

A rare cause of secondary cholangiopathy

Dr Frances Hughes, Dr Benjamin Rea
Sheffield Teaching Hospitals

Clinical history

52yr male

Background history of previous drug abuse-various substances

Presented to GP with new abdominal pain, urinary frequency and haematuria

Elevated LFTs on bloods

Referred for routine outpatient US scan

LFTs at presentation:

Total protein 70

Albumin 44

Globulin 26

Total bilirubin <3

Alkaline phosphatase 258

ALT 106

Ultrasound

- Diffuse hepatic steatosis with areas of focal fatty sparing
- No biliary dilatation
- Otherwise normal appearances of the abdominal and pelvic organs



One year later...

Admitted with worsening urinary symptoms and 3 stone weight loss within 6 months, nausea + vomiting

Tachycardic, raised neutrophils and suprapubic pain on palpation

Rising LFTs

LFTs:

Albumin 40

Total protein 73

Total bilirubin 12

Alkaline Phosphatase 984

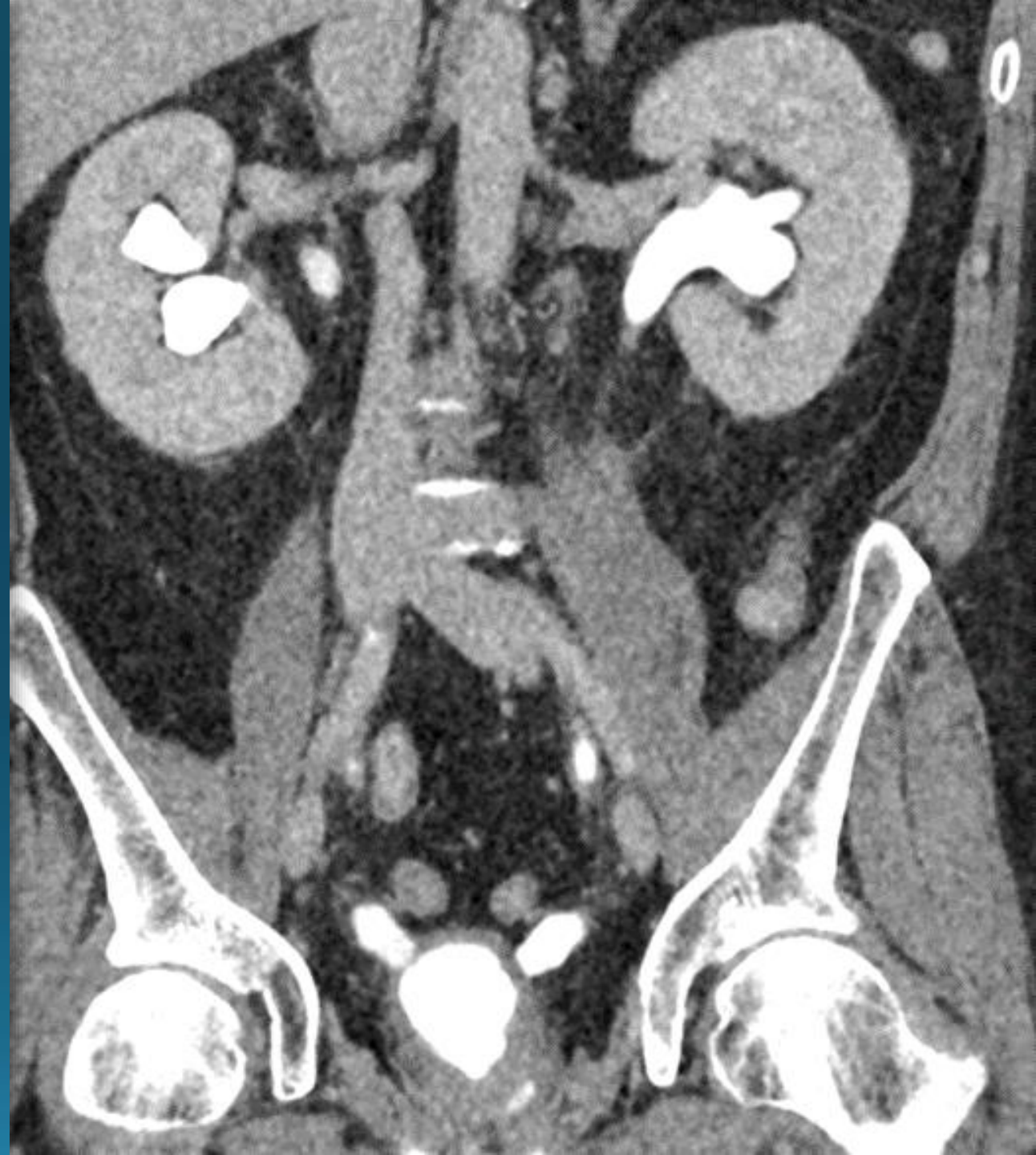
AST 419

ALT 770

GGT 2898

CT under urology team

- Bilateral hydronephrosis and hydroureter down to urinary bladder
- Thickening of ureters and urinary bladder
- Incidental partial duplex kidney on the right-proximal ureters fuse at L4.
- No other significant findings
- Proposed diagnosis-**Ketamine bladder**

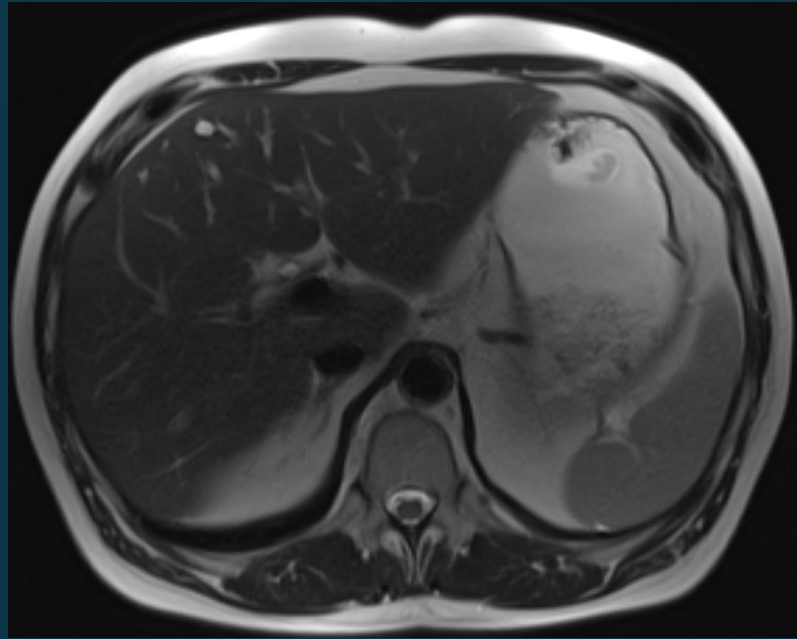


Next
steps...

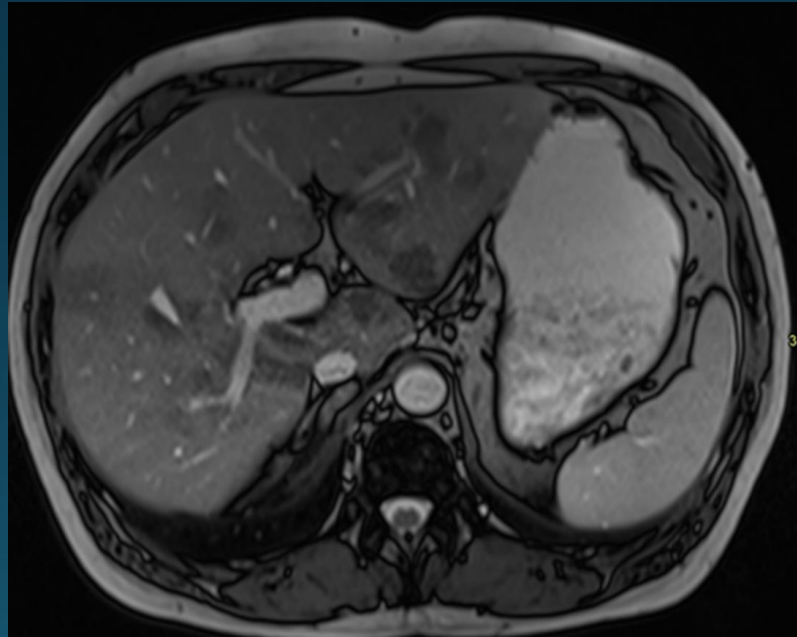
Outpatient cystoscopy with
biopsies confirmed chronic
inflammation

MRCP for further assessment
for rapidly rising LFTs and
on-going abdominal pain

MRCP

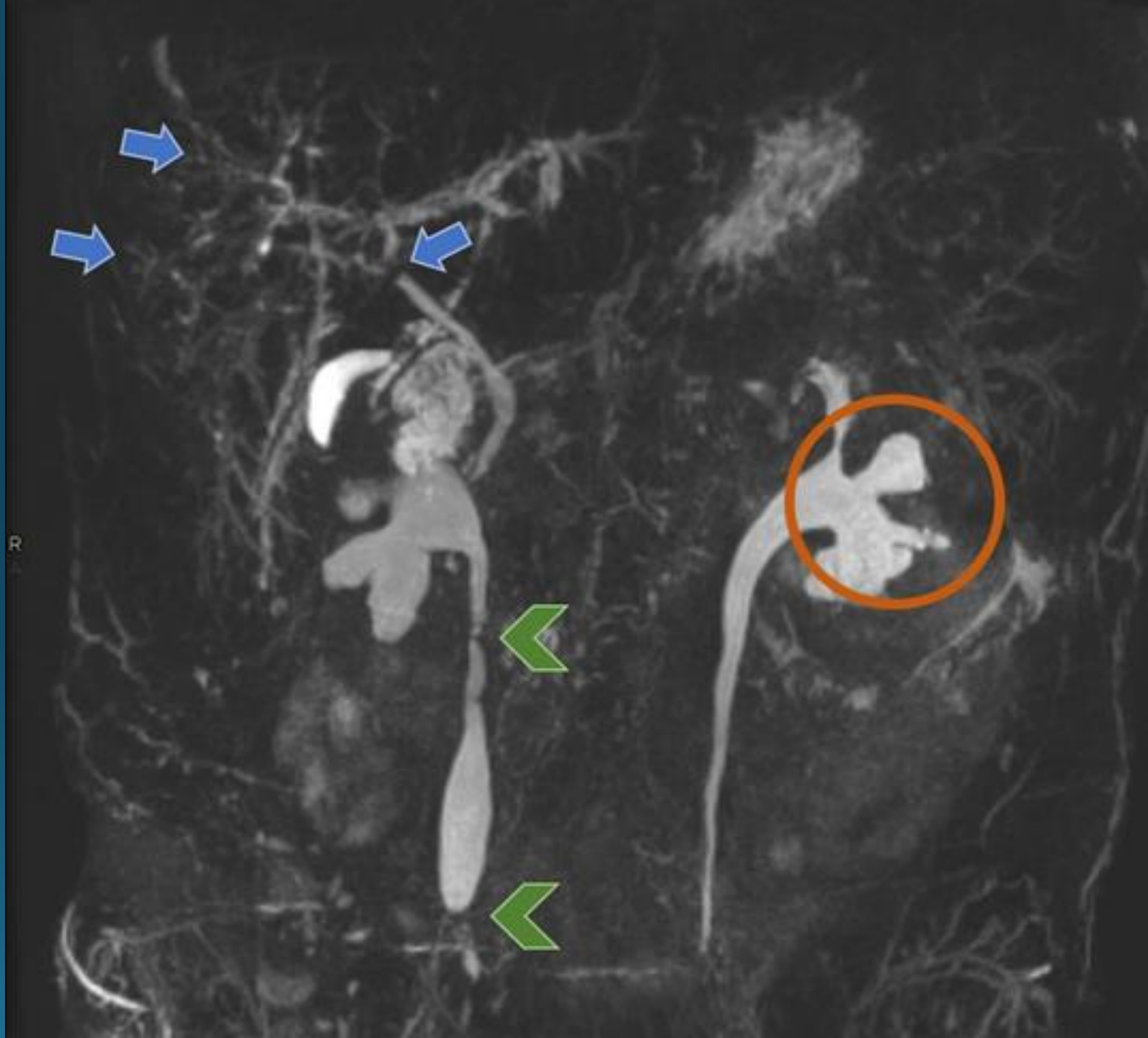


Axial T2-weighted MRI image
Dilatation of the peripheral
intrahepatic ducts



Axial T2 Trufi image
Diffuse background hepatic
steatosis

- Coronal T2-weighted MIP Image
- The biliary tree is grossly abnormal with irregular bile ducts and multifocal strictures within the intrahepatic bile ducts (blue arrows)
- Biliary appearances suggestive of PSC
- Ureteric strictures (green chevrons)
- Bilateral hydronephrosis (orange circle)



Diagnosis

Possibility of PSC (Primary sclerosing cholangitis) raised on MRCP however ketamine abuse listed as another potential cause

Patient seen by hepatology and disclosed a previous history of Ketamine abuse 20 years ago- successfully stopped for several years but restarted during Covid-19 lock-down due to anxiety.

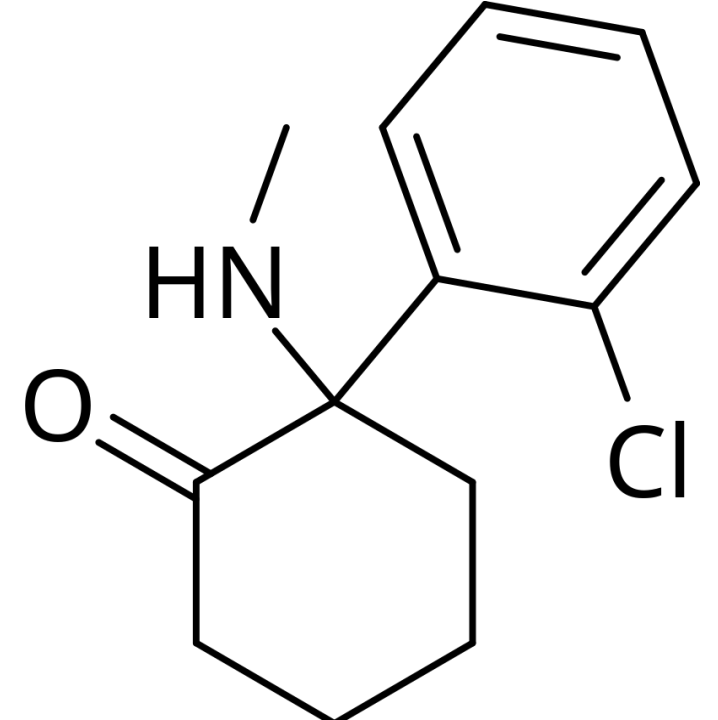
Patient discussed in Hepatology MDT meeting-Ketamine-induced cholangiopathy felt to be the most likely diagnosis

It was felt that any intervention to the strictures would be high risk and therefore supportive treatment including cessation of Ketamine abuse and mental health support was advised.

Literature review

Ketamine was developed in 1962-it is a NMDA receptor antagonist which can be used in induction and maintenance of general anaesthesia. When used recreationally the powder can be inhaled or taken orally to generate hallucinations and dissociative phenomena.

Ketamine is a rare cause of secondary cholangiopathy ^(1,2)

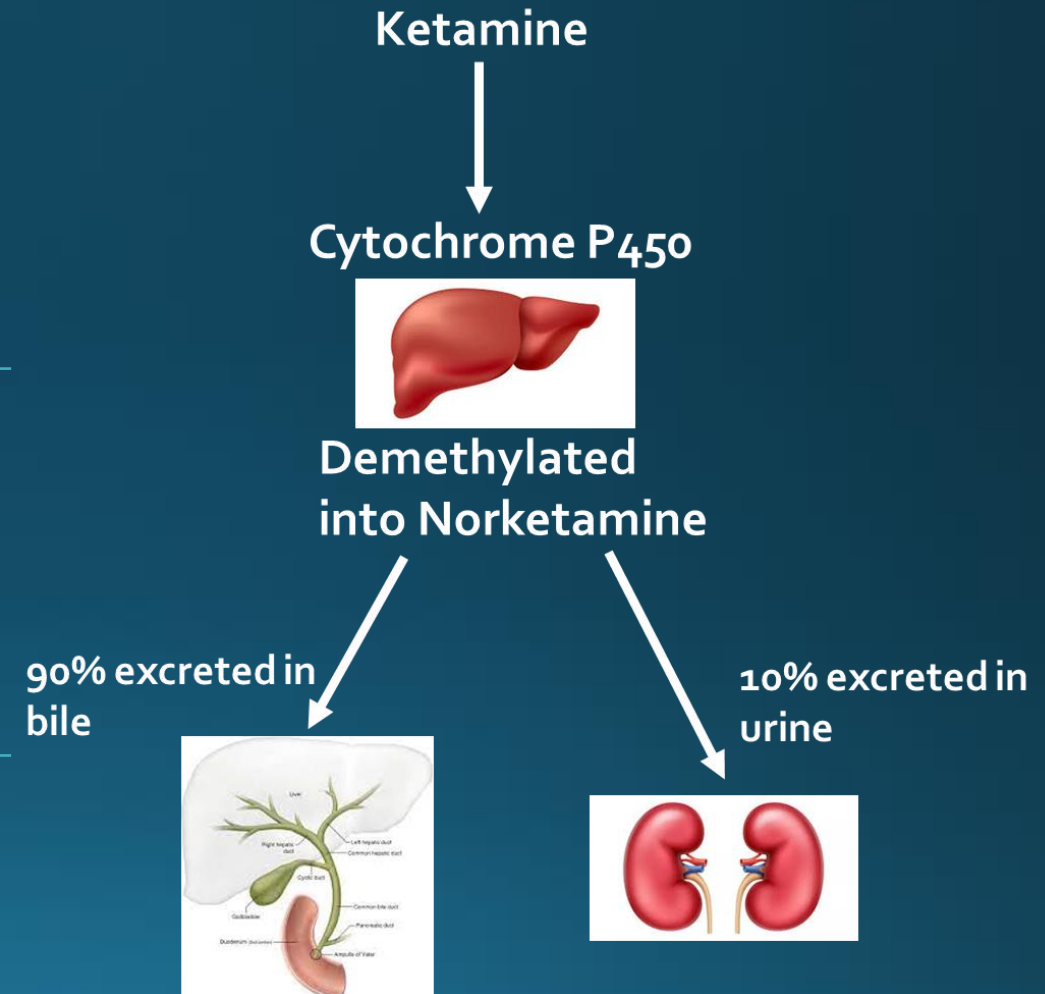


Literature review

Ketamine is metabolised by the cytochrome P₄₅₀ system in the liver and excreted predominantly in urine with the remainder through the biliary system. Therefore, pathology in both systems could be due to direct toxic injury to the epithelium ⁽⁶⁾.

It has also been proposed that the biliary dilatation may be due to increased flow resistance at the sphincter of Oddi ⁽³⁾. As animal studies have previously demonstrated this ⁽⁴⁾.

Ketamine-induced cholangiopathy usually affects drug users and burns patients. However, more recently it has been seen in ARDS/ COVID-19 patients who required mechanical ventilation with ketamine sedation ⁽⁵⁾.



Discussion and learning points

This case demonstrates the importance of having a detailed history including previous drug abuse when reporting studies demonstrating cholangiopathy-MDT meetings valuable for discussing these cases

Highlights the need to investigate abnormal LFTs/right upper quadrant pain in patients with ketamine bladder

Patients require early support from mental health/addiction teams to support medical therapy as cessation of drug taking is the main intervention though to benefit these patients

Awareness of the possibility of this diagnosis in Burns patients and those with previous episode of ARDS

References

1. Seto WK, Mak SK, Chiu K, Vardhanabhuti V, Wong HF, Leong HT, Lee PSF, Ho YC, Lee CK, Cheung KS, Yuen MF, Leung WK. Magnetic resonance cholangiogram patterns and clinical profiles of ketamine-related cholangiopathy in drug users. *J Hepatol.* 2018 Jul;69(1):121-128. doi: 10.1016/j.jhep.2018.03.006. Epub 2018 Mar 16. PMID: 29551711.
2. Al-Nowfal A, Al-Abed YA. Chronic biliary colic associated with ketamine abuse. *Int Med Case Rep J.* 2016 Jun 2;9:135-7. doi: 10.2147/IMCRJ.S100648. PMID: 27330331; PMCID: PMC4898409.
3. Wong SW, Lee KF, Wong J, Ng WW, Cheung YS, Lai PB. Dilated common bile ducts mimicking choledochal cysts in ketamine abusers. *Hong Kong Med J.* 2009 Feb;15(1):53-6. PMID: 19197097.
4. Thune A, Jivegård L, Pollard H, Moreau J, Schwartz JC, Svanvik J. Location of enkephalinase and functional effects of [Leu5]enkephalin and inhibition of enkephalinase in the feline main pancreatic and bile duct sphincters. *Clin Sci (Lond).* 1992 Feb;82(2):169-73. doi: 10.1042/cs0820169. PMID: 1311654.
5. Wendel-Garcia PD, Erlebach R, Hofmaenner DA, Camen G, Schuepbach RA, Jüngst C, Müllhaupt B, Bartussek J, Buehler PK, Andermatt R, David S. Long-term ketamine infusion-induced cholestatic liver injury in COVID-19-associated acute respiratory distress syndrome. *Crit Care.* 2022 May 23;26(1):148. doi: 10.1186/s13054-022-04019-8. PMID: 35606831; PMCID: PMC9125956.
6. Lin F, He Y, Zhang L, Zhang M, Zhang Y, Wen C. Assessment of the effect of ketamine on cytochrome P450 isoforms activity in rats by cocktail method. *Int J Clin Exp Med.* 2015 Mar 15;8(3):4335-41. PMID: 26064350; PMCID: PMC443184.