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CASE REPORT

Ketamine Abuse-Induced Obstructive Nephropathy and Kidney Injury

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KETAMINE is an anaesthetic agent characterized by a rapid onset and short duration of action, but it has increasingly been abused as a "club-drug" since the late 1980s. It can cause inflammation and contraction of the bladder, leading to possibly irreversible kidney damage. Since 2007, case reports are appearing in the medical literature describing severe bladder dysfunction and kidney injury in ketamine abusers.^{1,2} In this article, we report a case of obstructive nephropathy and kidney injury in a ketamine abuser.

CASE DESCRIPTION

A 24-year-old female patient complained of low back pain, frequent urination, odynuria, and dysuria for half a year. She was always lying in bed and eating less due to the illness above-mentioned. Medical examination at the local hospital showed that the patient was skinny, having poor skin elasticity, scaphoid abdomen, percussion tenderness over kidney region, and bilateral ureteral point tenderness. Initial investigations revealed renal insufficiency (urea 19.84 mmol/L, creatinine 249.3 μ mol/L). Liver function test results were abnormal (total bilirubin 22.9 μ mol/L,

alkaline phosphatase 919 U/L, γ -glutamyltransferase 1366 U/L, alanine transaminase 327 U/L, aspartate aminotransferase 249 U/L). Urine analysis was abnormal (white blood cell +++/high power field, urine protein +++). Renal ultrasound demonstrated chronic cystitis, bilateral hydronephrosis, and ureteral expansion. According to her history, the patient was a regular user of intra-nasal street ketamine for the past 6 years.

Based on the examination and test results, the patient was diagnosed with urinary tract infection and given anti-infective therapy. At the same time, she stopped taking ketamine because of hospitalization. The renal and liver function began to recover after 10 days (urea 9.91 mmol/L, creatinine 190.5 μ mol/L, alkaline phosphatase 470 U/L, γ -glutamyltransferase 882 U/L, alanine transaminase 193 U/L, aspartate aminotransferase 117 U/L), but the symptoms of urinary irritation were still obvious and the doctor could not give her a confirmed diagnosis. She therefore came to East Hospital of Tongji University.

After reviewing the patient's history, we noticed that she had visited a urologist in our hospital with the same complaints 2 years before. At that time, the patient had liver damage, but normal renal function and no hydronephrosis. Cystoscopy revealed a diffusely inflamed bladder with marked reduction in capacity but no obstruction. The bladder biopsy showed inflammatory change but no dysplasia or malignancy (Fig. 1). No definitive diagnosis

was reached and the patient was discharged. When the patient prepared for pregnancy, she stopped taking ketamine, and the symptoms were completely relieved. After her daughter was 6-month-old, the patient resumed the use of ketamine again, and the urinary irritation symptoms re-appeared.

After the patient was admitted into the department of nephrology, laboratory tests revealed that her renal function (urea 9.2 mmol/L, creatinine 133 μ mol/L) and liver function (alkaline phosphatase 490 U/L, γ -glutamyltransferase 638 U/L, alanine transaminase 116 U/L, aspartate aminotransferase 60 U/L) had not yet recovered to normal. Urine analysis was abnormal (white blood cells ++++/high power field, red blood cells 5-7/high power field, urine protein ++). 24-hour urinary protein was 0.5 g. Urine protein electro-phoresis showed glomerular proteinuria. Mid-stream urine culture and urine culture for acid fast bacilli were negative. Renal ultrasound demonstrated bilateral hydronephrosis and ureteral expansion. Magnetic resonance urography showed bilateral hydronephrosis (Fig. 2). No cause of the hydronephrosis was seen, in particular no calculi or tumor. Unfortunately, we could not perform renal biopsy because of hydronephrosis. Anti-infective therapy was prescribed at first. After a review of the literature, we found that ketamine abuse could cause inflammatory cystitis, low capacity of the bladder, and destruction of the lower urinary tract. The patient was therefore asked to stop ketamine and anti-infective therapy, to switch to medicines for liver protection, nitrogen level reduction and nutrition support. After 2 weeks, her urinary irritation symptoms were alleviated, liver and renal function alleviated spontaneously. Upon discharge, her serum creatinine was 100 μ mol/L and liver function was normal, yet ultrasound showed renal pelvis separation. The patient rejected urography and cystoscopy for recheck.

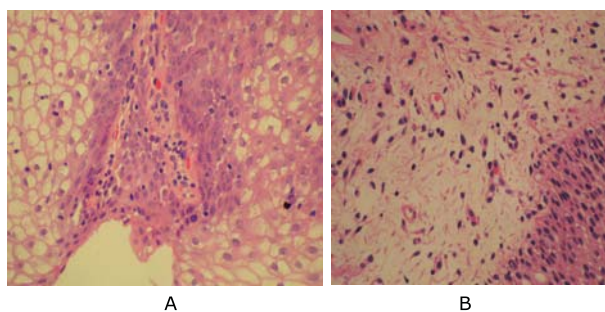


Figure 1. The bladder biopsy (A) and ureter pathology (B) show inflammatory infiltration predominantly consisting of lymphocytes and eosinophils, but no dysplasia or malignancy. (HE $\times$ 400)



Figure 2. Magnetic resonance urography shows bilateral hydronephrosis (arrows).

DISCUSSION

Ketamine is an anaesthetic agent, but is now becoming more widely used in clubs and parties, labeled a "club drug" by the National Institute on Drug Abuse (NIDA) of the United States. Its systemic side-effects on the central nervous system, respiratory system, and the cardiovascular system have been well recognized. However, its harmful effects on the upper and lower urinary tract have not been reported until recently.^{1,2} Recent reports suggest that approximately 20%-30% of ketamine abusers suffer from lower urinary tract symptoms,^{3,4} but the incidence is likely to be underestimated since people having suspicious symptoms may not visit doctors, therefore not counted as cases with side effects.⁴

The symptoms of ketamine abuse include a range of lower urinary tract symptoms, mainly irritability in nature. Typically, the patients may complain of urgent urination, extreme frequent urination, and intractable dysuria, and some patients have kidney and liver damage. Severe cases even need percutaneous nephrostomy. The underlying pathophysiological mechanism for the destruction of the urinary tract induced by ketamine is unknown. It was postulated that the high concentration of ketamine and its metabolites in the urine might cause direct toxic effects on the interstitial cells of the bladder, causing a significant chronic submucosal inflammatory response. In some abusers, the presence of papillary necrosis might be caused by the irreversible toxic effects of ketamine on the medullary interstitial cells, resulting in chronic renal insufficiency.⁴ Recent evidence in mice has shown that ketamine addiction leads to mononuclear inflammatory infiltration in the renal papilla, suggesting a possible pathogenesis of papillary necrosis.⁵

Currently, there is no definitive management for the patients with ketamine abuse-induced urinary tract symptoms, and the key issues are individualized care plans and the patients' compliance. However, the compliance of patients is often poor, and failure to abstain may lead to disease progression.^{1,6-9} Various treatments have been employed including antibiotic, oral non-steroidal anti-inflammatory drugs, steroids, anticholinergic therapy, and cystodistension.¹⁰ All have failed to provide significant and lasting improvements. So far, the treatment of lower urinary tract symptoms is to decrease the dose of ketamine at least and optimally to discontinue ketamine. Therapeutic strategies that may be useful may involve repairment of the urothelium. Pentosan polysulfate sodium (Elmiron), a low molecular weight heparin-like compound, has been tried in rebuilding the glycosaminoglycan layer of the damaged urothelium, and symptom relief after treatment was reported.¹

In conclusion, this article reported a case of inflammatory cystitis, reversible hydronephrosis, renal and liver dysfunction associated with ketamine abuse. Abuse of ketamine should be considered by nephrologists and urologists as a potential cause of unexplained hydronephrosis and bladder inflammation, especially when liver function is also abnormal. Some, if not all, of these symptoms appear to be reversible upon cessation of the drug.

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