Ketamine induced cholangiopathy - a growing concern in the context of rising misuse

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Background

Ketamine is a widely used anaesthetic, analgesic, and antidepressant with dissociative, psychedelic, and stimulant properties that have driven increasing illicit oral and inhalational use. In the UK, ketamine misuse has risen sharply over the past decade, with a 231% increase in reported use among individuals aged 16–24 years since 2013. National data published in March 2024 demonstrate record levels of consumption, prompting renewed debate regarding potential reclassification of ketamine from a Class B to a Class A substance [1]. Increasing use has been accompanied by growing recognition of ketamine-associated uropathy and cholangiopathy, with characteristic imaging findings met in clinical practice.

While ketamine-induced bladder dysfunction is relatively well recognised among clinicians, ketamine-induced sclerosing cholangitis remains rare and poorly understood, warranting further attention.

Learning objectives:

By the end of this poster, you should be able to:

- Recognise imaging features of ketamine-induced cholangiopathy (KIC)
- Identify when to suspect ketamine misuse
- Understand how KIC mimics primary sclerosing cholangitis (PSC)
- Appreciate the diagnostic challenge

Case presentation

Patient A

A 22-year-old man with a history of ketamine misuse presented with persistently elevated cholestatic liver function tests (ALP 886 U/L, GGT 1230 U/L), urinary incontinence, dysuria, and bilateral flank pain. Additional laboratory findings included an eGFR of 33 mL/min, Creatinine 231, haemoglobin of 78 g/L, and a positive urine ketamine screen.

- Liver screening tests for viral, autoimmune and metabolic panels were normal. Other causes of secondary sclerosing cholangitis were excluded, with normal IgG4 levels, CA 19-9, and HIV serology.
- USS liver showed both intrahepatic and extrahepatic biliary duct dilatation.
- MRCP revealed – mild intrahepatic biliary duct irregularities of the peripheral ducts with associated CBD dilatation; features in keeping with early ketamine induced cholangiopathy.
- Patient managed with Whitmore solution instillation into the urinary bladder, follow up renal USS and MRCPs. He is counselled for drug use.

Patient B

A 32-year-old female with a 10-year history of ongoing ketamine use (approximately 2 g/day) presented with persistently elevated liver function tests (GGT 463, ALP 321, ALT 116). Urine ketamine testing was positive. Renal function was normal, and no urinary symptoms were reported.

- Comprehensive liver screening, including viral, autoimmune, and metabolic panels, were unremarkable. Other causes of secondary sclerosing cholangitis were excluded, with normal IgG4, CA 19-9, HIV serology, and alpha-1 antitrypsin levels. There was no evidence of coeliac disease or haemochromatosis.
- Ultrasound demonstrated normal liver and renal appearances.
- MRCP showed - dilated common bile duct (12 mm) with abrupt tapering at the ampulla, and a short stricture of the proximal left main intrahepatic bile duct with mild upstream dilatation.

Patient was scheduled for an ERCP for direct visualisation of the ampullary narrowing.

Metabolism and clinical symptoms

Ketamine is metabolised in the liver to nor-ketamine, which is the primary active metabolite excreted in the urine. Elimination therefore occurs predominantly via the renal route (90%), with a smaller proportion (10%) undergoing biliary excretion [2].

Consequently, its toxic effects most commonly involve the urinary tract followed by hepatobiliary system, with increasing recognition of these complications in chronic users (frequent, repeated use) [3].

Common presenting symptoms include abdominal pain, nausea, vomiting, urinary symptoms, and deranged liver function tests, with both the duration and cumulative dose of ketamine misuse directly influencing symptom severity and organ damage [2].

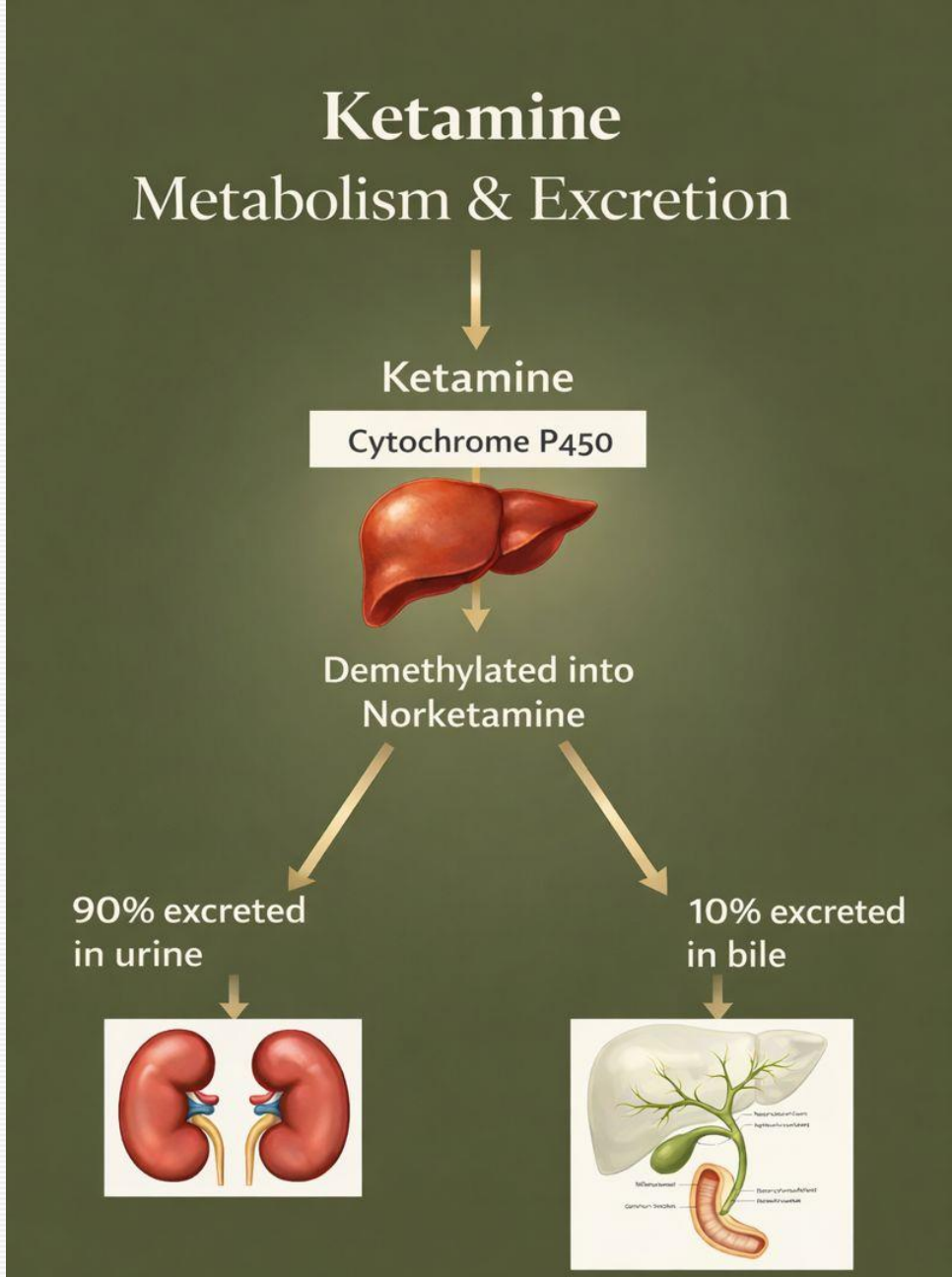


Fig. 1 Image generated using artificial intelligence and reviewed by the authors.

Ketamine induced hepatobiliary changes

Chronic ketamine misuse, typically over a period of around two years, has been associated with the development of a cholangiopathy resembling primary sclerosing cholangitis (PSC) [4]. Acute exposure may result in biochemical drug-induced liver injury, while prolonged or heavy use more commonly leads to cholangiopathy, presenting with abdominal pain, jaundice, and a cholestatic pattern of liver enzymes. On MRCP, multifocal intrahepatic and extrahepatic biliary strictures and dilatation are frequently seen in chronic users. Ketamine-induced cholangiopathy (KIC) also shares biochemical and histological features with PSC, making it a significant diagnostic challenge [5].

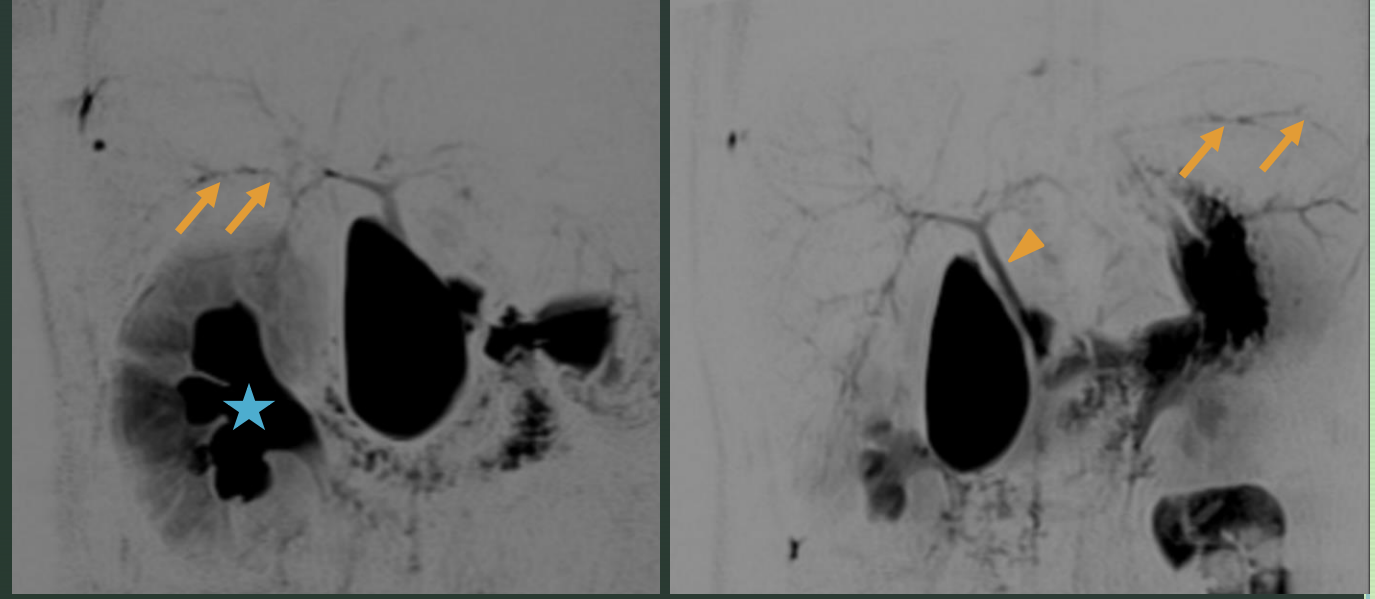


Fig. 2. (Patient A) Inverted and windowed 2D MRCP images demonstrating normal CBD (**arrowhead**), and irregularities of the distal intrahepatic biliary ducts (**arrows**) in keeping with features of early ketamine induced cholangiopathy. Note right hydronephrosis (**star**) associated with ketamine bladder (not shown).

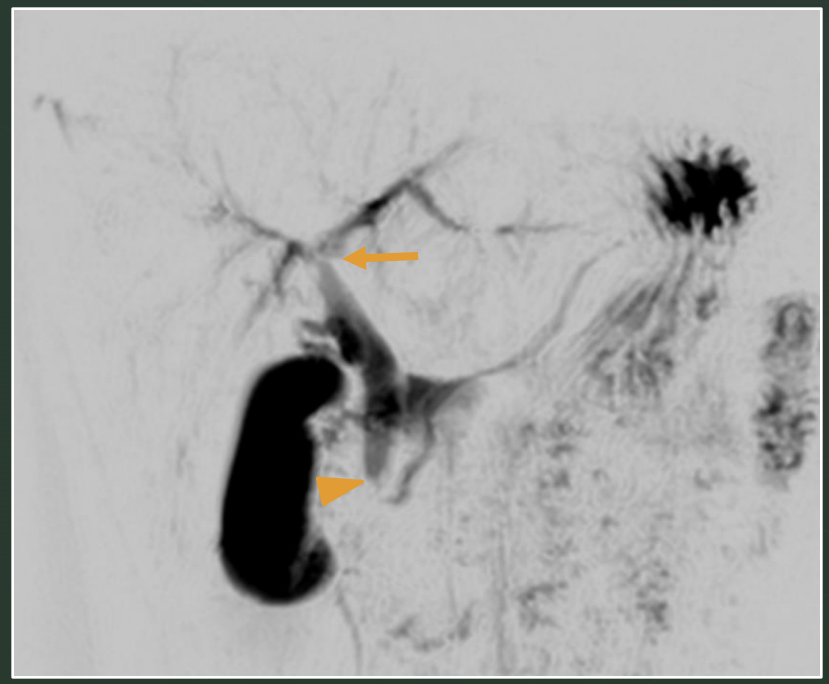


Fig. 3. (Patient B) Inverted and windowed 2D MRCP image demonstrating CBD dilatation with abrupt ampullary tapering, consistent with stricture (**arrowhead**), and proximal left intrahepatic duct stricture (**arrow**) at the hilum causing left ductal dilatation (not well demonstrated here).

KIC typical patient profile

- Young adult
- Cholestatic pattern: ↑ ALP, ↑ GGT ± ↑ ALT
- History of recreational ketamine misuse
- MRCP - biliary dilatation, irregularity, and/or strictures on imaging with no mechanical obstruction present
- No known inflammatory bowel disease or autoimmune disease
- Ketamine uropathy + new cholestatic LFTs = think ketamine-induced cholangiopathy.

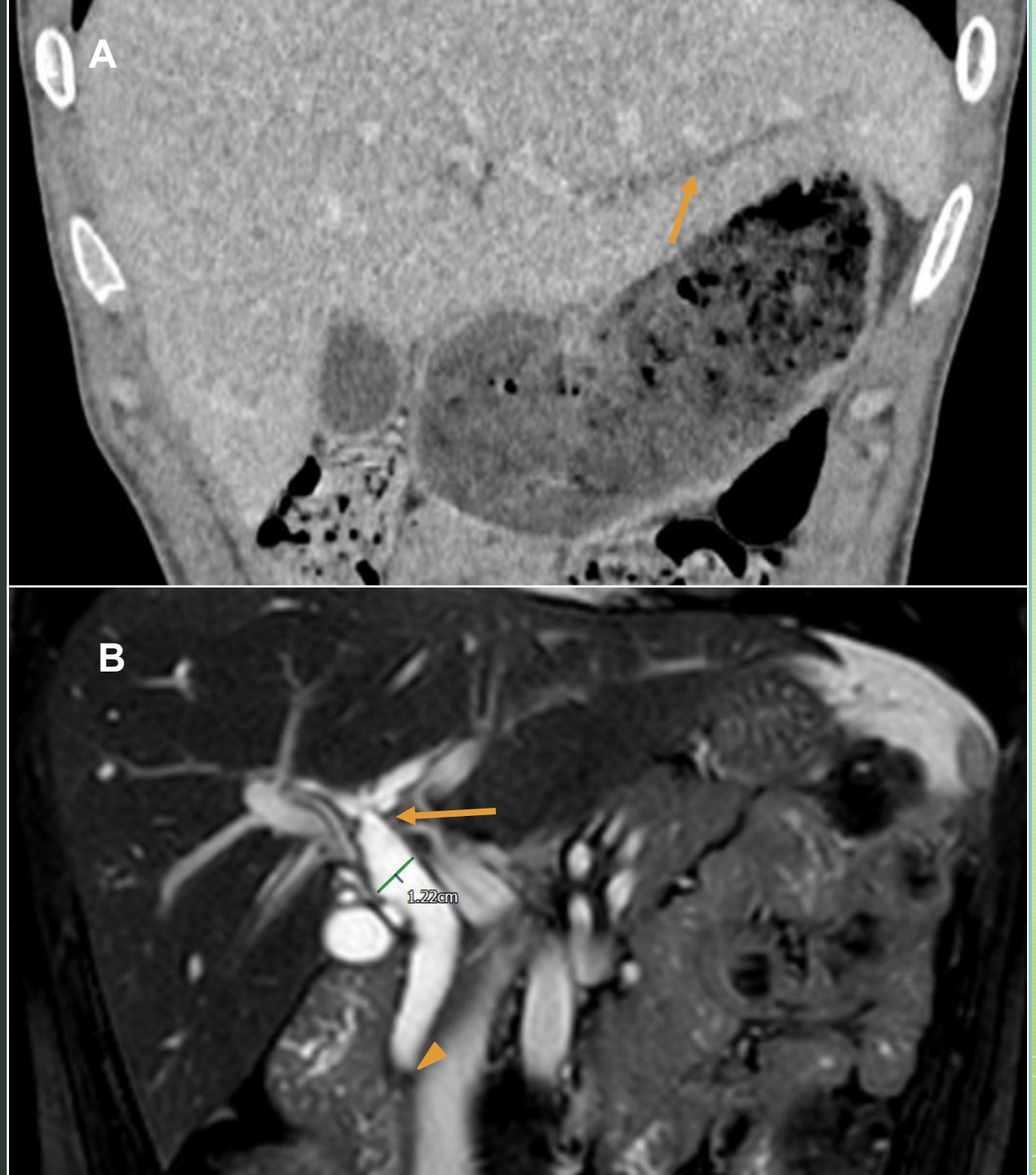
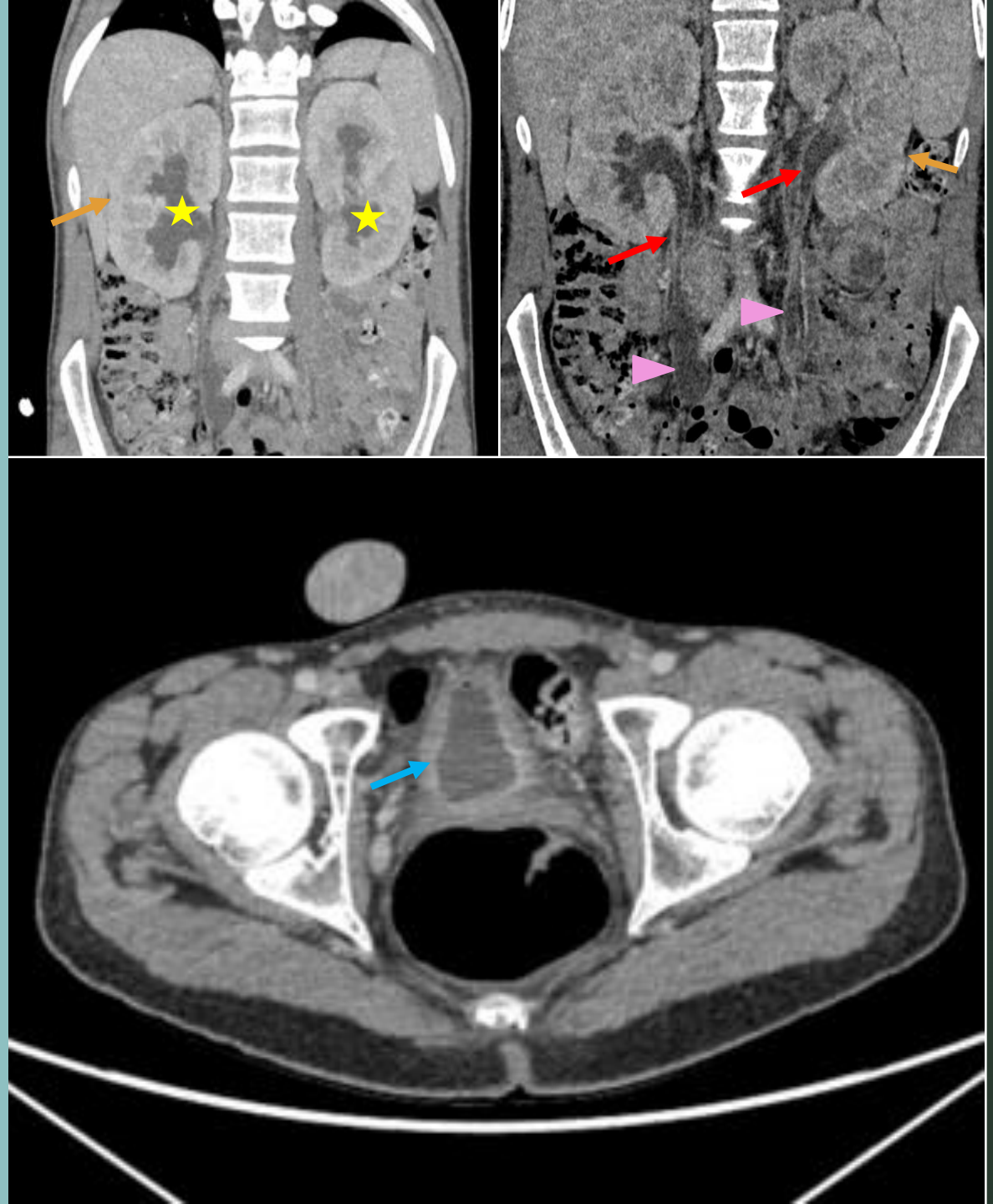


Fig.4 **A – patient A**, Coronal CT image of the liver demonstrates mild intrahepatic biliary duct dilatation (**arrow**), predominantly affecting left lobe of liver.
B – patient B, Coronal TSE sequence shows marked CBD dilatation at 12mm with abrupt distal tapering (**arrowhead**) and associated left hepatic duct dilatation due to a stricture at the hilum (**arrow**)



KIC and Ketamine bladder association

Ketamine-associated uropathy is a well-recognised complication of chronic misuse and should prompt consideration of ketamine-induced cholangiopathy in patients with newly deranged cholestatic liver function tests.

Fig.5 Demonstrated coronal and axial CT images of the abdomen for Patient A with bilateral hydronephrosis (**star**) and severe bilateral hydroureters (**arrowheads**). There is urothelial thickening and enhancement of the ureters (**red arrow**) and bladder (**blue arrow**) in keeping with ketamine induced uropathy. Several ureteric strictures (not shown) and renal cortical scarring is also present (**orange arrows**).

Differential diagnoses:

- Primary sclerosing cholangitis
- IgG4-related cholangitis
- HIV cholangiopathy
- Other causes for secondary sclerosing cholangitis (critically ill patients, ischaemic, iatrogenic)

PSC resemblance and diagnostic challenges

- Same stricture pattern
- Similar ductal irregularity
- Overlapping biochemistry
- Histological similarities

- Underreported drug history
- Imaging indistinguishable from PSC
- Biopsy often non-specific

***Pearl:**
Ask about ketamine use in young patients with PSC-like imaging.

KIC Reversibility?

The reversibility of ketamine-induced cholangiopathy following cessation remains uncertain in the published literature. Previous studies have reported a reduction in extrahepatic bile duct calibre and improvement in liver enzyme abnormalities following abstinence, particularly when cessation occurs early in the disease course [4,6]; however, consistent improvement in intrahepatic cholangiopathy has not been demonstrated. These findings suggest that established disease may be only partially reversible, particularly in the context of prolonged ketamine use.

Discussions and learning points:

- Ketamine-induced cholangiopathy is an increasingly recognised but still underdiagnosed cause of secondary sclerosing cholangitis.
- Patients may withhold a history of drug misuse, making radiologists a key link in raising suspicion
- It predominantly affects individuals with chronic recreational ketamine use with severity of symptoms being directly proportional with the dose, frequency and prolonged used.
- Imaging appearances closely mimic primary sclerosing cholangitis, creating a major diagnostic challenge
- A high index of suspicion is required for ketamine as an aetiology in cases of unexplained deranged liver function tests with or without radiological changes, particularly in younger people.
- Early recognition and cessation of ketamine are critical to prevent irreversible biliary damage.

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