Panorama *of* Emergency Medicine

Vol. 4 No. 1 2026 Case Report

A Near-Fatal Anaphylactic Reaction to Biliary Contrast: A Cautionary Case During Laparoscopic Cholecystectomy

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ABSTRACT

Anaphylactic reactions to iodinated contrast agents during intraoperative cholangiography (IOC) are extremely rare, although such reactions are well documented with intravenous (IV) administration. We present the case of a 71-year-old female with a known allergy to iodinated contrast, who experienced a life-threatening anaphylactic reaction immediately after intraoperative cholangiography (IOC) during laparoscopic cholecystectomy. Shortly after the administration of iodinated contrast into the biliary duct, the patient developed supraventricular tachycardia and profound hypotension. This case underscores the risk of systemic absorption and hypersensitivity reactions from biliary-administered contrast agents, even in the absence of intravenous exposure. It highlights the need for a comprehensive preoperative allergy evaluation in high-risk patients undergoing biliary procedures and the importance of considering alternative imaging methods to avoid serious complications.

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Submitted: 13 Sep 2025
Accepted: 27 March 2026

Published by New Health Concept
panoramaoem.cloud

INTRODUCTION

Cholecystitis, inflammation of the gallbladder mostly due to obstruction of the cystic duct by a gallstone, is considered one of the most frequent indications for laparoscopic cholecystectomy [1]. Intraoperative cholangiography (IOC) is performed during cholecystectomy to visualize the biliary anatomy and identify any residual obstruction [2]. The technique involves inserting a catheter into the cystic duct and injecting an iodinated contrast agent to highlight the biliary tree under fluoroscopy. While this contrast agent is generally safe and plays a crucial role in optimizing surgical outcomes, its use carries a very low risk of hypersensitivity reactions [3]. Although contrast is administered directly into the biliary tree rather than intravenously, iodinated agents can still be absorbed into the systemic circulation, potentially triggering hypersensitivity reactions, including anaphylaxis [4]. While such events are rare during intraoperative cholangiography (IOC), they are clinically significant due to their rapid onset and the potential for general anesthesia to obscure early warning signs like respiratory distress [5]. In this report, we present a critical case involving a 71-year-old female who experienced intraoperative anaphylactic shock following the administration of iodinated contrast dye during IOC in the course of a

How to cite this paper? Hamdar H, Abdelhadi A, Al Ayash D, Harb Y, Chaarani N, et al. A Near-Fatal Anaphylactic Reaction to Biliary Contrast: A Cautionary Case During Laparoscopic Cholecystectomy. Panorama of Emergency Medicine. 2026,4(1)
https://doi.org/10.26738/poem.v4i1.11

laparoscopic cholecystectomy for acute cholecystitis. This case highlights the importance of heightened awareness and preparedness for anaphylaxis during interventional oncology procedures.

CASE PRESENTATION

A 71-year-old woman with a medical history of coronary artery disease (status post placement of two coronary stents), hypothyroidism, diabetes mellitus, and hepatocellular carcinoma (was on tyrosine kinase inhibitor-lenvatinib) presented for one week history of epigastric and right upper quadrant pain, along with postprandial nausea and vomiting. The patient also reported being allergic to intravenous iodinated contrast, characterized by a self-resolving mild skin rash after previous exposure. Abdominal ultrasound **(Figure 1)** revealed acute cholecystitis, and the patient was planned for cholecystectomy. Preoperative transthoracic echocardiography (TTE) **(Figure 2)** showed a good left ventricular ejection fraction (60%-65%) with mild septal hypokinesia.

The patient underwent a laparoscopic cholecystectomy under general anesthesia. During the procedure, the surgeons began by dissecting Calot's triangle, followed by the introduction of iodinated contrast for intraoperative cholangiography (IOC) **(Figure 3)** to assess for any residual stones in the bile duct.

Within minutes, the patient developed tachycardia at a rate of 188 bpm, hypotension with a nadir of 80/56 mm Hg, mydriasis, and absence of brainstem reflexes. The ECG **(Figure 4)** revealed supraventricular tachycardia (SVT).

HIGHLIGHTS

1. Anaphylactic shock from intra-biliary contrast is a potentially fatal complication during IOC.
2. Consider alternative imaging techniques for those with high-risk preoperative allergic evaluations.
3. Awareness for signs of coagulopathy following contrast administration.

The operating room team promptly performed synchronized cardioversion to restore sinus rhythm and administered 300 mg of intravenous Amiodarone. Following this intervention, the SVT converted to atrial fibrillation, as shown in ECG 2.

The differential diagnoses considered included anaphylactic shock, septic shock, acute coronary syndrome, cerebrovascular accident, and pulmonary embolism. A postoperative TTE **(Figure 5)** showed a normal ejection fraction with no signs of myocardial ischemia. Additionally, echocardiography revealed no evidence of right ventricular strain, effectively ruling out pulmonary embolism. Moreover, CT brain was normal **(Figure 6)** and Echo Doppler venous lower limbs ruled out deep venous thrombosis. Further investigations, including a non-contrast abdominal computed tomography, excluded other potential causes such as biliary tract perforation and postoperative bleeding.

Considering the timing of IOC administration and the lack of alternative explanations, an anaphylactic reaction to the biliary iodinated contrast was deemed the most likely diagnosis, complicated by disseminated intravascular coagulation (DIC) at day 3 post-op.

TABLE 1 - Presents laboratory tests pre and post operatively

Lab test	Pre-Op	Post-Op (Day 1)	Post-Op (Day 2)	Post-Op (Day 3)	Post-Op (Day 4)	Post-Op (Day 5)	Post-Op (Day 6)	Post-Op (Day 8)	Post-Op (Day 10)
Cbc: Hg (12-15)	11.4	11.2	9.7	9.7	9.7	9	9	8.7	9
Wbcs (4-10)	4.15	10.88	12.27	12.63	11.37	9.1	7.96	7.37	8.96
Platelets (150-500)	172	226	134	63	28	48	62	88	155
Creatinine (0.4-1)	0.64	0.79	1.12	1.35	1.16	0.86	0.62	0.6	0.54
INR	1.18	1.21	1.44	2.99	3.07	2.41	1.57	1.32	1.13
Fibrinogen (200-400mg/dl)	-	388	320	177	181	-	210	-	-
D-Dimer (<500)	-	-	8068	3755	-	-	-	-	-
SGPT (<55)		38	106	140	166	100	54	41	24
SGOT (<55)		86	328	303	313	103	51	38	21
GGT (9-36)		421	535	605	703	683	689	633	389
Alk. Phos (40-150)		-	199	237	-	383	421	382	188
LDH (125-220)		307	734	603	589	242	218	195	-

The patient was transferred to the intensive care unit (ICU) for close monitoring. Upon admission, the patient received 0.3 mg of Adrenaline intramuscularly and 100 mg of Hydrocortisone intravenously, followed by 50 mg IV of Hydrocortisone every 6 hours. Intravenous antibiotics were initiated, including Amikacin 1 g, Vancomycin 2 g, and continued Meropenem at 1 g IV every 8 hours. Norepinephrine was also infused to maintain MAP > 65 mm Hg.

On the third postoperative day, Magnetic resonance cholangiopancreatography (MRCP) **(Figure 7)** was performed to investigate the persistently elevated cholestatic liver enzymes; however, the results were normal. Over the following days, the patient's clinical condition improved significantly. She was successfully extubated and weaned off vasopressors. Esophagogastroduodenoscopy was performed on day 6 post-op for persistent nausea, revealing candidal esophagitis and multiple gastric polyps. The patient was treated with antifungal agents and subsequently tolerated enteral feeding.

The pathology of the resected gallbladder confirmed chronic cholecystitis with multiple yellow stones and wall thickening.

DISCUSSION

This case represents only the third reported instance in the literature of anaphylactic shock following the administration of iodinated contrast into the biliary tree during intraoperative cholangiography (IOC), highlighting its rarity and potential lethality [4, 6]. While anaphylaxis is a recognized risk associated with intravenous iodinated contrast, its occurrence via non-vascular routes, such as the biliary system, is exceptionally rare. However, systemic absorption of contrast through the biliary tree can occur, particularly in the presence of inflammation, which may enhance vascular permeability and facilitate entry into the systemic circulation [7].

To date, only two prior cases have documented similar reactions. Moskovitz et al. described a case of anaphylactic shock following IOC during laparoscopic cholecystectomy in a patient with no prior intravenous contrast exposure, suggesting that biliary administration alone can trigger severe hypersensitivity reactions [4]. Although only available as an abstract, the report highlights the rapid onset of symptoms, including hypotension and respiratory distress, consistent with our patient's presentation [4]. Similarly, Ishiyama et al. reported an intraoperative allergic reaction to biliary contrast that progressed to disseminated intravascular coagulation (DIC), emphasizing the potential for severe systemic complications [6]. The abstract details a case where the reaction led to significant coagulopathy, mirroring the DIC observed in our patient on postoperative day 3 [6]. These cases, despite being limited to abstracts, underscore the clinical relevance and severity of anaphylactic reactions to biliary contrast, particularly in sensitized individuals.

The pathophysiology of anaphylactoid reactions to iodinated contrast media (ICM) involves non-IgE-mediated mechanisms, primarily through direct activation of mast cells and release of mediators such as histamine, prostaglandins, and bradykinins [8]. Inflammation in the biliary tree, as seen in acute or chronic cholecystitis, may exacerbate systemic absorption, increasing the risk of such reactions [7]. Recent studies suggest that some immediate reactions may involve IgE-mediated pathways, supported by elevated histamine and tryptase levels in affected patients [8]. In our case, the patient's history of a mild iodinated contrast allergy, combined with rapid cardiovascular collapse and laboratory evidence of DIC (e.g., elevated D-dimer, decreased platelets, and prolonged INR on day 3), strongly supports an anaphylactoid reaction complicated by coagulopathy.

The occurrence of DIC in this context is exceptionally rare. A review by Andreucci M et al. notes that iodinated contrast can trigger DIC through endothelial injury and activation of the coagulation cascade, particularly in patients with underlying inflammatory conditions [9]. The elevated D-dimer (8068 on day 2, 3755 on day 3) and decreased fibrinogen (177 mg/dl on day 3) in our patient align with this mechanism, suggesting that the anaphylactoid reaction may have initiated a systemic inflammatory response leading to DIC. The absence of other causes, such as sepsis or massive hemorrhage, further supports this association.

Management of anaphylactoid reactions requires immediate intervention. Epinephrine, administered intramuscularly, remains the cornerstone of treatment for systemic symptoms like hypotension and bronchospasm [5]. Our patient received 0.3 mg of adrenaline and hydrocortisone, with norepinephrine to support blood pressure, consistent with guideline-directed therapy. The subsequent development of DIC necessitated close monitoring and supportive care, including blood products if bleeding had occurred, though this was not required in our case.

To prevent such reactions, preoperative strategies are critical. Patients with a history of contrast allergy, even if mild, should be evaluated thoroughly. Premedication with corticosteroids and antihistamines is commonly used, but its efficacy is debated, as it does not eliminate the risk of severe reactions [5]. Alternative imaging modalities, such as intraoperative ultrasound, indocyanine green (ICG) fluorescence cholangiography, or preoperative magnetic resonance cholangiopancreatography (MRCP), offer safer options for visualizing the biliary tree [10]. ICG fluorescence, in particular, has gained attention for its safety profile and effectiveness in delineating biliary

anatomy without the risks associated with iodinated contrast [10]. Gadolinium-based agents, while used in some cases, carry their own risks and are not universally recommended for biliary imaging [11].

This case also highlights the need for surgical teams to maintain vigilance for rare complications like DIC. Monitoring for coagulopathy, including serial measurements of INR, fibrinogen, and D-dimer, is essential in patients with suspected anaphylactoid reactions to contrast. Future research should focus on identifying risk factors for such reactions and optimizing alternative imaging techniques to enhance patient safety during laparoscopic cholecystectomy.

CONCLUSION

Anaphylactic shock resulting from intra-biliary contrast administration is a rare but potentially fatal complication during IOC, particularly in patients with a known allergy to iodinated contrast, even those with only mild previous reactions. This case highlights the importance of thorough preoperative allergy evaluations, especially for high-risk individuals. It also underscores the need to consider alternative imaging techniques such as MRCP, intraoperative ultrasound, indocyanine green fluorescence cholangiography, or gadolinium-based agents to mitigate risk. Given the critical role of IOC in laparoscopic cholecystectomy, further research is warranted to develop strategies that minimize contrast-related risks and identify safer imaging options for vulnerable patients. Conversely, our case underscores another exceptionally rare adverse event linked to IOC: disseminated intravascular coagulation (DIC). While DIC is a recognized complication of iodinated contrast media, its occurrence following biliary administration is extremely rare and not well-documented in the literature. Clinicians should remain vigilant for signs of coagulopathy following contrast administration.

Keywords

Anaphylactic shock, Intra-op cholangiography, DIC

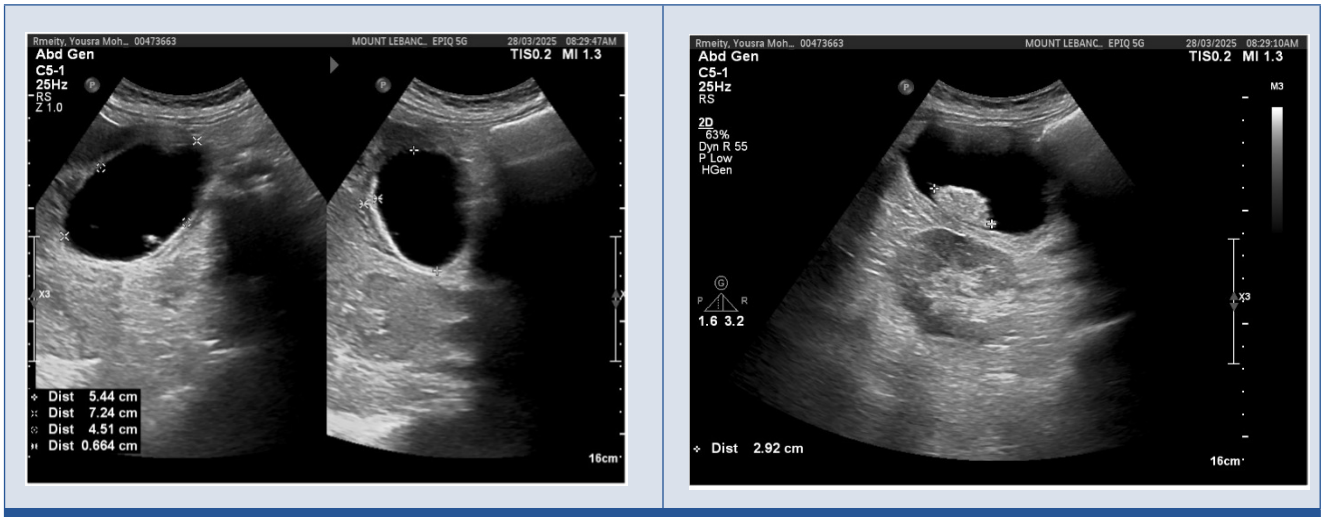

FIGURE 1 - The gallbladder is over-distended showing a large gallstone measuring up to 3 cm and multiple small calculi. It shows thickened walls measuring up to 1 cm and mild pericholecystic fluid. Findings are suggestive of acute cholecystitis

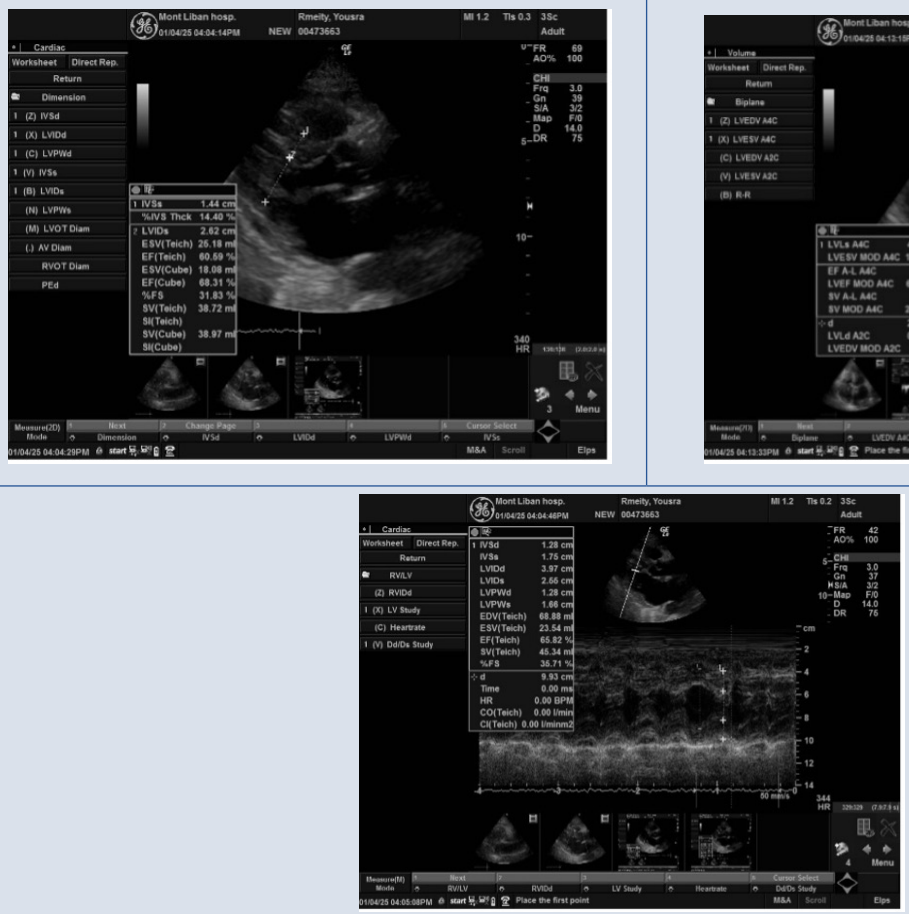

FIGURE 2 - Pre-operative TTE shows good systolic and diastolic left ventricular functions with estimated EF between 60% to 65%

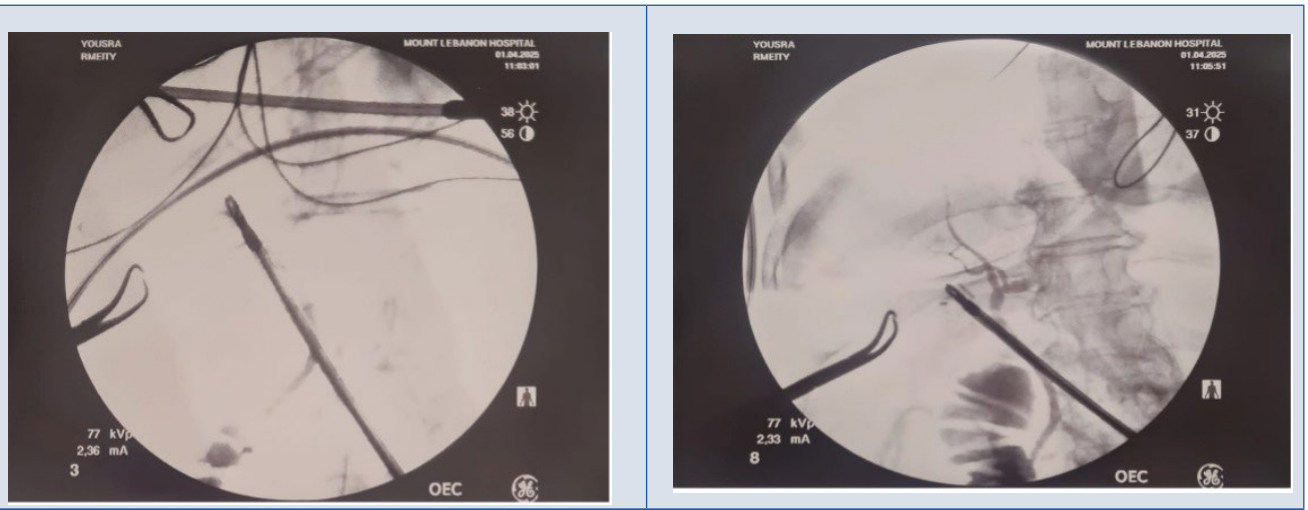

FIGURE 3 - Intraoperative cholangiography

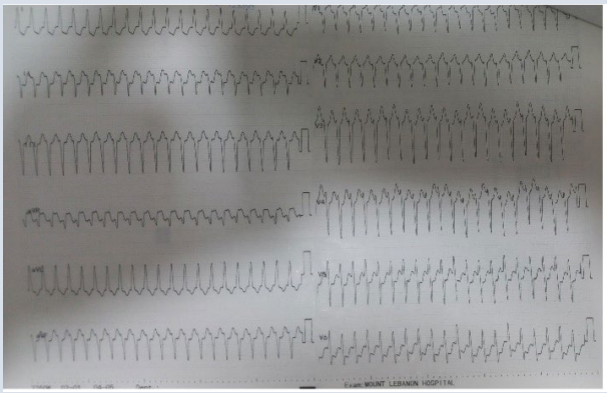

FIGURE 4 - ECG1: The ECG revealed supraventricular tachycardia (SVT)

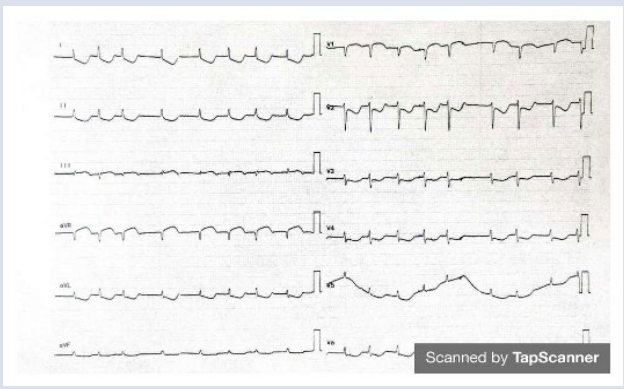

FIGURE 4 - ECG2: shows the SVT converted to atrial fibrillation, as shown in ECG 2

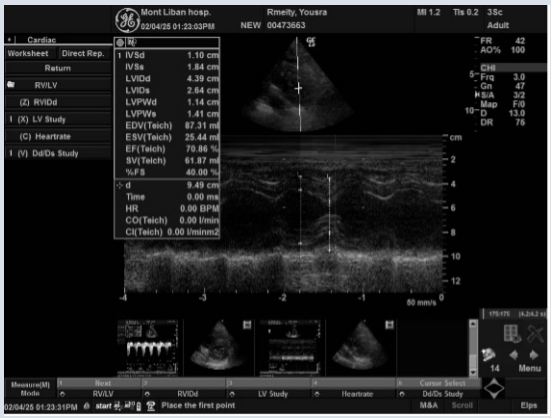

FIGURE 5 - Shows Post -operative TTE shows good systolic and diastolic left ventricular functions with estimated EF between 60%-70%

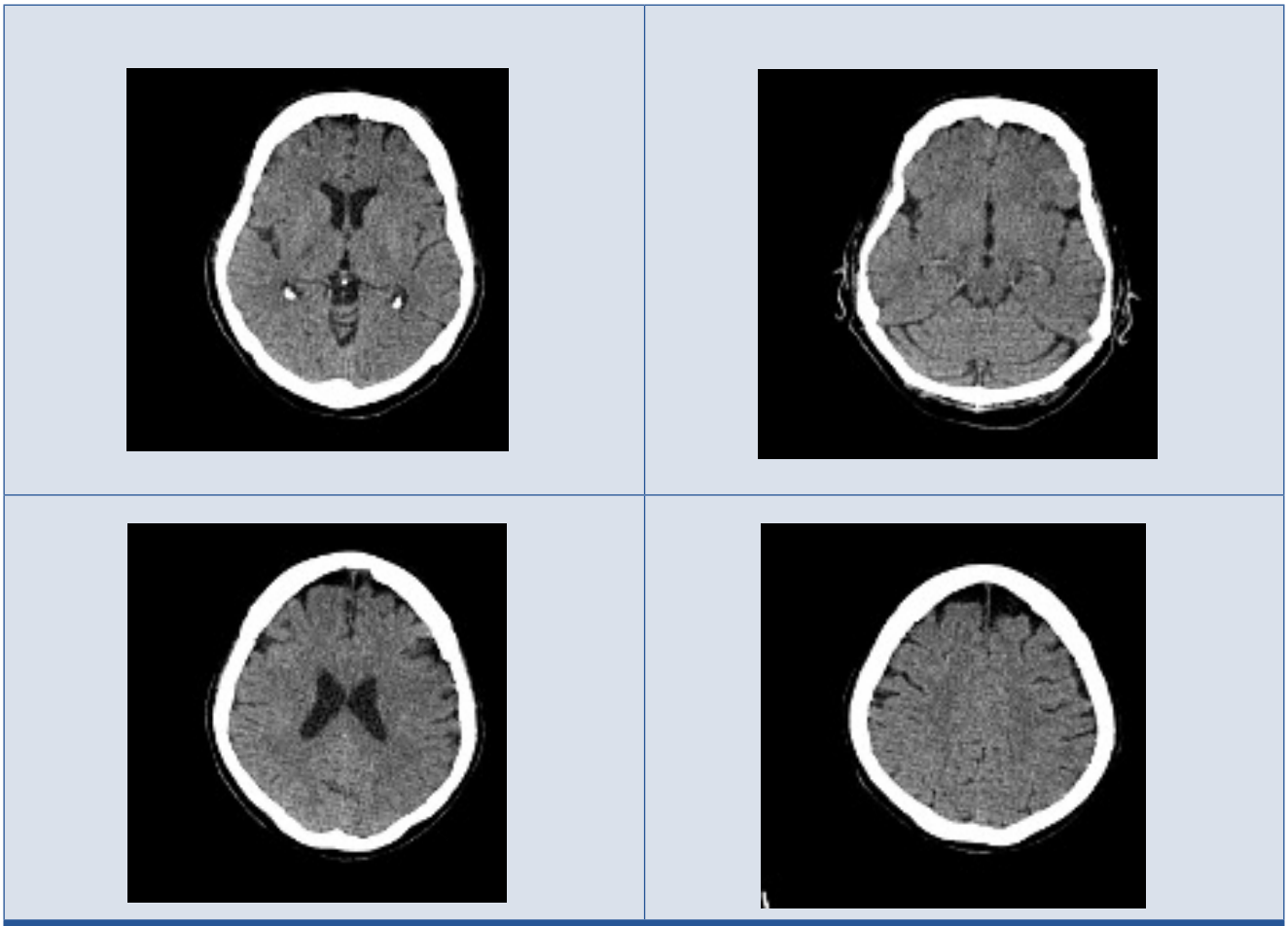

FIGURE 6 - Ct scan brain shows minimal age-related cortical atrophy with commensurate dilatation of the ventricles and subarachnoid spaces

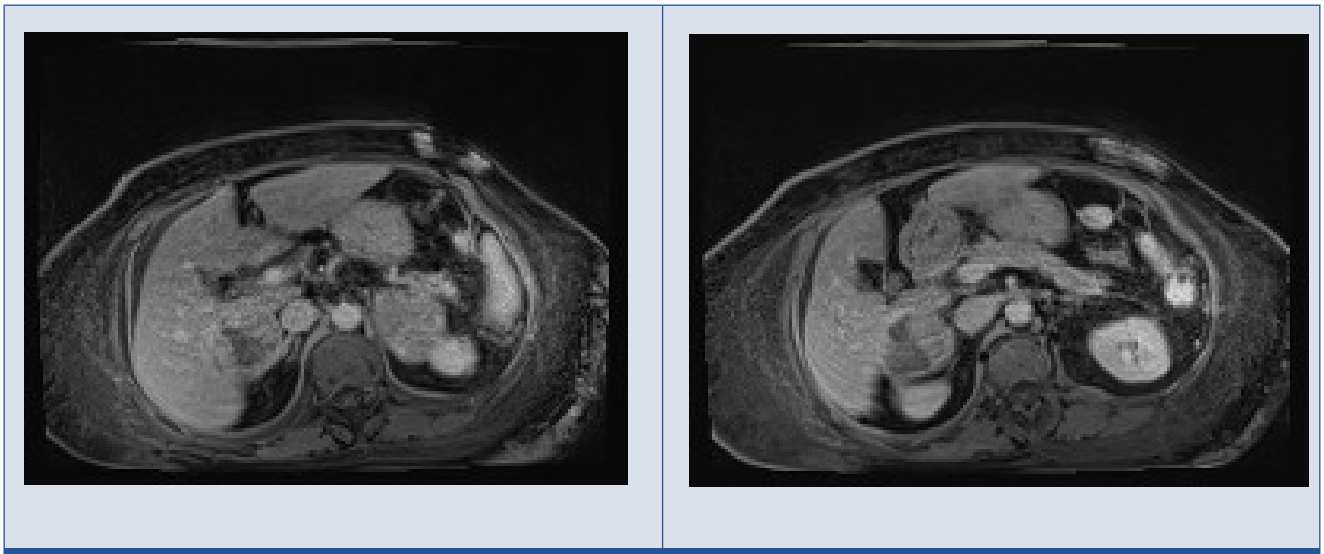

FIGURE 7 - MRCP shows no extra or intrahepatic bile duct dilation

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Author contributions

All authors contributed equally and validated the final version of record.

Declarations

Conflicts Of Interests

The Author declares that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Registration

No registration applicable.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical approval

Ethical approval for this study was not required.

Patient consent: authors confirmed that they have received patient consent to publish this case.

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