MEDICAL PRACTICE

Dilated common bile ducts mimicking choledochal cysts in ketamine abusers

EXPEDITED PAPER

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Substance abuse is a major health and social problem among Hong Kong youth and ketamine is the drug most commonly abused. Ketamine abuse is associated with a series of side-effects that include hallucination, nausea, vomiting, elevation of blood pressure, and urinary bladder dysfunction. Here we report three cases of ketamine abuse in which the abusers presented with recurrent epigastric pain and dilated common bile ducts that mimicked choledochal cysts on imaging. The dilated biliary tree may occur more frequently than was once assumed.

Introduction

Ketamine abuse is very common among Hong Kong youth. Data from the Central Registry of Drug Abuse (CRDA) in 2007[1] showed that ketamine was the drug most commonly abused by those below the age of 21 years. Overall, it is the second most commonly abused drug in Hong Kong. Once thought to be a 'safe' drug for abuse due to the absence of physical dependence, ketamine is now known to be associated with bladder dysfunction when abused[2-4] but its effect on the biliary tree has been largely ignored. In the past 6 months, three ketamine abusers have presented to our institution with epigastric pain and radiological features—dilated common bile ducts—that mimicked choledochal cysts. This suggests that ketamine has significant effects on the hepatobiliary system.

Case reports

Case 1

A 21-year-old woman presented to us in May 2008 with recurrent epigastric pain. She had a history of ketamine abuse (around once per 1 to 2 months) for 18 months, and complained of recurrent colicky epigastric pain in the past year, especially after taking ketamine. Gastroscopy showed mild antral gastritis only. Liver function tests performed on admission showed elevated alkaline phosphatase (ALP) level (122 IU/L) and alanine aminotransferase (ALT) levels (333 IU/L), and a normal bilirubin level (14 μmol/L). An ultrasound scan revealed a dilated common bile duct with a normal gall bladder. Subsequent computed tomography (CT) showed fusiform dilatation of the entire length of the common hepatic and bile duct up to 9 mm in diameter, which tapered smoothly to the pancreatic head. No gross obstructive lesions were seen on the CT scan. These clinical features were suggestive of a choledochal cyst. In view of the raised liver enzymes and abnormal CT findings, an endoscopic retrograde cholangiopancreatogram (ERCP) was arranged.

The ERCP showed a dilated common bile duct with a smooth tapered end (Fig 1a). A nasobiliary drain was inserted for biliary drainage. During this particular admission, the patient volunteered her lower urinary tract symptoms and admitted her history of ketamine abuse. Her symptoms and liver function gradually improved and the nasobiliary drain was removed. A surgical procedure that had been planned initially was cancelled and the patient ceased abusing ketamine after discharge. A follow-up magnetic resonance cholangiopancreatogram (MRCP) 3 months later showed resolution of the common bile duct dilatation, with the mid-common bile duct measuring 4 mm in diameter (Fig 1b). The patient's liver function had also returned to normal. Unfortunately, she took ketamine again in September and was admitted for epigastric pain. Once again her blood tests showed abnormal liver function with an elevated ALP (158 IU/L), although the ALT and the bilirubin levels were normal. She was treated conservatively and her symptoms subsided soon after admission. A further ultrasound examination revealed no dilatation of the common bile duct or the intrahepatic ducts.

Case 2

A 27-year-old man who had been abusing ketamine around twice a week for 2 years

Key words
Choledochal cyst; Common bile duct diseases; Dilatation, pathologic; Ketamine; Sphincter of Oddi dysfunction

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氯胺酮濫用者擬似膽管囊腫的膽總管擴張

濫用藥物是香港青年一個主要的健康及社會問題，而氯胺酮是其中一種最普遍被濫用的藥物。濫用氯胺酮與一連串副作用有關，如產生幻覺、噁心、嘔吐、血壓上升，以及膀胱功能失調。本文報告三宗濫用氯胺酮的病例。濫用者出現反複性上腹痛，和擬似膽管囊腫的膽總管擴張。

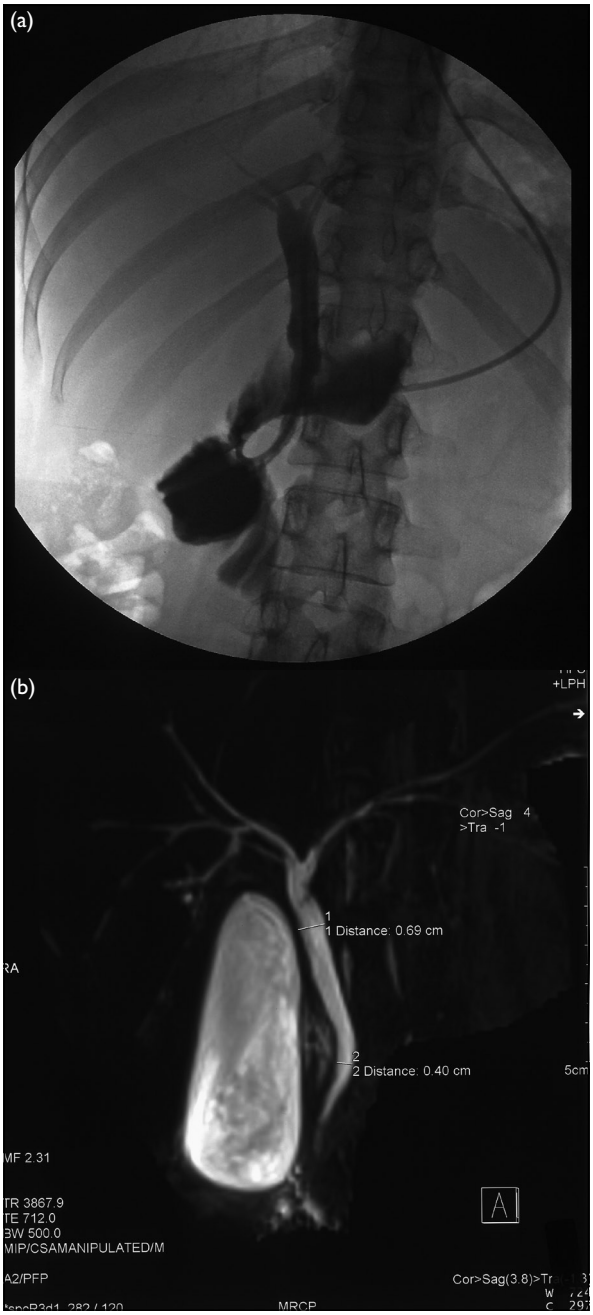

FIG 1. (a) Fusiform dilatation of the common hepatic and bile duct with minor irregularity shown on cholangiogram via the nasobiliary drain; and (b) magnetic resonance cholangiopancreatogram taken after cessation of ketamine abuse for 3 months, showing resolution of biliary tree dilatation

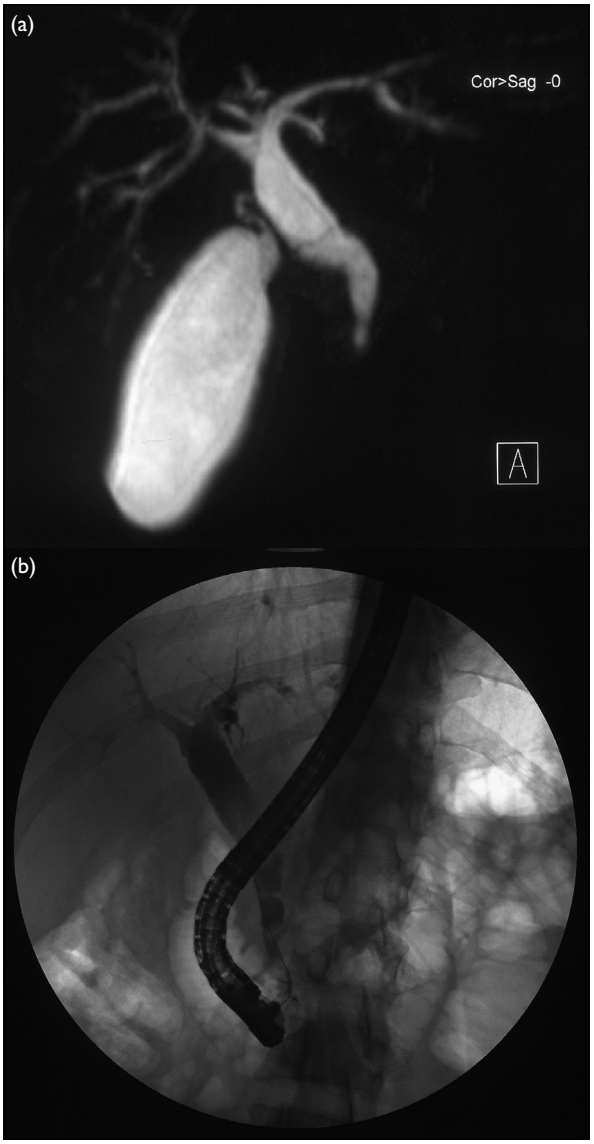

FIG 2. Films of (a) magnetic resonance cholangiopancreatogram showing fusiform dilatation of the common hepatic and bile duct; and (b) endoscopic retrograde cholangiopancreatogram showing slight decrease in the size of the common bile duct with a short segment of stricture at the distal common bile duct

complained of recurrent epigastric pain during that period and presented to a private hospital in Hong Kong in April 2008. Gastroscopy showed mild gastric erosion only, and a CT scan revealed a common bile duct dilated up to 17 mm in diameter, with no underlying obstructive lesion. A subsequent MRCP scan showed fusiform dilation of the common hepatic and bile duct (Fig 2a). The gall bladder was unremarkable and there was no sign of biliary obstruction. The overall picture was suggestive of a choledochal cyst.

On referral and admission to our institution, the patient's liver function was abnormal with raised ALP (137 IU/L) and ALT (75 IU/L) levels, although his bilirubin level was normal (7 μmol/L). An ERCP was performed and it showed a dilated common

bile duct with a short-segment distal common bile duct stricture. A plastic biliary stent was inserted for temporary drainage. Biliary tree brush cytology did not find any malignancy. The patient stopped abusing ketamine for 4 months and claimed a marked decrease in his epigastric pain. A repeat ERCP done in November 2008 showed a decrease in the size of the common bile duct, with a short-segment ring-like stricture at the distal common bile duct (Fig 2b). The biliary stent was removed and a free flow of bile was noted at the end of the procedure. The patient was discharged, and at follow-up it was noted that there was no further epigastric pain after the cessation of ketamine abuse.

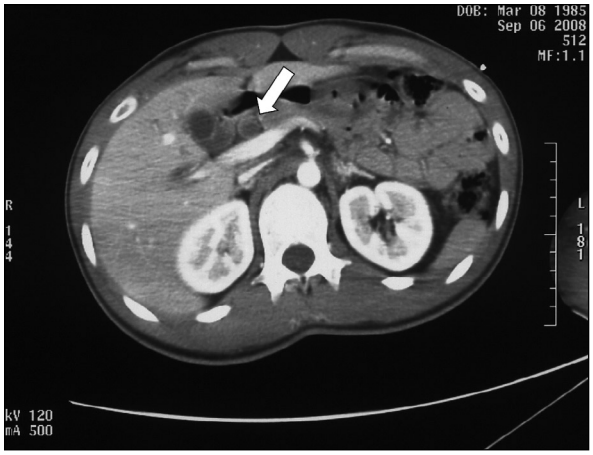

FIG 3. Computed tomographic film showing a dilated common bile duct (white arrow), measuring 11.2 mm in diameter

Case 3

The patient in the third case was a 23-year-old man who had been a chronic ketamine abuser from the age of 16 years. For most of that time he usually took ketamine once per week but for 3 months before admission he had inhaled ketamine almost every day. This patient presented to us in September 2008 with injuries caused by a fall from a height after taking ketamine. He had fractures of the left humerus, femur, and pelvis, managed with internal and external fixation. On admission, an urgent contrast CT scan was performed for a suspected intra-abdominal injury. The scan did not reveal any such injury, but the common hepatic duct and bile duct was found to have fusiform dilatation of up to 11.2 mm in diameter, which tapered distally to the pancreatic head (Fig 3). Again, no obstructing lesion was found upon CT scan. His liver function tests were normal on admission.

After being stabilised, the patient gave a detailed medical history. He had suffered occasional colicky epigastric pain in the past few years, and described an increase in that pain after taking ketamine; the pain would decrease when he temporarily ceased abusing the drug. The patient also described symptoms of ketamine-associated cystitis. In view of his normal liver function, he was treated conservatively and a follow-up ultrasound scan was arranged.

Discussion

Ketamine was developed by Parke-Davis in 1962 for use in anaesthesia. It is an N-methly-D-aspartate receptor antagonist, which can be used for the induction and maintenance of general anaesthesia, especially in paediatric anaesthesia. 'Street ketamine' (phencyclidine, a close analogue of ketamine but with a longer half-life) is now commonly abused for its intense psychotomimetic effects (hallucination and 'out of body' experiences). It is metabolised by hepatic microsomal enzymes and excreted in urine and bile.[5-8] The short-term side-effects include increases in heart rate and blood pressure, impaired attention, and even respiratory depression at high doses. Due to the absence of any physical withdrawal syndrome, ketamine is now the drug of choice among youth attending rave parties and other social gatherings.[1] It is now recognised that ketamine abuse is associated with cystitis and bladder dysfunction; the proposed mechanism is direct toxicity of ketamine metabolites on the urinary tract.[2-4] As ketamine is metabolised in the liver and excreted in bile, we postulate that this may be the reason for the dilation of the common bile duct that we observed.

Indeed, in a previous case series of 10 ketamine abusers with bladder dysfunction,[2] all 10 patients suffered from various degrees of liver function abnormality and seven of them had epigastric pain. As in our series, the abnormal liver function patterns mainly involved elevation in ALP and ALT levels. None of our patients were hepatitis B or C carriers. Their experiences suggest that their epigastric pain and abnormal liver function were associated with their intake of ketamine, as the symptoms improved after the cessation of ketamine abuse. Hence, the epigastric pain and impaired liver function seem to be reversible. The elevation in the liver enzymes may be caused by the hepatotoxicity of repeated ketamine abuse, as shown in an animal study.[9]

The biliary dilatation pattern seen in our series was uniform, with fusiform dilatation of the entire common hepatic and bile duct. Radiologically, it resembles Todani's type Ic choledochal cyst (diffuse fusiform dilatation of the common hepatic and bile duct).[10,11] In our cases, the maximal diameter of the dilated common bile duct ranged from 9 to 17 mm, whereas the mean common bile duct diameter in normal young adults is around 3.1 mm.[12,13] A similar case of ketamine abuse has been reported by Selby et al.[14] A 26-year-old male with ketamine-associated nephropathy was found to have abnormal liver function and a dilated common bile duct on

ultrasound, which resolved after cessation of his ketamine abuse. Nevertheless, the authors did not place any emphasis on the dilated biliary tree because they were focusing on nephropathy.

The reason for the biliary tree dilatation is unknown. It is not clear whether it is caused by dysfunction in the sphincter of Oddi or the formation of a benign biliary stricture. An animal study has shown that ketamine increases the flow resistance across the sphincter of Oddi, via the activation of opiate receptors on the sphincter.[15] Conversely, a recent study in humans showed that the use of low-dose ketamine for sedation in endoscopy did not significantly alter the phasic wave amplitude, duration, or frequency of the sphincter of Oddi.[16] Furthermore, none of our patients had histories of opiate abuse.

From the clinician's point of view, the drastic radiological features may cause diagnostic confusion when managing these young patients. The clinical picture of recurrent epigastric pain, abnormal liver function, and a dilated common bile duct on imaging matches that of a choledochal cyst. Misdiagnosing this condition as a choledochal cyst may lead to unnecessary investigations or even an operation. It is essential to identify the cause of the symptoms and radiological findings in these patients correctly, as the biliary tree dilatation may resolve completely after cessation of ketamine abuse. In addition, because the long-term effects of ketamine abuse on the hepatobiliary system are still unknown, clinicians should be mindful of the possibility of ketamine abuse in patients presenting with biliary tree dilatation. Furthermore, the general public needs to be made aware of this particular harmful side-effect of ketamine abuse.

Conclusion

Ketamine is absolutely not a 'safe' drug for abuse. It is not only associated with cystitis and urinary bladder dysfunction, but is also associated with liver function impairment and biliary tree dilatation. Although the effects seem to be reversible on cessation of abuse, clinicians should also be mindful about the possible long-term consequences for the hepatobiliary system.

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