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Fungal cholecystitis: Easily missed unless considered-A Case Report and Review of Literature

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Case Report

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Title: Fungal cholecystitis: Easily missed unless considered-A Case Report and Review of Literature

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ABSTRACT

Background: While gallstone disease remains the most common cause, a variety of other etiologies may also lead to acute cholecystitis. We present a rare case of acute cholecystitis in the backdrop of gall stone disease.

Case Presentation: A 50-year-old diabetic female with recent history of diabetic foot ulcer, presented with right upper abdomen pain with associated fever. She was diagnosed with acute cholecystitis at outside hospital and received parenteral antibiotics. In view of persistent fever, she was referred to our hospital. She was evaluated with relevant investigations including a CECT abdomen which showed ill-defined heterogeneously enhancing gall bladder mass lesion with extension into liver parenchyma. Ultrasound guided FNA from the mass lesion showed fungal elements (hyphae and pseudo-hyphae). In view of high suspicion of underlying malignancy, PET CT scan was done which revealed FDG avidity in neck and body of gall bladder (SUV max 6.6) with extension into segment 4a, 4b and 5 of liver (SUV max 8.1). However, USG guided biopsy done from gall bladder fossa mass didn't show any evidence of malignancy. Hence possibility of acute fungal cholecystitis with gall bladder perforation and liver abscess was considered. She was managed with liposomal

amphotericin B for 2 weeks, following which her symptoms resolved completely. Repeat CECT abdomen and PET CT scan demonstrated near complete resolution of the mass lesion in liver bed with mild residual symmetrical wall thickening of gall bladder. Now she has been listed for cholecystectomy.

Conclusions: High clinical suspicion and histopathological evaluation are required to diagnose acute fungal cholecystitis and liver abscess.

Keywords: Cholecystitis, Fungal infection, Diabetes, Gall stone disease, Candida

Background

Acute cholecystitis is a common gastrointestinal emergency encountered in patients with gallstones. Although superadded bacterial infection is common in the majority of cases requiring parenteral antibiotics, fungal infection warrants consideration, particularly in high-risk patients. Fungal cholecystitis is a rare cause of acute cholecystitis and is predominantly seen in immunocompromised individuals. Delayed diagnosis may result in complications, such as gallbladder perforation and fungal liver abscesses. These complex presentations often mimic gallbladder carcinoma both clinically and radiologically, posing a significant diagnostic challenge. We report a unique case of complicated fungal cholecystitis in a middle-aged woman with diabetes mellitus, highlighting the diagnostic dilemmas and therapeutic considerations associated with this uncommon entity.

Case Presentation

A 50-year-old female, with history of long-standing diabetes for 15 years, presented with right upper abdomen pain with fever for 2 months duration. She was evaluated at outside hospital for her symptoms and underwent ultrasound abdomen which showed acute calculous cholecystitis. She was managed with parenteral antibiotics; however, her fever spikes persisted. She was referred to our centre where she was initially evaluated at outdoor setting and abdomen CT scan was advised. Her CECT abdomen showed ill-defined heterogeneously enhancing gall bladder mass lesion with extension into liver parenchyma. Considering the possibility of underlying malignant etiology, USG guided fine needle aspiration (FNA) from the mass lesion revealed fungal elements with presence of hyphae and pseudo-hyphae [figure A-D]. On reviewing her history, she was found to have non healing ulcer over right great toe and sole since last couple of months. Also, she had an episode of pulmonary tuberculosis 3 years back for which she was treated with anti-tubercular therapy for 6 months. After discussion with the Infectious disease team and reviewing slides with the Mycology unit; possibility of candida infection was considered. She was started on parenteral liposomal amphotericin B after sending blood for fungal culture. Although her tumor markers were negative, due to high index of suspicion of underlying malignancy, PET CT scan was performed which showed FDG avidity in neck and body of gall bladder (SUV max 6.6) with extension into segment 4a, 4b and 5 of liver (SUV max 8.1) (Image IA-IB). USG guided biopsy done from gall bladder fossa mass didn't reveal any evidence of malignancy. A possibility of acute fungal cholecystitis with gall bladder perforation and liver abscess in the setting of gallstones and poorly controlled diabetes was considered and she was treated with 2 weeks antifungal therapy. Her symptoms improved

completely upon treatment with resolution of fever and pain abdomen. A repeat CECT abdomen was performed which demonstrated near complete resolution of the mass lesion in liver bed with mild residual symmetrical wall thickening of gall bladder. PET scan also showed significant reduction in the FDG uptake in the gall bladder fossa (SUV max 3.7) and liver bed (SUV max 6.2) (Image IIA-IIB). USG guided repeat biopsy from gall bladder neck region was done after the inflammation settled down which showed no evidence of malignancy. Currently she has been listed for cholecystectomy.

Review of Literature and Discussion

We did a comprehensive review of the literature by searching PubMed using combinations of the search terms “fungal,” “cholecystitis,” “Aspergillus,” “Candida,” “Fusarium,” "Histoplasma", "Mold", “Mucorales,” and “yeast.” Our search demonstrated several case reports, case series and reviews in the English language literature on acute fungal cholecystitis.

In our review of 44 cases of fungal cholecystitis encompassing both candida and non-candida fungi, majority of patients had significant predisposing risk factors for fungal infection. Early diagnosis, source control by cholecystectomy or cholecystostomy, and prompt antifungal therapy were associated with favourable outcomes, whereas delayed diagnosis, disseminated fungal infection, and severe immunocompromise were linked to increased mortality (Table 1). Fungal organisms are an infrequent cause of cholecystitis. Candida is the most frequent etiological agent. Of the 692 cholecystectomies conducted, Morris et al. showed an incidence of 1.3% at their institution [1]. Malignancy, long-term broad-spectrum antibiotic treatment, immunosuppressive medication, diabetes mellitus, total parenteral nutrition, and intraabdominal surgery are the documented risk factors for invasive Candida infection [2]. It is believed that the infection results from either haematogenous seeding during blood stream infection or ascending migration of organisms within the biliary tract [3]. The high mortality rates of gangrenous and acalculous cholecystitis in critically ill patients hospitalized to intensive care units (38–80%) are probably caused by widespread Candida infection and candidemia. Ariel et al assessed 42 cases of fungal cholecystitis and found that Candida was the sole organism isolated in 36 of the 42 cases (86%), and in only 14% an additional bacterial co-pathogen was found. Of the 42 cases (28 isolates, 67%), Candida albicans was the most prevalent species. Candida glabrata (6 isolates, 14%), Candida parapsilosis (5 isolates, 12%), and Candida tropicalis (3 isolates, 7%), were next in line. The most common site of concurrent Candida infection was blood (13 cases, 31%), followed by urine (10 cases, 24%) and peritoneal fluid (6 cases, 14%) in 20 patients (48%) with concurrent Candida infection [4]. Rare causes of other fungal organisms causing acute cholecystitis includes Fusarium, Histoplasma and Penicillium.

Literature on fungal liver abscess is scarce. In majority of causes it can be part of underlying polymicrobial etiology. Like fungal cholecystitis, here also candida is the commonest organism. It is usually seen in immunocompromised individuals with spread to the liver from the gastrointestinal or biliary tract resulting in either micro-abscesses or macro-abscesses. Often, they are part of ongoing polymicrobial infection. In a retrospective review of patients admitted with hepatic abscesses at The Johns Hopkins Hospital from 1973 to 1993, eight patients were diagnosed with pure fungal hepatic abscesses and 34 patients were identified with mixed fungal/pyogenic abscesses [5].

Our patient had long standing diabetes with macro (diabetic foot) and microvascular complications (diabetic neuropathy and nephropathy). In a large cohort study by Ratheesh et al there was a significant rise in gallstone rates in diabetic patients as compared to non-diabetics (OR = 2.30, 95%

CI: 1.89–2.79; p < 0.001). Multiple factors have been attributed including high prevalence of obesity and dyslipidaemia in diabetics which are known risk factors for gall stone disease, microvascular and neurological complications as well as hormonal changes in diabetes interfering with gall bladder emptying, and lastly dysfunction of sphincter of Oddi can increase bile concentration and risk of cholelithiasis [6]. Diabetes can increase the risk of both acute calculous and acalculous cholecystitis. Hence, surgery in such settings might be a little tricky. Serban et al in a retrospective study showed post operative risk of both major cardiovascular events as well as minor complications like surgical site infections were much higher in the diabetic subgroup (p=0.0254), however no statistically significant associations were found between diabetic patients and the severity of acute cholecystitis or requirement for conversion [7]. In a population-based study by Shebl et al demonstrated independent of body mass index, diabetes was significantly linked with gallbladder cancer (odds ratio [95% confidence interval] = 2.6 [1.5 – 4.7]) risk with biliary stones and low serum levels of high-density lipoprotein (HDL) were significant mediators of the effect on gallbladder cancer risk [8]. To summarize patients with diabetes has significantly higher risk of developing gall bladder malignancy.

The differentials of gall bladder fossa mass lesion can be diverse. Our case had a gall bladder fossa mass mimicking malignancy. Apart from those various other etiologies like xantho-granulomatous cholecystitis, IgG4 related acute cholecystitis, tubercular cholecystitis, adenomyomatosis, lymphoma, cholangiocarcinoma and hepatic metastasis can present as soft tissue mass lesion of gall bladder fossa (9). However fungal cholecystitis mimicking gall bladder malignancy is fairly rare. Dedicated history, clinical examination, imaging and tissue diagnosis can aid in differentiating underlying conditions.

The index patient presented with acute fungal cholecystitis with gall bladder perforation into surrounding hepatic parenchyma. Early cholecystectomy or percutaneous tube drainage of the inflamed gallbladder seem to be essential in such conditions if not improving with systemic antifungals. Amphotericin B and fluconazole are examples of systemic antifungals that have good fungicidal activity and bile penetration, making them suitable therapeutic adjuvants [10]. Duration of antifungal therapy should be of at least 2 weeks duration to ensure clearing of candidemia [11].

Conclusion: Invasive fungal infection with contiguous gall bladder and liver involvement is uncommon. High index of clinical suspicion and prompt initiation of anti-fungal therapy are the mainstays for successful treatment of fungal cholecystitis with liver abscess.

List of Abbreviations:

CECT: Contrast enhanced computed tomography

FDG-PET: Fluorodeoxyglucose-Positron emission tomography

FNA: fine needle aspiration

SUV: Standardized uptake value

USG: Ultrasound

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  - **Nilanjan Kar:** Conceptualization, Data Curation, Methodology, Writing - Original Draft.
  - **Radhika Srinivasan**: Data Curation, Visualization, Investigation, Supervision
  - **Sanjay Barada**: Data Curation, Visualization, Investigation, Supervision
  - ***Rajender Kumar****:* Data Curation, Visualization, Investigation, Supervision
  - **Pankaj Gupta**: Data Curation, Visualization, Investigation, Supervision
  - **Usha Dutta:** Conceptualization, Data Curation, Methodology, Software, Writing - Review & Editing.
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Image IA-IB: CECT abdomen and FDG-PET axial scan images showing ill-defined heterogenous mass lesion arising from fundus and body of gall bladder with infiltration into surrounding liver parenchyma and increased FDG uptake (SUV max Gall bladder-6.6, Liver – 8.1) on presentation

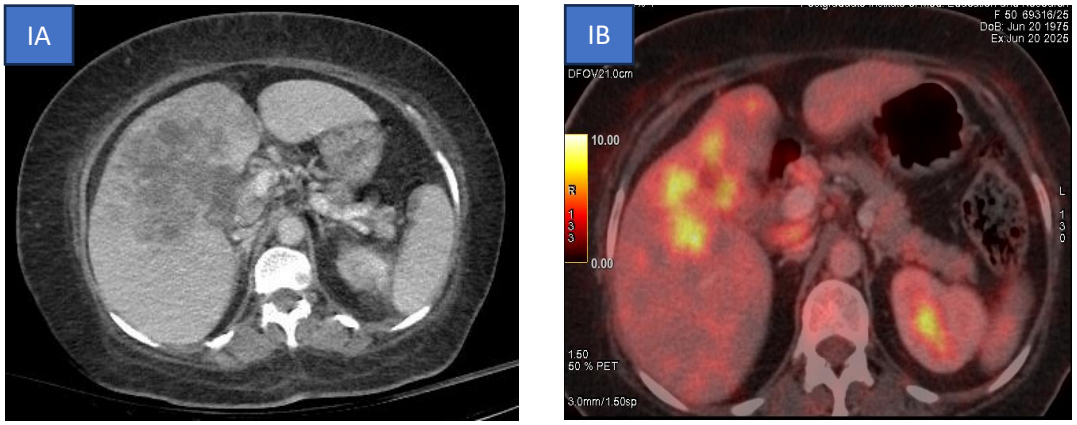


Image IIA-IIB: CECT abdomen and FDG-PET axial scan images showing significant resolution of the ill-defined mass lesion involving the gall bladder and surrounding liver parenchyma with reduction in FDG uptake (SUV max Gall bladder-3.7, Liver – 6.2) post anti-fungal treatment

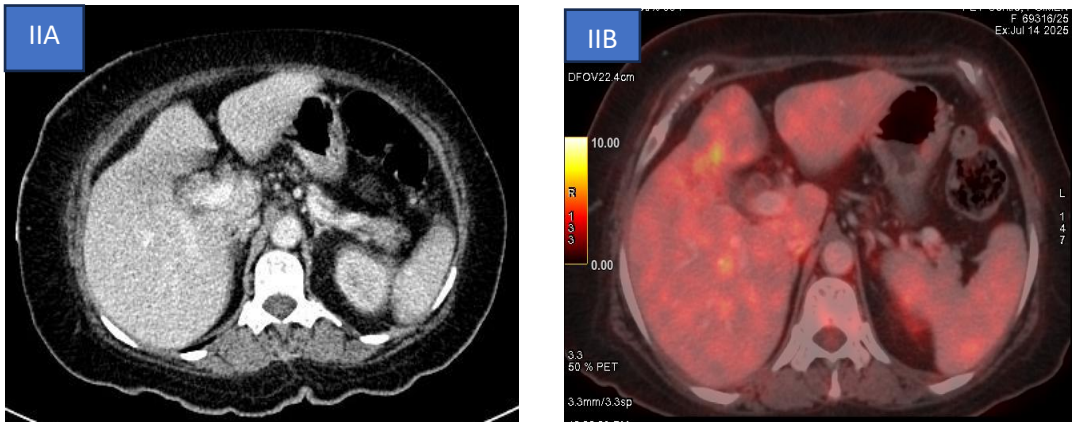


Fig A-D: A: Fine needle aspirate cytology smears from gall bladder lesion showing thin slender septate fungal profiles (MGG, 20X) B: Fungal profiles at higher magnification with lymphoplasmacytic infiltrate (MGG, 40X) C: Fungal profiles admixed with numerous bile plugs (black arrow) (H&E, 20X) D: Broad bulbous ends of the fungal profiles (H&E, 40X)

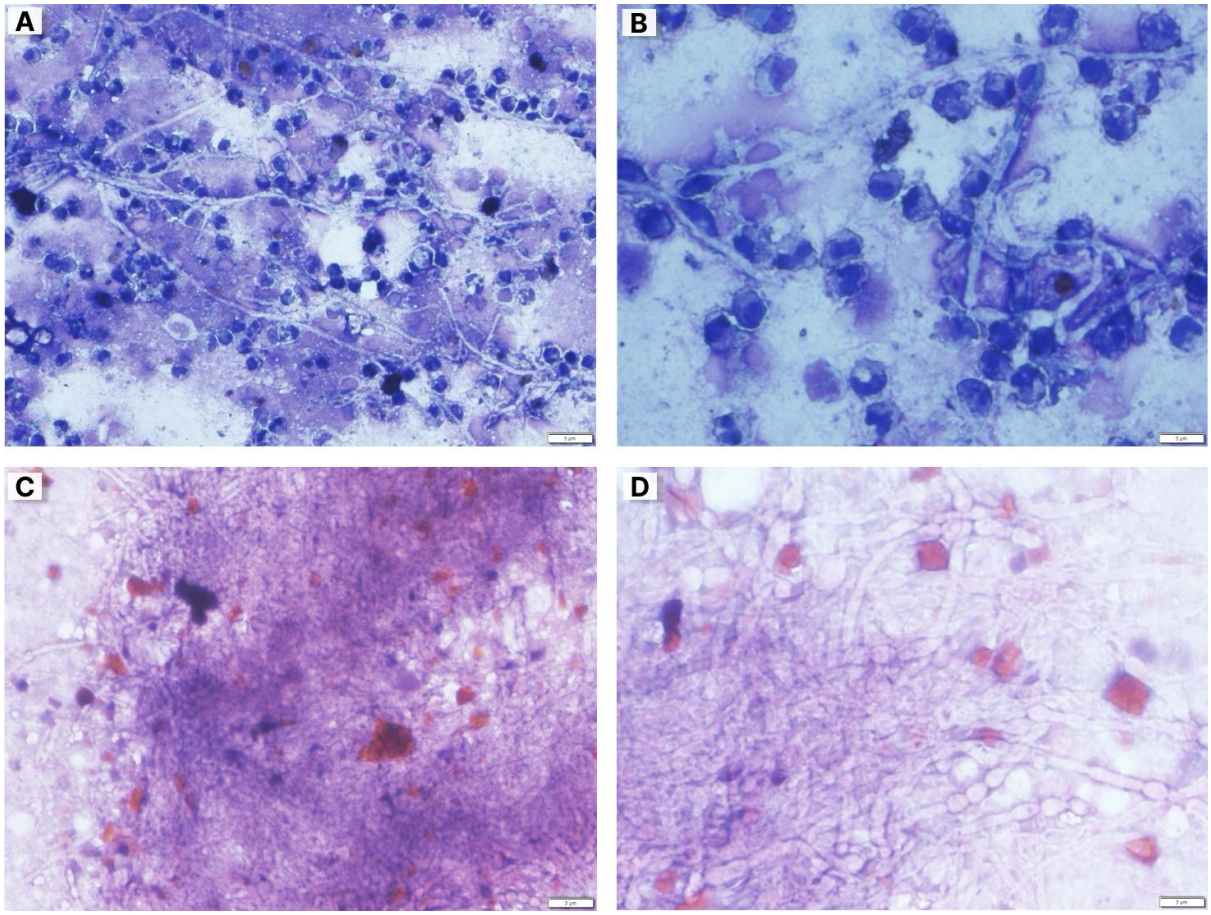


Table 1: Summary of case reports and case series on fungal cholecystitis from 1976-2026 including characteristics, predisposing factors, management, and outcomes

Serial no	Author	Age/Sex	Risk factors	Fungal organism	Specimen yielding fungus	Treatment	Outcome	Reference
1.	Miller	70/M	TPN	Candida glabrata	Gallbladder	Cholecystostomy	Survival	Arch Surg 1976
2.	Schreiber	12/M	Leukemia	Candida albicans	Gallbladder	Cholecystostomy + Amphotericin B	Survival	Am J Dis Child 1982
3.	Brooks	63/M	None	Candida albicans	Gallbladder	Cholecystectomy + azoles	Death	Arch Intern Med 1982
4.	Warren	53/M	Diabetes	Candida glabrata	Gallbladder	Cholecystectomy	Survival	Am J Clin Pathol 1982
5.	Irani	72/M	None	Candida albicans	Biliary tract	Amphotericin B	Death	Arch Pathol Lab Med 1986
6.	Valainis	55/F	None	Candida glabrata	Gallbladder	Cholecystectomy	Survival	J Infect Dis 1987
7.	Schneiderman	84/F	Diabetes	Candida albicans	Gallbladder	Cholecystostomy	Survival	British Journal of Surgery 1987
8.	Gomez-Mateos	58/M	TPN	Candida parapsilosis	Gallbladder	Surgery + Amphotericin B	Survival	J Infect Dis 1988
9.	Adamson	13/M	Malignancy (Sarcoma of femur)	Candida albicans	Gallbladder	Cholecystostomy + Amphotericin B	Survival	Pediatric Infectious Disease Journal 1989
10.	Morris et al.	9 cases	Mixed	Candida spp.	Gallbladder	Surgery ± antifungals	Mixed	Rev Infect Dis 1990

11.	Hiatt	4 cases	Polytrauma + Prolong ICU stay	Candida albicans	Gallbladder	Surgery + Amphotericin B	Survival in 2 patients, death in rest 2 cases	Am Surg 1991
12.	Gips	72/M	None	Candida albicans	Gallbladder	Cholecystectomy	Survival	European Journal of Surgery 1992
13.	McGuire	42/M	Leukemia	Candida tropicalis	Gallbladder	Surgery + Amphotericin B	Survival	Clinical Infectious Diseases 1992
14.	Paret	2/F	None	Candida albicans	Gallbladder	Cholecystectomy	Survival	Journal of Paediatric Surgery 1994
15.	Mandak	52/M	Heart transplant	Candida parapsilosis	Gallbladder	Cholecystectomy	Death	Am J Gastroenterol 1995
16.	Lopez Onrubia	68/F	Diabetes	Candida albicans	Gallbladder	Fluconazole + surgery	Survival	European Journal of Clinical Microbiology and Infectious Diseases 1995
17.	Takano	65/M	Diabetes	Candida albicans	Gallbladder	Fluconazole + surgery	Survival	Endoscopy 1996
18.	Diebel	7 cases	Prolong ICU stay	Candida spp.	Gallbladder	Surgery ± Amphotericin	Mixed	Surgery 1996
19.	Santos	30/F	None	Candida albicans	Gallbladder cytology	Cholecystectomy	Survival	Acta cytol 2004

20.	Christensen	NR	None	Aspergillus spp.	Gallbladder	Not reported	Reported	ACG Abstract 2004
21.	Lai	37/M	Diabetes	Candida glabrata + C. albicans	Cholecystostomy aspirate	Amphotericin B→ Fluconazole	Survival	World J Gastroenterol 2005
22.	Scheele	80/M	None	Candida albicans	Gallbladder	Voriconazole	Survival	Mycoses 2006
23.	Singh	65/F	AIDS	Cryptococcus spp.	Gallbladder	Cholecystectomy	Survival	AIDS 2007
24.	Rodriguez	85/F	None	Candida albicans	Gallbladder	Fluconazole	Survival	Rev Iberoam Micol 2007
25.	Yildirim	33/F	None	Candida lusitaniae	Gallbladder	Amphotericin B	Survival	Japanese Journal of Infectious Diseases 2008
26.	Misselwitz	76/F	Bladder carcinoma	Candida glabrata	Gallbladder aspirate	Voriconazole	Survival	Infection 2008
27.	Grosser	1/M	Kidney transplant	Candida albicans	Gallbladder	Cholecystectomy	Survival	Pediatr Transplant 2011
28.	Alave	23/M	AIDS	Histoplasma capsulatum	Cholecystectomy specimen	Amphotericin→ Itraconazole	Recovery	The Journal of Infection in Developing Countries 2011
29.	Lacarrière	59/M	AML + Neutropenia	Mucorales	Gallbladder	Liposomal amphotericin B + cholecystectomy	Death	Infection 2011
30.	Araujo	79/F	Diabetes	Candida famata	Cholecystostomy	Drainage	Death	Rev. Soc. Bras. Med. Trop 2013

					aspirate			
31.	Shinha	38/M	AIDS	Histoplasma capsulatum	Urine antigen	Amphotericin→ Itraconazole + surgery	Survival	ACG Case Reports Journal 2015
32.	Szvalb	33/F	AML	Fusarium spp.	Bile	Liposomal Amphotericin B+ voriconazole + drainage	Death	Mycoses 2019
33.	Karasuno	74/M	Corticosteroid use	Candida glabrata	Peritoneal fluid	Liposomal amphotericin B	Death	IDCases 2019
34.	Grewal	60/M	Diabetes	Coccidioides immitis	Aspirate from pericholecystic fluid collection	Liposomal Amphotericin B	Survival	*Journal of Investigative Medicine High Impact Case Reports*. 2020
35.	Sabzanov	55/F	Renal transplant	Histoplasma capsulatum	Urine antigen	Liposomal Amphotericin B + cholecystostomy	Survival	Cureus 2023
36.	Fernández	50/M	None	Histoplasma capsulatum	Urine antigen	Amphotericin B → Itraconazole	Survival	Cureus 2024
37.	Pouriki	58/F	Diabetes + ESRD	Candida auris	Cholecystectomy specimen	Micafungin + surgery	Survival	Cureus 2024
38.	AlNuaimi	58/F	None	Conidiobolus coronatus	Hilar biopsy	Antifungal + ERCP/PTBD	Survival	Journal of Surgical Case

								Reports 2025
39.	Swaiti	68/M	None	Candida glabrata	Cholecystostomy aspirate	Micafungin	Death	ACG Case Rep J 2025
40.	Raab	69/M	DM + CKD	Aspergillus fumigatus	Cholecystectomy specimen	Cholecystectomy	Survival	Medical Ultrasonography2025
41.	Hamamah	47/F	None	Apophysomyces ossiformis	Cholecystectomy specimen	Liposomal Amphotericin B + Posaconazole	Death	Cureus 2025
42.	Mullai	28/F	None	Syncephalastrum spp.	Cholecystectomy specimen	Cholecystectomy	Survival	Diagnostic Microbiology & Infectious Disease 2025
43.	Dayal	35/F	None	Candida albicans	Cholecystectomy specimen	Cholecystectomy	Survival	Acta Medica Bulgarica 2025
44.	Dumais	28/F	Acute Myeloid Leukemia	Lomentospora prolificans	Bile culture & cholecystectomy specimen	Voriconazole → Fosmanogepix + cholecystectomy	Survival	Eur J Clin Microbiol Infect Dis 2026

Consent: patient has given written informed consent for her personal and clinical details along with any identifying images to be published in this study.

CARE Checklist has been provided in the supplementary file.

Availability of data: the data supporting the findings are available from the corresponding author upon reasonable request, subject to applicable patient confidentiality and institutional requirements.

Ethical section: Not applicable

Supplementary Files

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- CAREchecklistEnglish2013.docx