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Severe Cholestatic Jaundice With Negative Biliary Imaging in Decompensated Liver Cirrhosis: A Case Report

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Male, 63-year-old
Final Diagnosis: Severe cholestatic jaundice due to decompensated liver cirrhosis
Symptoms: Anorexia • clay-colored stool • dark urine • fatigue • generalized pruritus • intermittent abdominal pain • progressive jaundice • weight loss
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology
Objective: Unusual clinical course
Background: Cholestatic jaundice with markedly elevated bilirubin levels usually raises concern for extrahepatic biliary obstruction or malignant hepatobiliary disease. However, marked conjugated hyperbilirubinemia can occasionally occur in patients with cirrhosis despite repeatedly negative biliary imaging, creating substantial diagnostic uncertainty and management challenges.
Case Report: We report a diagnostically challenging case of a 63-year-old Egyptian man presenting with progressive jaundice, dark urine, pale stool, pruritus, abdominal pain, fatigue, anorexia, weight loss, and recent ascites. Laboratory investigations revealed severe conjugated hyperbilirubinemia with total bilirubin level reaching 19.45 mg/dL. Extensive infectious and viral investigations were negative. Autoimmune assessment demonstrated only weak anti-smooth muscle antibody positivity with otherwise negative autoimmune markers. Radiological evaluation including ultrasonography, contrast-enhanced computed tomography, magnetic resonance imaging, and magnetic resonance cholangiopancreatography demonstrated cirrhotic liver morphology, portal hypertension, splenomegaly, and gallbladder calculi without evidence of common bile duct obstruction, biliary dilatation, or pancreatic mass. The marked discrepancy between the severity of cholestasis and the absence of obstructive pathology created substantial diagnostic uncertainty, while the marked discrepancy between severe cholestasis and persistently negative biliary imaging raised concern for a possible nonobstructive cholestatic process associated with advanced chronic liver disease. The patient was treated conservatively with supportive medical therapy and careful clinical monitoring.
Conclusions: This case highlights that severe cholestatic jaundice in patients with cirrhosis does not necessarily indicate extrahepatic biliary obstruction. Integrating clinical, serological, and multimodal radiological findings is essential for excluding alternative etiologies and preventing unnecessary invasive biliary procedures.
Keywords: Jaundice, Obstructive • Case Reports • Hyperbilirubinemia • Gallstones • Hypertension, Portal • Liver Cirrhosis
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Introduction

Cholestatic jaundice represents a complex diagnostic challenge with a broad differential diagnosis that includes obstructive biliary pathology, autoimmune hepatobiliary disease, infiltrative disorders, drug-induced liver injury, and advanced cirrhosis. Patients commonly present with jaundice, pruritus, dark urine, pale stool, and constitutional symptoms associated with predominantly conjugated hyperbilirubinemia. However, identifying the underlying etiology may be difficult in cases with inconclusive imaging findings or overlapping hepatic abnormalities [1].

Cryptogenic cirrhosis remains a diagnosis of exclusion after elimination of viral, metabolic, autoimmune, and obstructive causes. Such patients may initially present with manifestations of portal hypertension, splenomegaly, ascites, or progressive cholestasis without a clearly identifiable cause despite extensive evaluation [2]. Furthermore, autoimmune and inflammatory cholangiopathies can mimic obstructive or malignant hepatobiliary disease both clinically and radiologically, further complicating the diagnostic approach [3].

In recent years, uncommon causes of severe cholestasis, including drug-induced and infiltrative hepatobiliary disorders, have increasingly been recognized in the literature, emphasizing the importance of a systematic multidisciplinary evaluation in patients with unexplained cholestatic jaundice [4,5].

Herein, we report a diagnostically challenging case of severe cholestatic jaundice in a 63-year-old Egyptian man with decompensated cirrhosis and portal hypertensive manifestations despite repeatedly negative multimodal biliary imaging. The present report aims to highlight the importance of structured exclusion-based evaluation in patients with cirrhosis with marked conjugated hyperbilirubinemia before attributing the presentation to extrahepatic biliary obstruction or proceeding to invasive intervention.

Case Report

A 63-year-old Egyptian man presented to the hepatology unit with progressive jaundice of 2 months' duration associated with intermittent abdominal pain. The patient also reported having dark urine, clay-colored stool, mild generalized pruritus, anorexia, fatigue, and significant unintentional weight loss. Approximately 10 days before admission, he developed ascites that was medically managed.

His past medical history was significant for type 2 diabetes mellitus for 15 years, previous schistosomiasis with completed treatment, and lumbar disc surgery performed 20 years

earlier. He was a former smoker with a remote smoking history of approximately 3 years. Family history was positive for diabetes mellitus in both parents.

The patient denied the use of nonsteroidal anti-inflammatory drugs, herbal medications, or other potentially hepatotoxic agents during the 2 months preceding presentation despite his history of abdominal pain.

On physical examination, the patient appeared deeply jaundiced, pale, and cachectic. Vital signs were stable, with blood pressure of 110/80 mm Hg, heart rate of 90 beats/minute, respiratory rate of 18 breaths/minute, and Glasgow Coma Scale score of 15/15. Skin examination revealed diffuse hyperpigmentation. Neurological examination demonstrated fine hand tremors without flapping tremor or evidence of hepatic encephalopathy. No lower limb edema was detected.

Laboratory investigations demonstrated marked conjugated hyperbilirubinemia with a total bilirubin level of 19.45 mg/dL, direct bilirubin level of 13.78 mg/dL, and indirect bilirubin level of 5.67 mg/dL. Urinalysis revealed bilirubin positivity with dark yellow urine. Viral serological markers including hepatitis A virus, hepatitis B surface antigen, hepatitis C virus antibody, HIV, Epstein-Barr virus (EBV), and cytomegalovirus (CMV) IgM were negative, while CMV IgG was positive, indicating previous exposure. Brucella serology was also negative. Autoimmune workup demonstrated negative antinuclear antibody, anti-mitochondrial antibody, and liver-kidney microsomal antibody type 1. Anti-smooth muscle antibody was weakly positive at a titer of 1: 40. Detailed laboratory investigations are summarized in **Table 1**, while the serological and autoimmune investigations are summarized in **Table 2**. The white blood cell count was $4.5 \times 10^3/\text{mm}^3$ without leukocytosis, and the C-reactive protein level was within the reference range (3.2 mg/L). Together with the absence of supportive imaging findings, these results made acute cholecystitis and cholangitis unlikely.

Abdominal ultrasonography demonstrated coarse hepatic echotexture and irregular liver surface suggestive of chronic liver disease, associated with splenomegaly and multiple gallbladder stones. Mild ascites was also noted without evidence of intrahepatic or extrahepatic biliary dilatation (**Figure 1**). Contrast-enhanced computed tomography of the abdomen showed manifestations of portal hypertension, including splenomegaly and collateral circulation, in addition to gallbladder wall thickening with hyperdense gallstones (**Figure 2**). Magnetic resonance cholangiopancreatography (MRCP) of the gallbladder and biliary tree demonstrated multiple small gallbladder calculi without biliary dilatation or obstructing lesions (**Figure 3**). High-resolution thick-slab maximum intensity projection reconstruction of the biliary tree confirmed a normal caliber common hepatic duct and common bile duct

Table 1. Hematological and biochemical laboratory investigations.

Investigation	Result	Reference Range
Hemoglobin	12.1	13.1-17.2 g/dL
Red blood cells	4.2	4.2-5.6 × 10 ³ Cells/μL
Hematocrit	34.6	39%-50%
Mean corpuscular volume	82.38	80-100 fL/cell
Mean corpuscular hemoglobin	28.81	27-34 pg/cell
Mean corpuscular hemoglobin concentration	34.97	32-37 g/dL
Red cell distribution width	14.5	11.5%-14.5%
Platelet count	112	150-440 × 10 ³ /mm ³
Mean platelet volume	8.3	8.0-12.0 fL
Platelet distribution width	16.2	10.0%-18.0%
Plateletcrit	0.093	0.1-0.5%
White blood cells	4.5	4.5-11.0 × 10 ³ /mm ³
Neutrophil	3.6	1.8-7.7
Lymphocytes	0.7	0.8-4.8
Monocytes	0.2	0.2-0.9
Eosinophils	0.1	0-0.8
Basophils	0	0-0.1
C-reactive protein-quantitative	3.2 mg/L	Up to 6.0mg/L
Prothrombin time	18.8 s	8.2-13.1 s
Prothrombin concentration	37%	70%-120%
International normalized ratio	1.80	0.9-1.27
Total bilirubin	19.45 mg/dL	0.5-1.2 mg/dL
Direct bilirubin	13.78 mg/dL	Up to 0.25 mg/dL
Indirect bilirubin	5.67 mg/dL	Up to 1 mg/dL
Aspartate aminotransferase	65	Up to 37 U/L
Alanine aminotransferase	49	Up to 45 U/L
Alkaline phosphatase	96	40-130 U/L
Gamma-glutamyl transferase	26	10-71 U/L

Table 2. Serological and autoimmune investigations.

Investigation	Result	Reference range
HAV	Negative	Negative
HBV	Negative	Negative
HCV	Negative	Negative
HIV	Negative	Negative
EBV	Negative	Negative
CMV IgG	Positive (2.5 U/mL)	Negative < 1 U/mL
CMV IgM	Negative (< 0.1 U/mL)	Negative < 1 U/mL
<i>B. abortus</i>	Negative	Negative
<i>B. melitensis</i>	Negative	Negative
ANA	Negative	Negative
AMA	Negative	Negative
LKM-1	Negative	Negative
ASMA	Positive (1: 40)	Negative < 1: 40
Urine bilirubin	Positive	Absent
Urine glucose	Positive	Absent
Urine urobilinogen	Trace	Normal
PMNL count	280 cells/mm ³	Less than 250 cells/mm ³

Abbreviations: HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; EBV, Epstein-Barr virus; CMV IgG, cytomegalovirus immunoglobulin G; CMV IgM, cytomegalovirus immunoglobulin M; *B. abortus*, *Brucella abortus*; *B. melitensis*, *Brucella melitensis*; ANA, antinuclear antibody; AMA, antimitochondrial antibody; LKM-1, liver-kidney microsomal type 1 antibody; ASMA, anti-smooth muscle antibody; PMNL, polymorphonuclear leukocyte.

with smooth outlines and no filling defects or intrahepatic biliary dilatation (Figure 4).

Overall radiological evaluation demonstrated cirrhotic liver changes, portal hypertension manifestations, splenomegaly, and gallbladder calculi. No significant biliary dilatation, stricture, sizable filling defect, or pancreatic head mass was identified on abdominal ultrasonography, contrast-enhanced computed tomography, magnetic resonance imaging (MRI), or MRCP. Detailed radiological findings are summarized in Table 3.

Diagnostic paracentesis revealed a polymorphonuclear leukocyte count of 280 cells/mm³ in the ascitic fluid. The patient was treated conservatively with N-acetylcysteine, pantoprazole, lactulose, and ondansetron with close clinical follow-up.

A liver biopsy was not performed, because the multidisciplinary team determined that it was unlikely to alter the patient's treatment. Given the patient's decompensated cirrhosis, thrombocytopenia (platelet count, 112 × 10³/mm³), prolonged prothrombin time (18.8 s), and elevated international normalized ratio (1.80), the potential procedural risks were judged

to outweigh the expected diagnostic benefit. Furthermore, the patient declined to undergo the procedure after being informed of its potential risks and limited expected effect on management. Accordingly, conservative supportive management was pursued.

Discussion

Severe cholestatic jaundice in the absence of definite biliary obstruction represents a significant diagnostic challenge, particularly in patients with underlying chronic liver disease. Our patient presented with progressive conjugated hyperbilirubinemia, pruritus, pale stool, dark urine, constitutional symptoms, and radiological evidence of cirrhosis and portal hypertension without evidence of common bile duct obstruction on MRCP. Similar diagnostic complexity has been reported in patients with multifactorial jaundice and cirrhosis [1,2].

The differential diagnosis in this case included obstructive biliary disease, autoimmune cholangiopathy, infiltrative liver disease, drug-induced cholestasis, and cryptogenic cirrhosis.

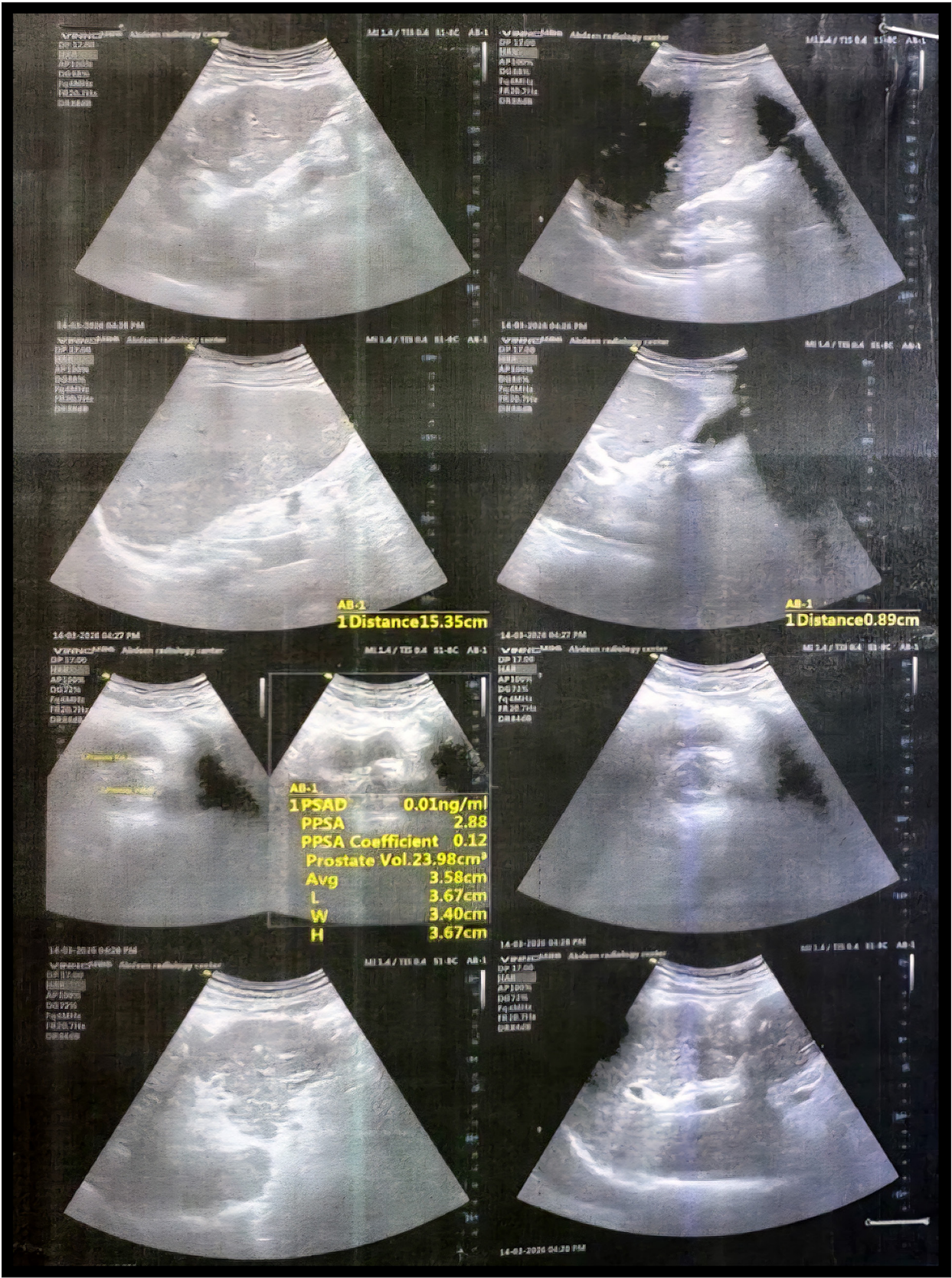


Figure 1. Abdominal and pelvic ultrasonography findings.

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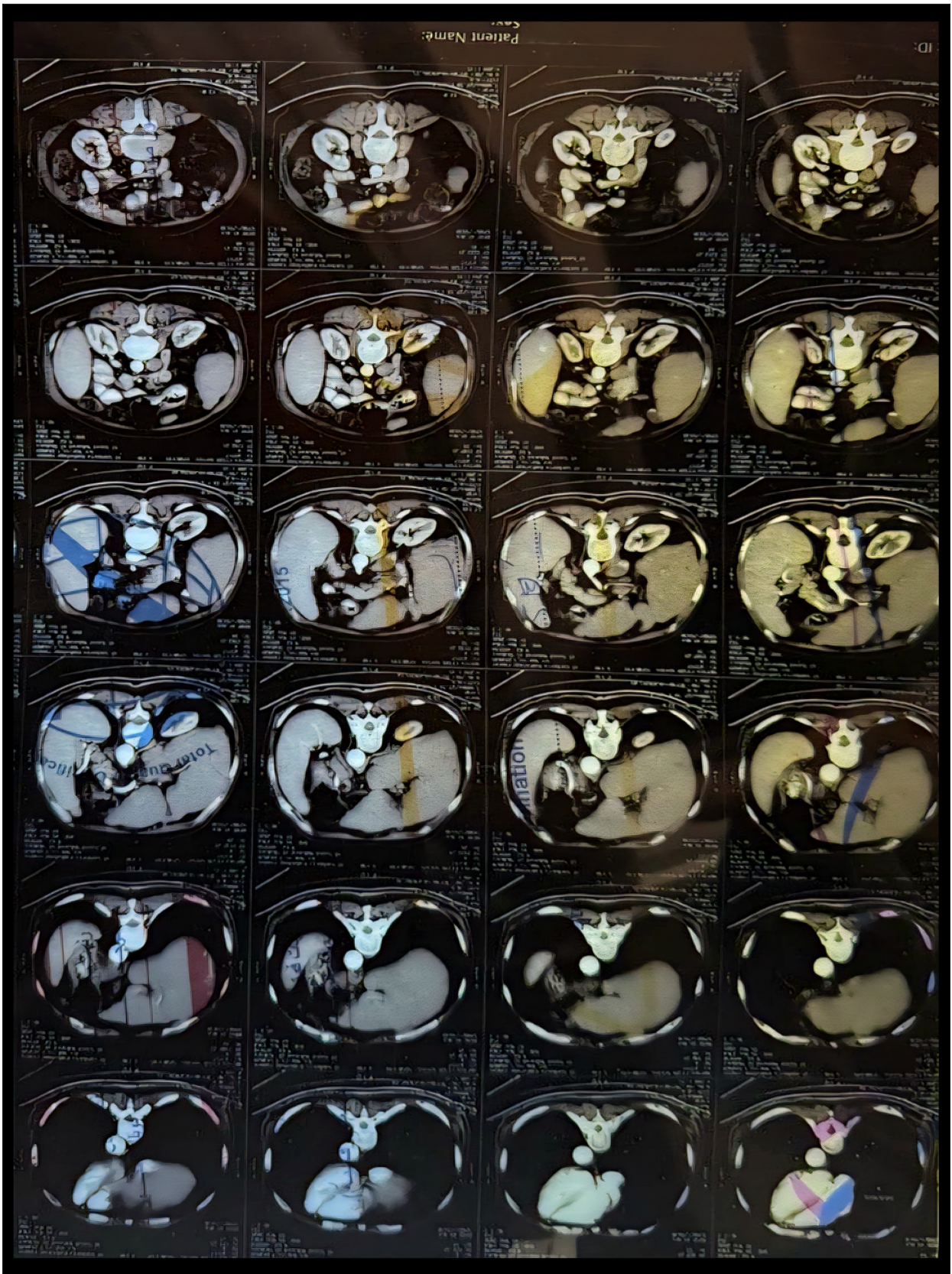


Figure 2. Contrast-enhanced computed tomography of the abdomen.

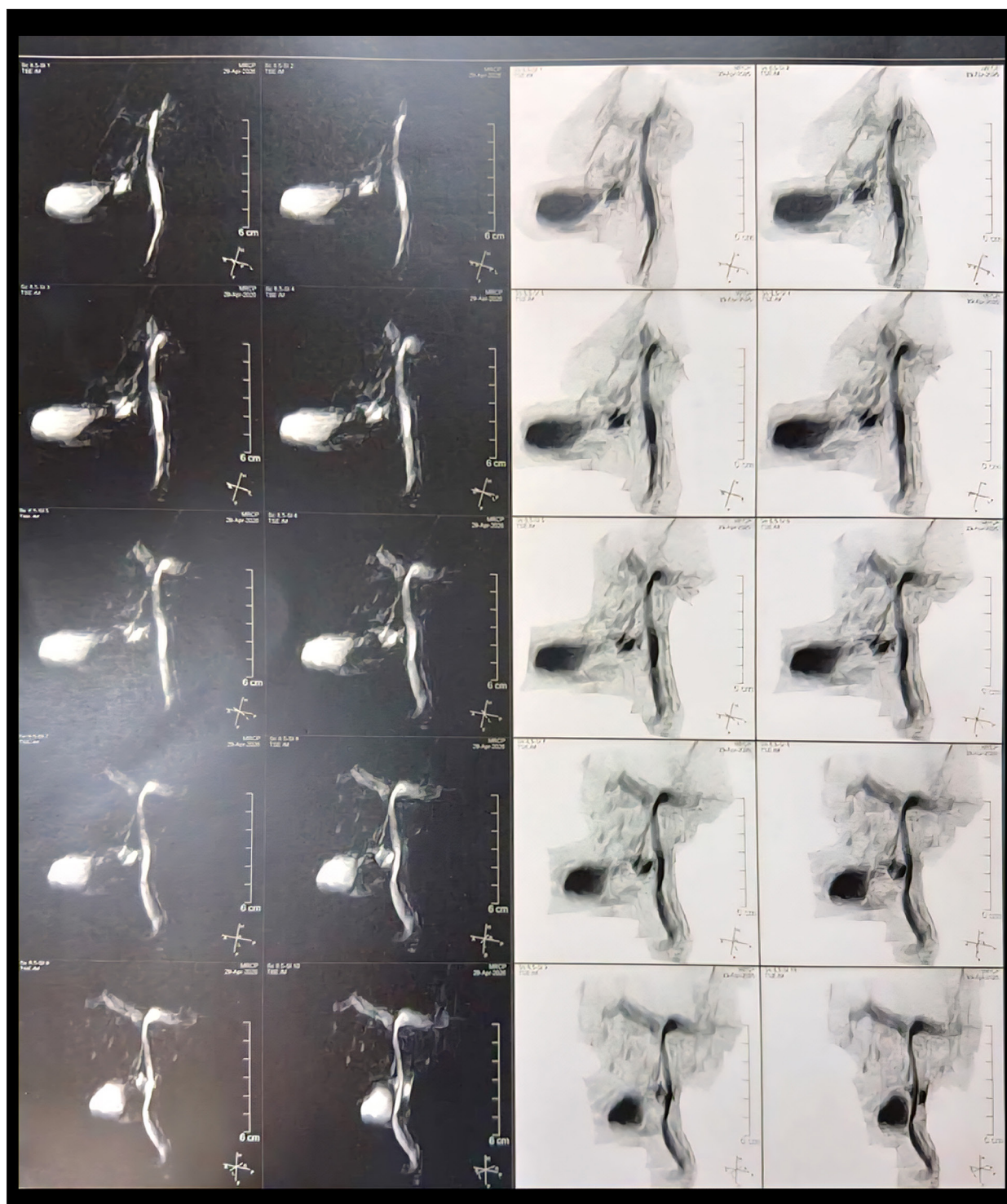


Figure 3. Magnetic resonance cholangiopancreatography on gallbladder and biliary tree.

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Figure 4. High-resolution thick-slab maximum-intensity projection reconstruction of the biliary tree using magnetic resonance cholangiopancreatography.

Table 3. Radiological findings of the patient.

Imaging Modality	Main findings
Abdominal ultrasonography	Features suggestive of chronic liver disease with splenomegaly and gallbladder stones
Contrast-enhanced CT abdomen	Portal hypertension manifestations including splenomegaly and collateral circulation, in addition to gallbladder wall thickening with hyperdense gallstones
MRCP on gallbladder & biliary tree	Coarse cirrhotic liver with regenerative nodules and splenomegaly. Multiple small gallbladder calculi were identified with no biliary dilatation, strictures, or obstructing lesions
High-resolution thick slab MIP reconstruction of the biliary tree (MRCP)	Normal caliber common hepatic duct and common bile duct with smooth outlines and no sizable filling defects or intrahepatic biliary dilatation

Although gallbladder stones were detected on multiple imaging modalities, no biliary dilatation or obstructing lesion was identified. This emphasizes the importance of advanced imaging modalities such as MRI and MRCP in excluding extrahepatic obstruction in patients with cholestatic presentations [2]. Autoimmune liver disease was also considered because anti-smooth muscle antibody was weakly positive. However, anti-nuclear antibodies, antimitochondrial antibodies, and liver/kidney microsomal type 1 antibodies were negative, and imaging did not support autoimmune pancreatitis or IgG4-related sclerosing cholangitis. Previous reports have shown that autoimmune hepatobiliary disorders may mimic obstructive jaundice and create diagnostic uncertainty [3].

Extensive infectious investigations including viral hepatitis markers, Brucella serology, EBV, and CMV IgM were negative, reducing the likelihood of infectious hepatitis. Infiltrative and systemic causes of cholestasis were also considered. A previous case report described severe cholestasis as an unusual presentation of systemic amyloidosis, highlighting the broad differential diagnosis of nonobstructive cholestasis [4].

Drug-induced cholestatic injury may also produce progressive cholestasis and secondary biliary cirrhosis. Severe cholestatic liver injury associated with semaglutide use has previously been reported to radiologically resemble chronic biliary disease [5]. However, no clear offending medication was identified in our patient.

Although infection was considered a potential precipitating factor for hepatic decompensation, this was considered less likely because the patient had no leukocytosis (WBC $4.5 \times 10^3/\text{mm}^3$), a normal C-reactive protein level (3.2 mg/L), and extensive infectious investigations, including hepatitis A, hepatitis B, hepatitis C, HIV, EBV, CMV IgM, and Brucella serology, were negative. Furthermore, repeated imaging showed no evidence of acute cholecystitis or cholangitis. Overall, the coexistence of cirrhotic morphology, portal

hypertension, gallstones, and marked direct hyperbilirubinemia without demonstrable ductal obstruction was considered compatible with a possible multifactorial or nonobstructive cholestatic process superimposed on advanced chronic liver disease. Although the exact mechanism of cholestasis could not be definitively established, the case primarily highlights the importance of structured exclusion of obstructive and alternative etiologies using multimodal evaluation. Similar perplexing cholestatic presentations have been previously described in the literature [1,6]. This present case highlights the importance of integrating clinical, serological, and radiological findings to avoid unnecessary invasive biliary procedures and optimize conservative management and serves as an incremental contribution to the existing literature, illustrating that patients with decompensated cirrhosis may present with severe cholestatic jaundice despite repeatedly negative biliary imaging and the absence of an identifiable obstructive or infectious etiology. By reinforcing this critical diagnostic boundary, it highlights the importance of a systematic, exclusion-based diagnostic approach and careful interpretation of multimodal imaging—particularly in distinguishing incidental gallstones from true obstruction—to avoid unnecessary invasive procedures and support appropriate conservative management.

Conclusions

This case highlights the diagnostic complexity of severe cholestatic jaundice in patients with cirrhosis with negative multimodal biliary imaging. Despite marked conjugated hyperbilirubinemia and the presence of gallstones, advanced imaging studies repeatedly failed to demonstrate significant biliary dilatation or obstructing lesions. The present report emphasizes the importance of structured exclusion-based diagnostic evaluation before attributing severe jaundice to extrahepatic biliary obstruction or proceeding to invasive biliary intervention. Careful integration of clinical, laboratory, and radiological findings remains essential in similar diagnostically challenging presentations.

Institution Where Work Was Done

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Patient Permission/Consent Declaration

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A signed authorization from the patient is available for review by the Editor-in-Chief of the journal upon request.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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