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## ORIGINAL ARTICLE

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# Ketamine-related Urological Complications: Radiological Features

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### ABSTRACT

**Objective:** To describe the radiographical features of patients with ketamine-related urological complications.

**Methods:** All ketamine users who presented to the Urology Division of our hospital during June 2006 to July 2009 were included in this study. Investigations including renal function test, ultrasound, intravenous urogram, micturating cysto-urethrogram, antegrade pyelogram, renal scintigraphy, and computed tomography were performed as appropriate. Their medical records, radiological reports, and corresponding images were reviewed.

**Results:** A total of 36 patients were included in this study, in which 19% had bilateral hydronephrosis, 8% had unilateral hydronephrosis, and 72% of the patients had no hydronephrosis. Moreover, 6% of the patients with bilateral hydronephrosis had renal stones, and 6% had increased renal parenchymal echogenicity on ultrasound; 11% of patients had episodic or continuously elevated serum creatinine levels. Bilateral ureteral narrowing was demonstrated in 14% of the patients, and features of cystitis were documented in 39%. Bladder stones were detected in 6% of patients, and 11% had a percutaneous nephrostomy.

**Conclusion:** Ketamine abuse can lead to irreversible damage to the urinary tract, causing cystitis, urinary tract stones, hydronephrosis, renal parenchymal disease, and renal failure. Radiological investigations such as ultrasound and intravenous urogram have an important role in the assessment of these complications. Percutaneous nephrostomy offers relief of significant urinary tract obstruction.

**Key Words:** Cystitis; Hydronephrosis; Ketamine; Substance-related disorders; Urologic diseases

## 中文摘要

### 與氯胺酮有關的泌尿系統併發症：放射影像學特徵

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**目的：**描述與氯胺酮有關的泌尿系統併發症的病人的放射影像特徵。

**方法：**2006年6月至2009年7月期間，所有到本院泌尿科應診的氯胺酮濫用者都納入研究範圍。替病人進行的檢查包括有腎功能測試、超聲、靜脈尿路造影、排尿式膀胱尿道造影、逆行腎盂造影、腎核醫學閃爍造影及CT。回顧病人的病歷紀錄、放射學報告及有關圖像。

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Submitted: 14 Oct 2011; Accepted: 17 Feb 2012.

**結果：**本研究的36名病人中，19%有雙腎積水，8%有單腎積水，72%無腎積水。雙腎積水患者中6%有腎石，6%超聲有腎實質性迴聲增強，11%有間歇或不斷上升的血清肌酐水平。14%病人有雙側輸尿管收窄，39%有膀胱炎症狀。6%有膀胱石，11%接受經皮腎穿刺造瘻術。

**結論：**濫用氯胺酮可以對輸尿管道造成永久性傷害，引致膀胱炎、尿路結石、腎積水、腎實質性病及腎衰竭。影像檢查如超聲及靜脈尿道顯影對於檢查這些併發症很重要。此外，經皮腎穿刺造瘻術可以減輕尿路梗阻的病情。

## INTRODUCTION

Cases of ketamine-related cystitis have been reported in the literature in recent years. Presenting symptoms include frequency, urgency, dysuria, pelvic pain, urge incontinence, and haematuria. Quality of life and daily activities can be affected. Contracted bladder, detrusor overactivity, vesico-ureteric reflux, ureteric obstruction, hydronephrosis, and complications such as renal impairment and papillary necrosis have been reported.<sup>1</sup> The lower urinary tract is more commonly affected than the upper tract.<sup>1</sup> Upper urinary tract damage may be secondary to poor bladder compliance and vesico-ureteric reflux.<sup>1</sup> Our study aimed to document the radiological findings commonly encountered with ketamine-related urological complications.

## METHODS

This study was approved by the local ethics committee. Any patient who had consumed ketamine was considered a ketamine user. This study included all ketamine users who presented to the Urology Division of the Department of Surgery of our hospital for urinary tract symptoms during the period June 2006 to July 2009. Patients who had no documented radiological results or had defaulted follow-up were excluded. In all, 36 eligible patients were identified and their imaging findings were retrospectively reviewed.

Ultrasonography was performed on all patients. Other imaging studies included intravenous urogram (IVU),

**Table 1.** Imaging of patients.

Modality	No. of patients
USG	36
IVU	9
CT	13
Renal scintigraphy	2
Fluoroscopy	3

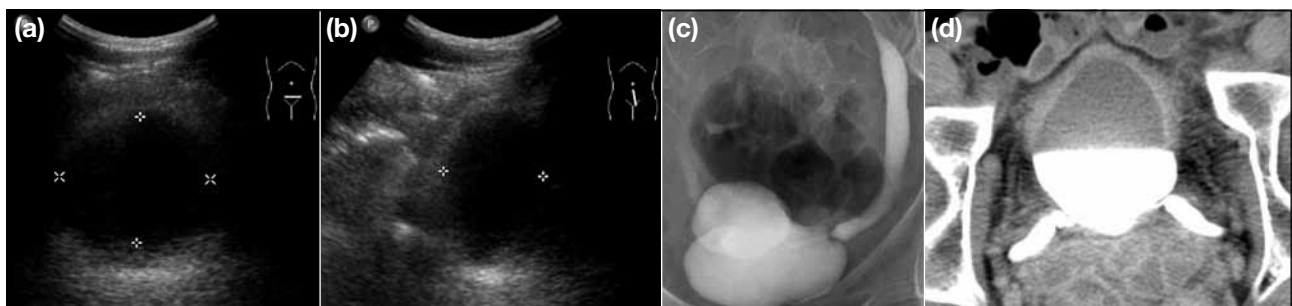
Abbreviations: USG = ultrasonography; IVU = intravenous urogram; CT = computed tomography.

**Table 2.** Imaging findings of patients.

Findings	No. of patients
No significant imaging abnormalities	9
Renal abnormalities	
Bilateral hydronephrosis*	7
Unilateral prominent renal pelvis <sup>†</sup>	3
Renal parenchymal disease	2
Renal stone	2
Ureteric abnormalities	
Bilateral ureteric narrowing	5
Bladder abnormalities	
Imaging evidence of cystitis	14
Bladder stone	2

\* Hydronephrosis is defined as renal pelvis anteroposterior diameter of >1 cm.

<sup>†</sup> Prominent renal pelvis is defined as renal pelvis anteroposterior diameter of <1 cm.



**Figure 1.** Ultrasonography (USG) and computed tomography (CT) images of different patients. (a and b) USG of the bladder in axial plane showing thickened bladder wall (6 mm) and small bladder volume of less than 50 ml. (c) Antegrade pyelogram examination showing a contracted bladder and tight stricture of the distal ureter. (d) Axial CT of the lower pelvis showing that the bladder and both ureters are opacified during the delay phase. Bladder wall thickening and distal ureteric narrowing are seen.



**Figure 2.** Ultrasonography showing hydronephrosis; tiny echogenic foci within the renal pelvis very likely represent debris.

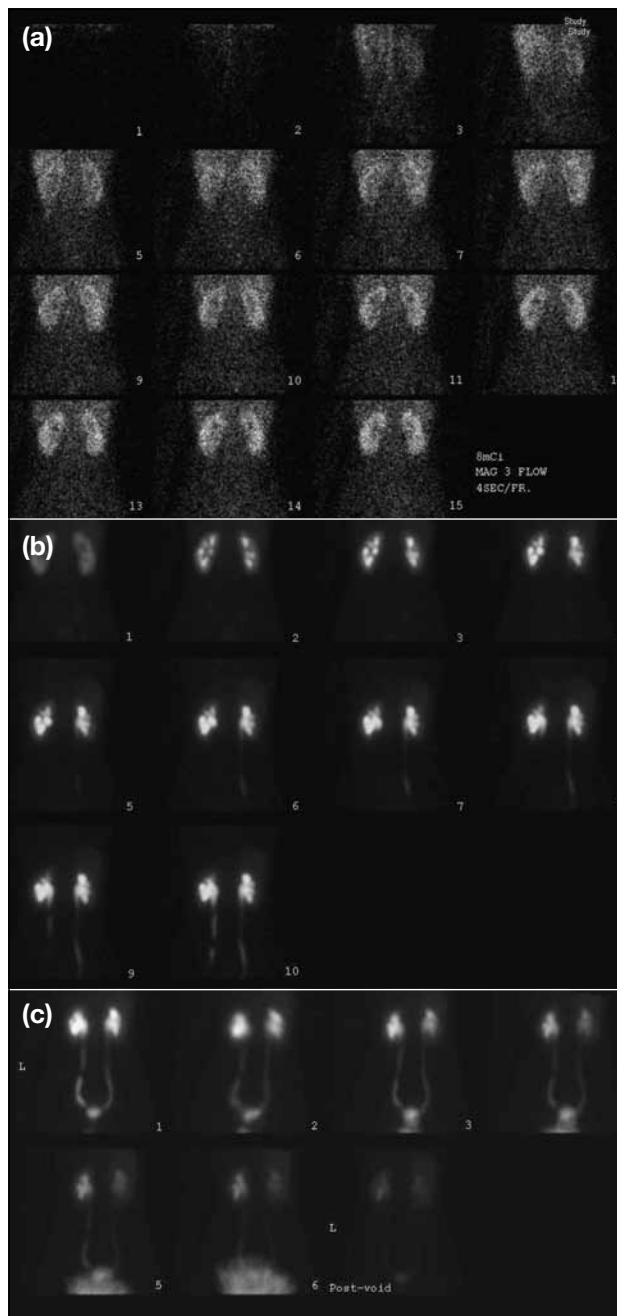
computed tomography (CT), and renal scintigraphy. Fluoroscopic examinations including a micturating cysto-urethrogram and an antegrade pyelogram (AP) were performed on three patients. These investigations are summarised in Table 1.

## RESULTS

The age range of the 36 patients was 16 to 36 (mean, 26) years, and the male-to-female ratio was 1:1.

Among these patients, nine (25%) had no significant imaging abnormalities, which was probably related to early presentation to the Urology Division. By contrast, seven (19%) had bilateral hydronephrosis, and three (8%) had unilateral hydronephrosis. Two (6%) of the patients with bilateral hydronephrosis had renal stones, two (6%) had increased renal parenchymal echogenicity on ultrasound suggestive of parenchymal disease. Four (11%) of the patients with bilateral hydronephrosis had episodic or continuously elevated serum creatinine levels; the highest recorded creatinine levels ranged from 101 to 502  $\mu\text{mol/L}$  (reference range, 39-76  $\mu\text{mol/L}$  for female and 55-103  $\mu\text{mol/L}$  for male). In all, 26 (72%) of the patients had no hydronephrosis.

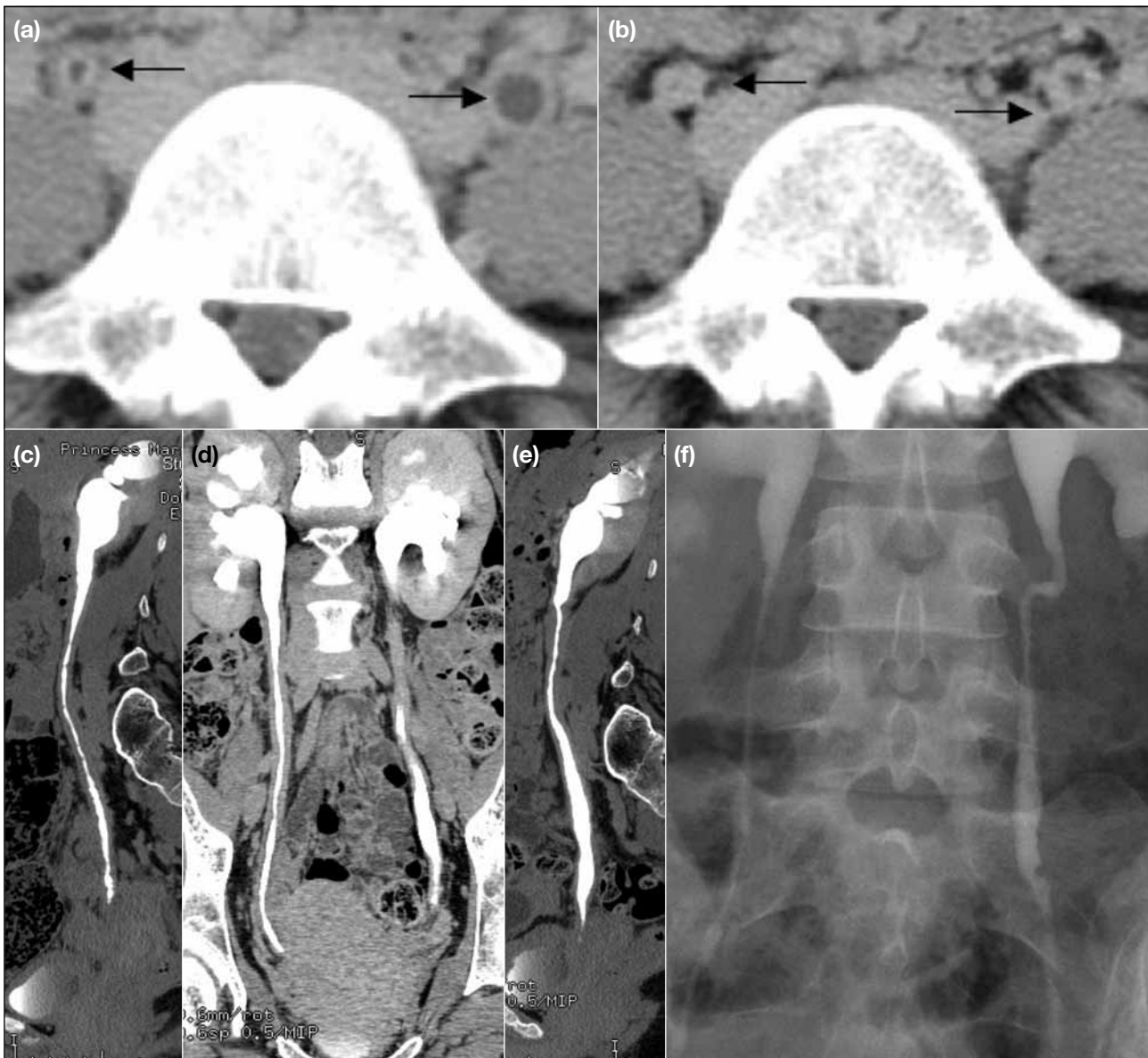
Bilateral ureteric narrowing was demonstrated by IVU, AP, or cross-sectional studies in five (14%) of the patients. Contracted or small bladders, failure to attain a normal full size, and bladder wall thickening (all compatible with cystitis) were documented in 14 (39%) of the patients, and bladder stones in two (6%). Four (11%) of the patients were referred to the Department of Radiology for percutaneous nephrostomy (PCN); in three of them acute renal failure was the indication, and the subsequent serum creatinine level decreased to normal or near-normal levels in all of them, so that they could all wean off PCN. However, the remaining



**Figure 3.** Tc-99m Mercaptoacetyltriglycine (MAG3) scan. (a) Bilateral hydronephrosis with satisfactory perfusion. (b) There was progressive accumulation of tracer in the collecting systems. (c) Drainage was observed after lasix injection at 20 minutes.

one patient had bilateral PCNs for a severely contracted bladder with bilateral tight ureteric strictures and gross hydronephrosis, and in her the bilateral drainage continued. These findings and interventions are summarised in Table 2.

The lower urinary tract is more frequently involved than the upper tract, and in our patients the commonest



**Figure 4.** Computed tomography (CT) and intravenous urogram (IVU) of a patient with ureteric narrowing.

(a) Axial CT showing that both ureters are dilated with wall thickening (arrows). (b) CT taken 2 years later on the same patient shows interval increase in ureteric wall thickening. The curve multiplanar reformat (MPR) images in the sagittal plane of the (c) right and (e) left ureters are shown. (d) The curve MPR image of bilateral ureters in the coronal plane is shown. The collecting systems are opacified on delay phase. Ureteric wall thickening and hydronephrosis are seen. Ureteric lumens are mildly irregular. (f) The release image of this patient's IVU for correlation. Subtle ureteric irregularities are seen.

radiological findings were bladder wall thickening and a small contracted bladder (Figure 1). With obstruction and hydronephrosis, debris may be seen within the dilated collecting system (Figure 2). Renal function may be evaluated by renal scintigraphy (Figure 3). Ureteric narrowing and wall thickening (Figure 4) are probably under-reported, because ureteric imaging by cross-sectional study or contrast was not performed on all patients. Most (5/7) of the patients with bilateral hydronephrosis had distal ureteric narrowing (Figure 5).

## DISCUSSION

Ketamine is a dissociative anaesthetic, which is also being used for recreational purpose in rave parties and nightclubs. Its use results in analgesia, anaesthesia, cardiovascular and respiratory stimulation, as well as hallucinations, psychosis, psychomotor and cognitive impairment.<sup>2</sup> There is a dramatic increase in youth ketamine use in Hong Kong in recent years, from less than 1% of drug users under the age of 21 years in 1999 to 61% in 2005.<sup>3</sup> Apart from cardiovascular,



**Figure 5.** Bilateral distal ureteric narrowing are seen on antegrade pyelogram.

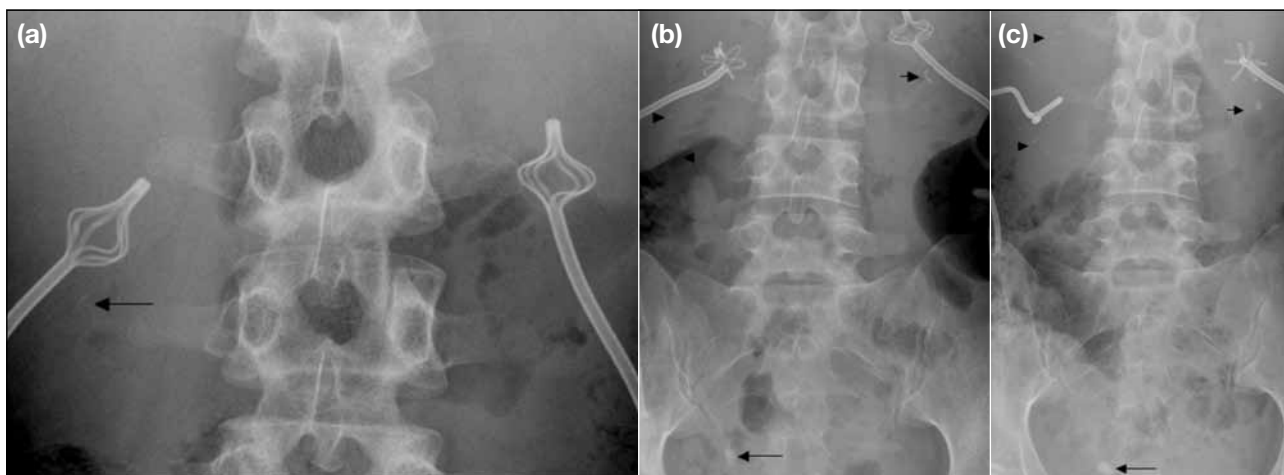
respiratory, and psychiatric sequelae, ketamine abuse also has urological complications. Ketamine-related urological complications constituted a new disease entity discovered in recent years.

The actual mechanism by which ketamine and / or its metabolites causing urinary tract damage is unknown. Chu et al<sup>1</sup> have proposed three possible mechanisms,

including direct toxicity to the urinary tract interstitium, microvascular damage to the urinary tract leading to chronic ischaemia and fibrosis, and a ketamine-induced autoimmune reaction.

The investigation protocol for such young patients should emphasise the need to minimise radiation doses. We would like to propose a stepwise approach starting with ultrasound to look for evidence of urinary tract obstruction, renal parenchymal disease and cystitis, together with renal function tests to look for renal impairment. Further investigations could depend on features of significant obstruction. IVU involves a lower radiation dose than CT. A study by McTavish et al<sup>4</sup> estimated that the total effective dose of CT urography (including pre-contrast, nephrographic and pyelographic phases) approximately doubled that of IVU. IVU can provide information on presence of radio-opaque renal stones, hydronephrosis, papillary necrosis, ureteric stricture and significant obstruction, which can all be indicated by the holding up of contrast. Detailed assessment of the bladder by urologists includes cystoscopy, bladder biopsy, and urodynamic studies. These investigations are adequate to assess for cystitis, ulceration, contact bleeding, bladder volume, detrusor instability, and vesico-ureteric reflux.

Our finding that the lower urinary tract is more commonly affected than the upper tract is consistent with findings by Chu et al.<sup>1</sup> In our series, imaging evidence of cystitis (thickened bladder wall and small



**Figure 6.** Serial plain radiographs (kidney, ureter, and bladder [KUB]) of a patient showing accelerated renal stone formation. (a) A stone is present at lower pole of right kidney (long arrow); KUB three months before (not shown) showed no radio-opaque stone. (b) The stone shows enlargement after 6 months and has propagated down the right ureter (long arrow). New small stones are present at the lower pole of left kidney (short arrow) and right kidney (arrowheads). (c) The KUB 9 months later shows multiple new right renal stones (arrowheads).

contracted bladder) was the commonest finding, followed by bilateral hydronephrosis and bilateral ureteric narrowing. Upper urinary tract damage may be secondary to poor bladder compliance and vesico-ureteric reflux.<sup>1</sup>

Mason et al<sup>5</sup> reported on 23 ketamine users who presented with severe urological symptoms. Our patients differ from theirs in that their symptoms ranged from mild to severe. Small bladders with thickened walls, ureteric wall thickening, and strictures were common in both patient groups.

Urinary tract stones were detected in four (11%) of the patients in our series; stones were visible on plain X-rays in three, and as a tiny calcific focus on CT in one. One of these patients showed progressive urinary stone formation (Figure 6). The rate of stone formation of this patient was much faster than in others in our series or in the general population. The phenomenon of accelerated renal stone formation has not been discussed in the literature. The underlying mechanism may be related to urine stasis and dehydration. Whether renal stone growth is related to use of ketamine requires further observation and studies.

As the vast majority of ketamine users are young adults or teenagers, ketamine-related complications can cause significant life-long morbidity. A standard treatment protocol has not yet been established for this new disease entity. Total abstinence from ketamine is the most important step, but may also be the most difficult to achieve. Medical therapies have been prescribed. Chu et al<sup>1</sup> reported that none of their patients responded to antimuscarinic agents. A case series of ketamine-associated ulcerative cystitis by Shahani et al<sup>6</sup> reported improvement in lower urinary tract symptoms with cessation of ketamine abuse and the use of pentosan polysulfate.<sup>6</sup>

Whether surgical procedures should be offered to ketamine abusers is controversial. Chu et al<sup>7</sup> reported one patient who underwent augmentation enterocystoplasty. This patient had initial clinical improvement but continued to abuse ketamine. He later developed gross bilateral hydronephrosis and acute renal failure.<sup>7</sup>

Currently, in our institution patients with ketamine-

related cystitis are treated with oral oxybutynin, and intravesical administration of sodium hyaluronate solution or hydrodistention. PCN catheters are inserted for patients with obstructive uropathy. Further studies are needed to assess the outcome and long-term effects of these therapies.

There were potential sources of bias in our study owing to the small sample size and because patients who did not have radiological investigations or defaulted follow-up were not included. It is difficult to obtain accurate information on the duration, amount, frequency and purity of ketamine used, as such information was not definitively documented in the case notes. Therefore whether there is any correlation between radiological findings and the pattern of ketamine usage cannot be determined.

## CONCLUSION

Ketamine abuse can lead to irreversible damage to the urinary tract, and can cause cystitis, urinary tract stones, hydronephrosis, renal parenchymal disease, and renal failure. Radiological investigations such as ultrasound and intravenous urography have important roles in the assessment of these complications. PCN offers relief if there is significant urinary tract obstruction.

## ACKNOWLEDGEMENT

We gratefully acknowledge Dr PO Lee for her advice in the writing of this article.

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