2–1.2 mg/L
Urea	104.9 mg/L	5–45 mg/L
Serum ceruloplasmin	20mg/dL	15–30 mg/dL
Urine copper	0.5 µmol/L	<0.9 µmol/L
Serum ferritin	200 ng/mL	12–300 ng/mL
serum iron	90 µg/dL	60–180 µg/dL
Alpha-1 antitrypsin	1.5g/L	0.90–2.0 g/L
Antinuclear antibody	NEGATIVE	NEGATIVE
Anti-mitochondrial antibody	NEGATIVE	NEGATIVE
Anti-smooth muscle antibody	NEGATIVE	NEGATIVE
Anti-liver kidney microsomal antibody	NEGATIVE	NEGATIVE

Ultrasound examination of the abdomen demonstrated a liver with coarse echotexture and irregular margins, consistent with chronic liver disease. Multiple echogenic

lesions were identified in the right hepatic lobe, the largest measuring approximately 5 × 6.8 cm, with Doppler signals suggestive of hepatocellular carcinoma. Mild splenomegaly was also noted. These findings are illustrated in Figure 1**.**

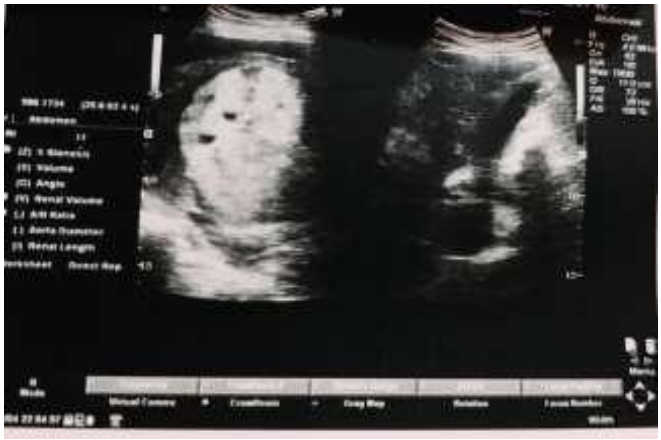

Figure 1: Ultrasound Scan Image of Abdomen

Further evaluation with contrast-enhanced computed tomography (CT) of the abdomen revealed irregular hepatic contours with features of cirrhosis. The portal vein showed evidence of thrombosis, and multiple hepatic lesions were observed, consistent with hepatocellular carcinoma. Additionally, splenomegaly with splenic varices was noted. These imaging findings are demonstrated in Figure 2**.**

Histopathological examination following percutaneous liver biopsy revealed micronodular cirrhosis without evidence of steatosis, iron deposition, or other metabolic liver diseases, confirming the diagnosis of cryptogenic cirrhosis.

Based on clinical, laboratory, imaging, and histopathological findings, a final diagnosis of cryptogenic decompensated chronic liver disease complicated by hepatocellular carcinoma and portal vein thrombosis was established.

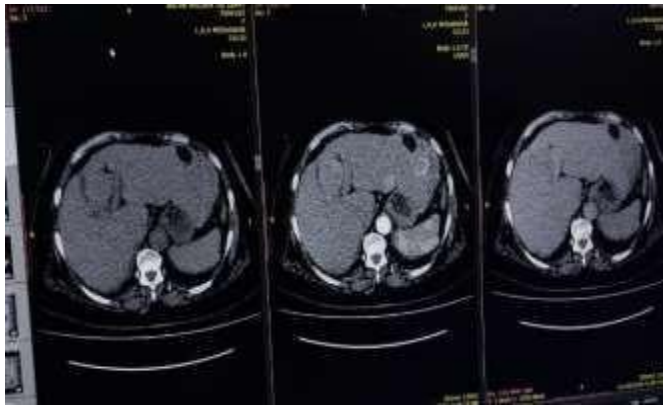

Figure 2: CT scan of the Abdomen

DISCUSSION

Cirrhosis represents the final common pathway of chronic liver disease (CLD) and is characterized by progressive fibrosis, architectural distortion, and the formation of regenerative nodules, ultimately leading to impaired hepatic function [(9)]. The most common etiologies include alcohol-related liver disease, chronic viral hepatitis, and non-alcoholic fatty liver disease (NAFLD), although a subset of cases remains unexplained and is classified as cryptogenic cirrhosis [(3)].

Cryptogenic cirrhosis (CC) is considered a diagnosis of exclusion when no specific cause can be identified despite comprehensive clinical, serological, and histopathological evaluation. Historically, it accounted for approximately 5–30% of cirrhosis cases; however, with advances in diagnostic techniques, this proportion has decreased to around 5% [(5)]. Increasing evidence suggests that many cases of CC may represent advanced or "burnt-out" non-alcoholic steatohepatitis (NASH), particularly in patients with underlying metabolic risk factors such as obesity and diabetes mellitus [(10, 11)]. However, in the absence of definitive biomarkers or histological confirmation, this association remains challenging and should be interpreted cautiously.

Similar to other forms of cirrhosis, CC is associated with a range of complications, including portal

hypertension, portal vein thrombosis, and hepatocellular carcinoma (HCC) (6). The occurrence of portal vein thrombosis in cirrhotic patients has been increasingly recognized and may contribute to disease progression and adverse outcomes (7). In the present case, the patient exhibited both portal vein thrombosis and significantly elevated alpha-fetoprotein levels, raising strong suspicion for HCC.

The development of HCC in patients with cryptogenic cirrhosis is an emerging concern. Although traditionally considered to have a lower oncogenic potential compared to viral or alcoholic cirrhosis, recent studies suggest that the risk of HCC in CC may be comparable, particularly in cases associated with underlying metabolic dysfunction (7,8). The absence of clearly defined etiological factors and specific surveillance strategies often leads to delayed diagnosis and poorer prognosis in these patients.

Our case highlights the diagnostic challenges associated with cryptogenic cirrhosis complicated by HCC and portal vein thrombosis. The absence of identifiable etiological factors, combined with overlapping clinical and radiological features, makes early diagnosis difficult. This underscores the importance of comprehensive evaluation and vigilant surveillance in patients with CLD, even when the underlying cause remains unidentified.

CONCLUSION

Cryptogenic cirrhosis complicated by hepatocellular carcinoma represents a challenging clinical entity due to the absence of identifiable etiological factors and the potential for delayed diagnosis. This case highlights the importance of thorough diagnostic evaluation and a high index of suspicion for malignancy in patients with chronic liver disease of unknown origin. Early recognition, appropriate surveillance, and multidisciplinary management are essential to improve clinical outcomes in this high-risk population.

DISCLOSURES

CONFLICT OF INTEREST: The authors declare no conflict of interest.

Human/Animal Rights: This case report complies with the ethical standards of the Declaration of Helsinki. No experiments involving human participants or animals were conducted.

Informed consent: Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. All efforts have been made to protect the patient's privacy and confidentiality, and no identifiable- information-has-beend-closed.

AUTHORS CONTRIBUTIONS

Concept & Design of Study: Shafiq Ur Rahman

Drafting of Manuscript: Rahman Syed

Critical Review: Ameer Afzal Khan, Bilal Iqbal

Final Approval of Manuscript: All authors approved the final version

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