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Biliary Cryptococcus Neoformans Manifesting as Obstructive Jaundice Managed by Whipple Surgery: A Rare Case Report

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1. Abstract

A 66-year-old male presented with several episodes of right upper quadrant pain, fever, and elevated inflammatory markers, suggesting a biliary infection. The patient's initial presentation was complicated by the unusual manifestation of Cryptococcus neoformans infection in the duodenum, leading to obstructive jaundice in a patient without known immunodeficiency. This atypical presentation and subsequent diagnosis of ascending cholangitis with duodenal stricture preventing ERCP significantly complicated the diagnostic and management process. Conservative management with antibiotics initially proved ineffective, necessitating further investigation and, ultimately, a Whipple procedure. Histopathology revealed a complex picture, confirming fungal infection of the gallbladder and IgG4-related disease involving the duodenum. This case throws light in the importance of considering rare diagnoses and underscores the challenges of differentiating between infectious and autoimmune processes in complex biliary conditions. It serves as a reminder of the need for a multidisciplinary approach involving infectious disease and surgical specialties to manage these challenging cases effectively.

2. Introduction

This case report presents a unique and challenging presentation of biliary Cryptococcus neoformans infection in a 66-year-old male without known immunodeficiency, leading to obstructive jaundice [1,11]. While C. neoformans is typically associated with immunocompromised individuals, this case highlights an uncommon manifestation of the infection, particularly in the biliary tract. The initial diagnosis of ascending cholangitis, based on dilated intrahepatic biliary ducts and gallstones, proved inaccurate, as recurrent symptoms and further investigations revealed a duodenal stricture caused by a mass. This mass, subsequently identified as a C. neoformans infection, required a Whipple procedure for definitive treatment. The excised specimen revealed no malignancy but indicated the presence of dematiaceous fungi, raising the possibility of IgG4-related disease. This case highlights the intricate interplay between fungal infections and autoimmune disorders, contributing to a deeper understanding of their complex mechanisms.

3. Case Presentation

A 66-year-old male presented with severe generalized abdominal pain, multiple episodes of vomiting, anorexia, dark urine, 39.0 °C fever, and tachycardia (136 beats/min). The patient experienced these symptoms for the first time and denied weight loss or other symptoms. On examination, he was agitated and febrile, with right upper quadrant and epigastric tenderness and guarding. Figure 1(A and B). An abdominal CT scan with IV contrast on November 25, 2020, revealed pneumobilia, characterized by extensive

intrahepatic biliary channel dilatation and air within the (CBD), alongside a dilated gallbladder without signs of acute cholecystitis. Other potential causes of acute surgical abdomen were ruled out. A subsequent MRI/MRCP on November 26, 2020, it confirmed the presence of sludge in the gallbladder and dilatation of the biliary system, suggesting an incompetent Oddi sphincter as shown in Figure 2. Laboratory results revealed markedly elevated inflammatory markers, including procalcitonin (49.47 ng/mL), CRP (82.02 mg/L), and lactate (9.33 mmol/L), while other laboratory values remained within normal limits. A (CT CAP) was performed on November 29, 2020, to rule out malignant tumors. It showed acute calculus cholecystitis with a high risk of rupture in the hepatic fifth segment and small micro-abscesses that could not be evacuated (Figure 3A&3B). Attempted ERCP revealed a benign stricture and fistula at the D1/D2 junction, explaining pneumobilia. While the ERCP was aborted, meropenem successfully treated the infection. On August 4, 2021.The patient presented with two days of abdominal pain, nausea, vomiting, and dark urine. He had a positive Murphy's sign and elevated white blood cell count (11.3 × 109/L), ALT (40 U/L), and total bilirubin (23.2 μmol/L). A second MRCP done on August 5, 2021, was compared to the one done during the first admission. It showed chronic CBD and intrahepatic duct dilatation and distal CBD constriction (Figure 4). The patient was treated conservatively. The patient presented on November 30, 2021, with same previous presentations and elevated white blood cell count (12 × 109/L), GGT (410 U/L), ALP (220 U/L), and total bilirubin (122 μmol/L). ERCP done on December 2nd ,2021 revealed a severely deformed D1 with an obstructing mass, requiring a trans-nasal endoscope for visualization. Biopsies were unremarkable (Figure 5). On December 5, 2021, Figure 6 confirms a PTC catheter was implanted. The details of the values of the hematological tests are shown in Table 1. On January 25, 2022, the patient was admitted for elective (ERCP). A fistula with bile drainage was found; sphincterotomy was done successfully, and a stent was placed in the CBD. The biopsies taken from the ampulla and stenotic area reveal different findings. The ampulla biopsy shows superficial inflammation and slough with microorganisms consistent with Cryptococcus neoformans, suggesting a fungal infection. The biopsy from the stenotic area demonstrates unremarkable Brunner glands (Figure 7). The patient took oral fluconazole at 400 mg once daily on 15th February 2022. A follow-up cholangiogram showed improved CBD, suggesting treatment effectiveness, as shown in Figure 8. However, a month later, PTC (Figure 9) showed severe dilation of intrahepatic biliary radicles and the proximal CBD, indicating persistent obstruction. The patient's condition, despite multiple treatments, remains unchanged, with a persistent mass causing duodenal stricture and biliary obstruction. Imaging shown in Figure 10 reveals a concerning lesion in the head of pancreas of approximately 2.8 x 3.1 cm, likely a tumor, causing obstruction. The decision to perform a Whipple procedure was decided with patient.

Histological investigation of resected specimens showed no cancer. Dematiaceous fungi were found in the gallbladder and biliary tree, which are suggested by the reported characteristics and confirmed by microbiology testing shown in Figure 11. IgG4/IgG ratios over 40% and over 50 IgG4-positive plasma cells in a high-power field were detected. These observations are associated with periampullary fibrous response. These findings raise IgG4-related disease risk. The patient's postoperative course was uneventful after he underwent the Whipple procedure and started antifungal treatment. Currently, the patient is undergoing follow-up in the outpatient clinic.

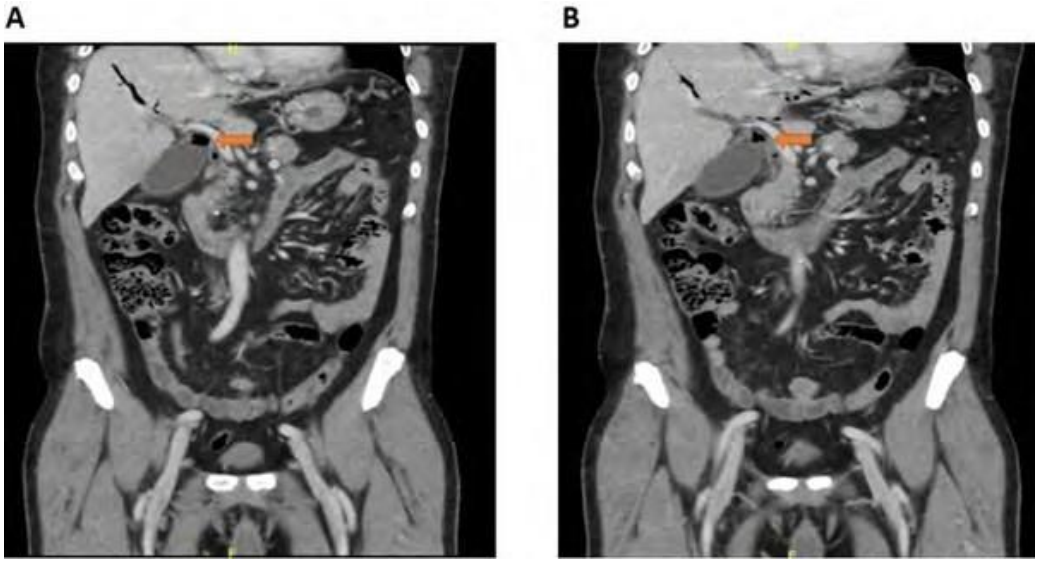

Figure 1: Abdominal CT scan images (A and B) with IV contrast. Pneumobilia was confirmed by extensive intrahepatic biliary channel dilatation and air within the (CBD). A dilated gallbladder (indicated by arrowheads) was present without evidence of acute cholecystitis.

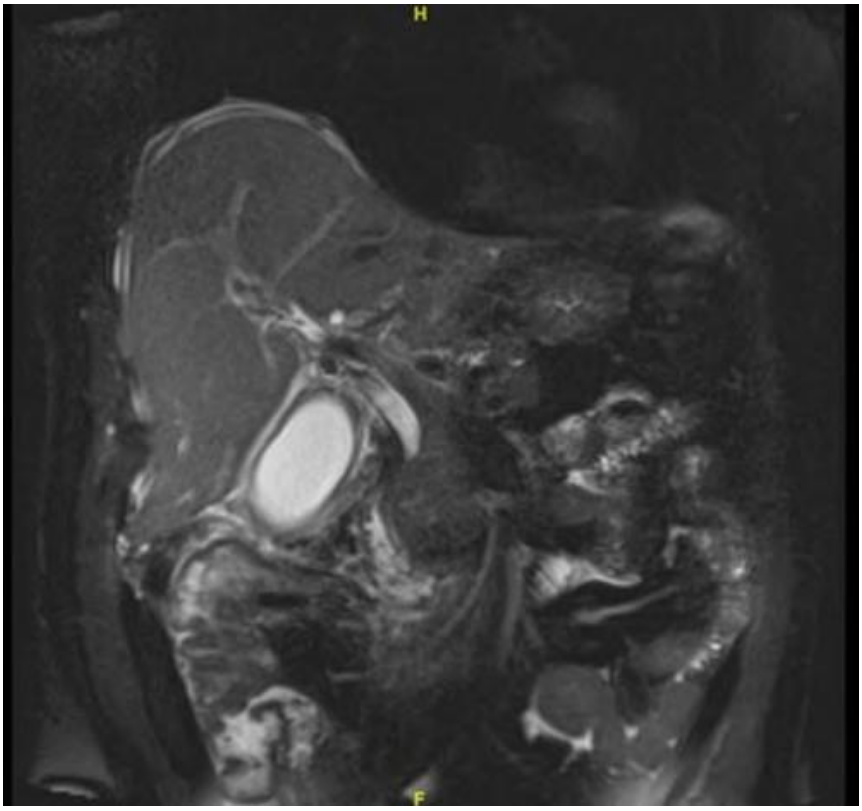

Figure 2: A prominent intrahepatic and extrahepatic biliary system with signal void foci in keeping with known pneumobilia; however, no definite distal CBD stone.

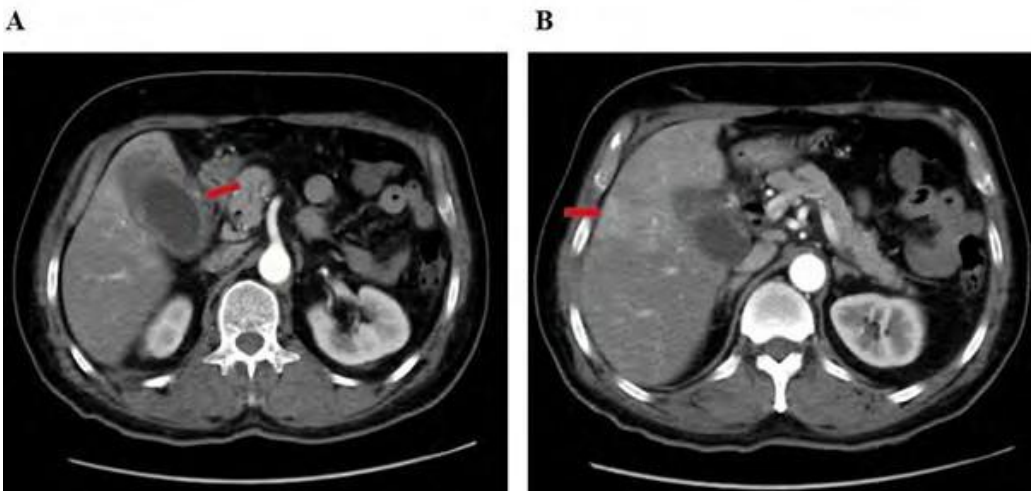

Figure 3: Acute calculus cholecystitis with impending rupture in hepatic segment #5 and non-drainable small micro-abscesses.

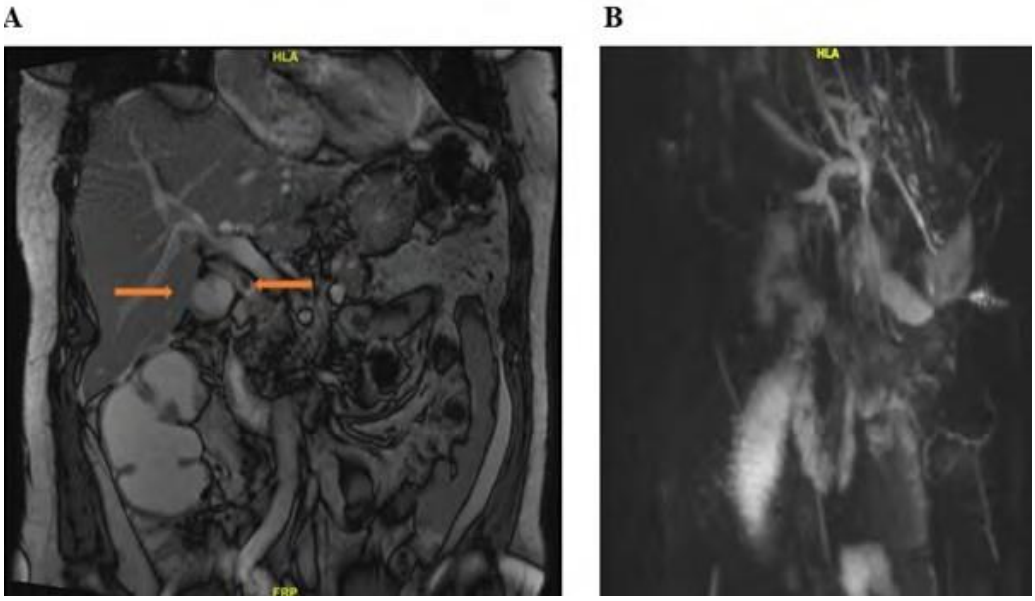

Figure 4: Persistent CBD and intrahepatic duct dilatation and improvement of the gallbladder abnormality shown in **Figure A,** with persistent mild inflammation and a focal narrowing distally in CBD, are shown in **Figure B.**

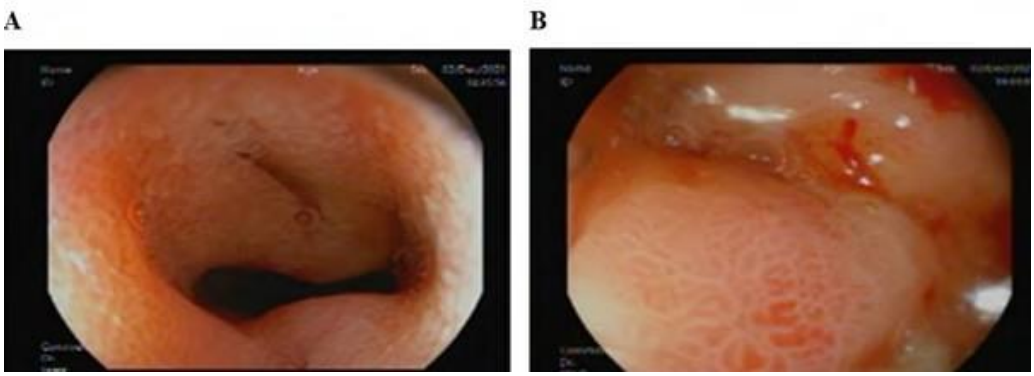

Figure 5: severely deformed D1 with an obstructing mass, requiring a trans-nasal endoscope for visualization. Normal D2. Biopsies were unremarkable.

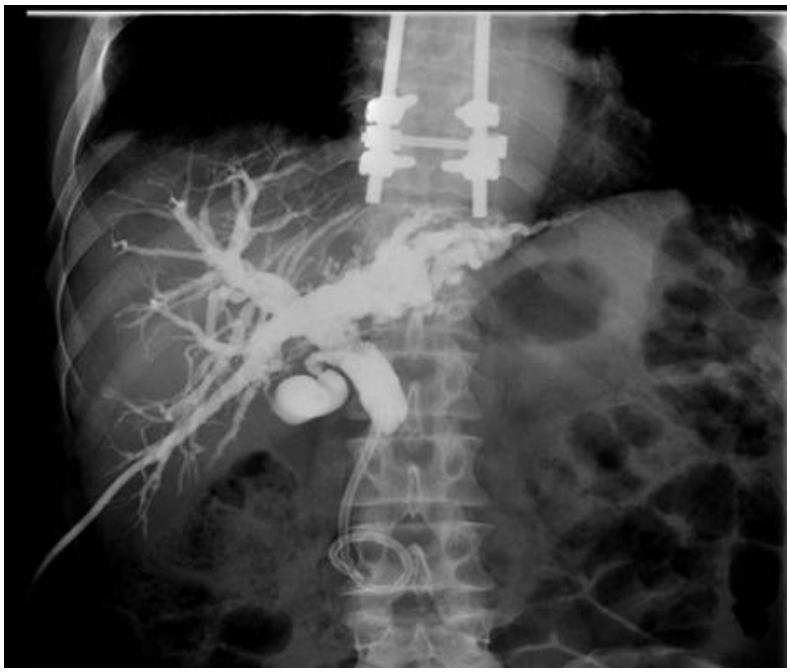

Figure 6: (PTC) catheter implantation.

Table 1: Patient details in 1st, 2nd, and 3rd admission. (CRP- C-Reactive Protein, WBC- White Blood Cells, ALT- Alanine aminotransferase, AST- Aspartate aminotransaminase, Gamma GT- Gamma-glutamyl Transferase).

Lab Tests	Value			Abnormal	Normal Range
	1st Admission	2nd Admission	3rd Admission		
Procalcitonin	49.47	NA	NA	High	<0.5 ng/mL Low risk >2.0 ng/mL High Risk
CRP	82.02	NA	NA	High	<5
Lactate	9.33	NA	NA	High	0.5 - 2.2
WBC	NA	11.35	12	High	3.5 to 11
ALT	NA	37	40	High	Upto 40
AST	NA	22	44	High	Upto 40
Alkaline Phosphate	NA	100	220	High	40 to130
Bilirubin-Total	NA	23.2	122	High	0 to17.1
Conjugated	NA	8	105	High	0 to3.4
Gamma GT	NA	272	410	High	8 to 61
Protein	NA	69	78	High	64 to 83
Albumin	NA	38	34	High	35 to 52
Globulin	NA	31	44	High	16 to 37

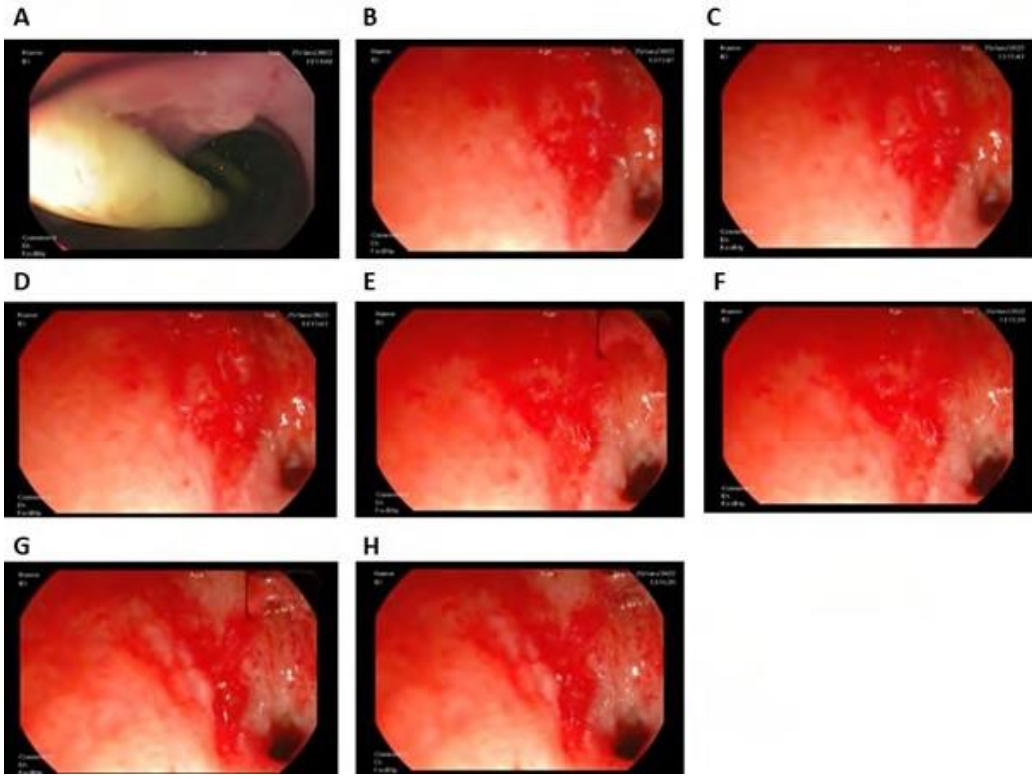

Figure 7: The biopsies taken from the ampulla and stenotic area.

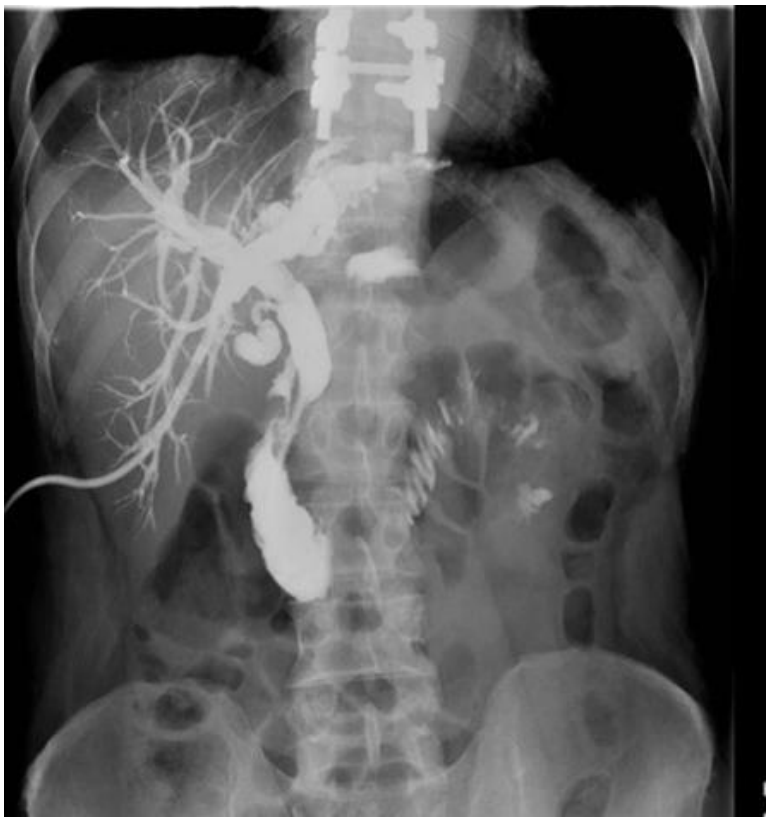

Figure 8: Cholangiogram showing Slight improvement of retro-duodenal CBD.

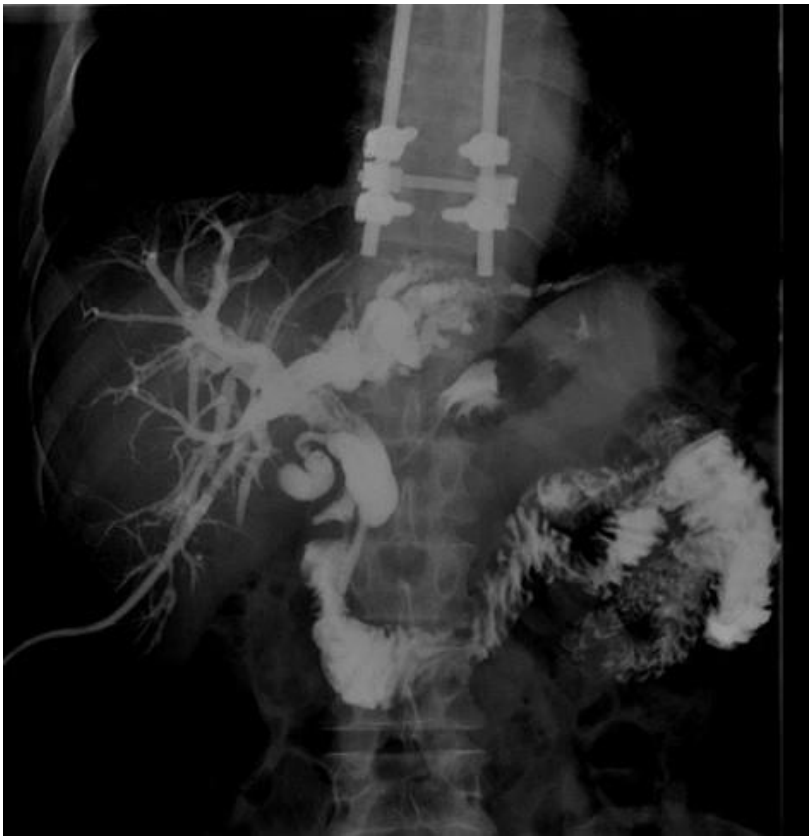

Figure 9: (PTC) shows severe dilatation of intrahepatic biliary radicles and proximal (CBD), which shows obstruction at the mid-zone followed by drainage of contrast through the CBD stent down to the duodenum and mild reflux toward the stomach.

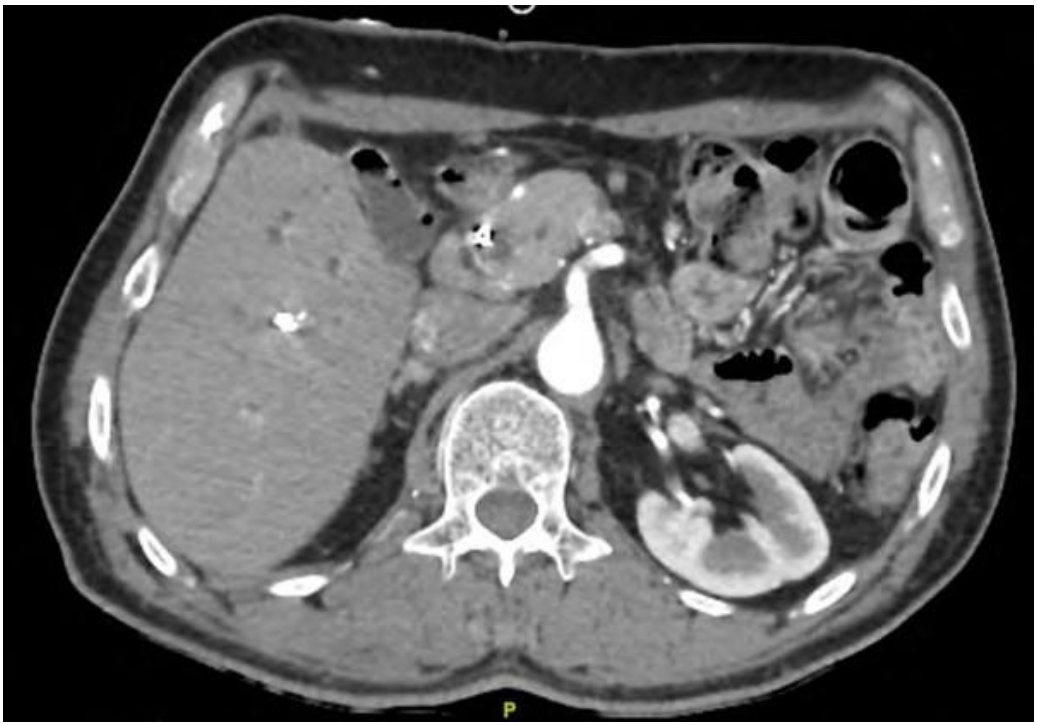

Figure 10: Intra-pancreatic duct dilatation is seen with a pancreatic head hypodense lesion measuring around 2.8 x 3.1 cm.

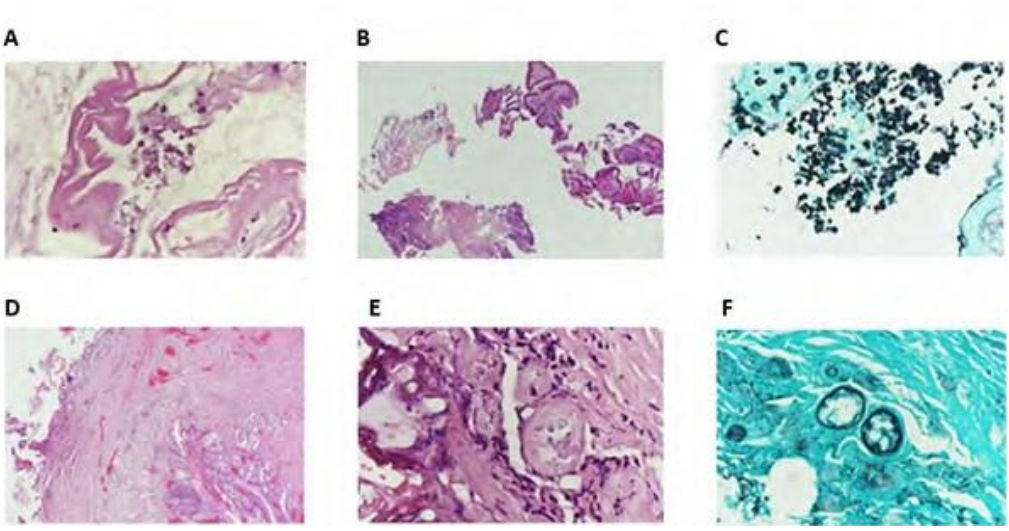

Figure 11. Whipple procedure the histopathological images of the resected specimen.

4. Discussion

A peculiar manifestation of biliary Cryptococcus neoformans manifesting as obstructive jaundice [2] is highlighted in this case report. Cryptococcus neoformans, a fungus commonly found in the environment, typically affects immunocompromised individuals and often causes no symptoms in healthy people. Since 1985, only 12 cases of biliary cryptococcosis, including this one, have been documented, with a mix of immunocompromised and immunocompetent patients [3]. These cases demonstrate diverse presentations, including abdominal pain, fever, jaundice, dark urine, and pale stool. Diagnoses often rely on biopsies, cytology, or cultures and involve multiple organs in most cases. Treatment with antifungals has resulted in complete recovery in most patients, except for one HIV-positive individual who succumbed to a separate respiratory infection, highlighting the importance of early diagnosis and management in this rare but potentially life-threatening condition. As far as we have been able to determine, this is the first reported instance where a Whipple procedure was employed as the definitive treatment. This case report delves into the complex interplay of biliary cryptococcosis, a rare fungal infection caused by Cryptococcus neoformans, and IgG4-related disease (IgG4-RD), a chronic immune disorder [5]. While C. neoformans typically affects immunocompromised individuals, this case highlights its potential in immunocompetent patients, throwing light on the need for a broad differential diagnosis in unexplained biliary strictures. The patient presented with common biliary symptoms, including abdominal

pain, fever, jaundice, and altered stool color, further complicating the diagnosis. Initial imaging revealed gallstones, intrahepatic biliary duct dilatation, and ascending cholangitis, leading to conservative treatment. A rare case of biliary Cryptococcus neoformans is obstructive jaundice. MRCP [7] and ERCP [10] are valuable diagnostic imaging techniques for identifying the underlying cause of obstructive jaundice. However, persistent symptoms required further investigation, ultimately revealing a duodenal stricture caused by a C. neoformans mass. Histopathology confirmed the fungal infection and suggested IgG4-RD, highlighting the importance of meticulous investigation and careful differentiation between these conditions. While most reported cases of cryptococcal cholangitis have shown complete recovery with antifungal therapy, this case demonstrates the potential for severe complications, emphasizing the need for early diagnosis and appropriate management in this rare but potentially life-threatening condition.

5. Conclusion

This case underscores the significance of a comprehensive diagnostic and therapeutic approach in managing complex biliary pathology. This case demonstrates the importance of considering uncommon causes, especially in patients with persistent symptoms and inconclusive initial investigations. This complex case exemplifies the diagnostic challenges of biliary disease and highlights the importance of multidisciplinary collaboration in achieving optimal patient outcomes.

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