

Ketamine Abuse Associated with Vesicoureteral Reflux

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INTRODUCTION

Ketamine (K) is a non-competitive N-methyl-D-aspartic acid receptor antagonist that can act as a short-acting general anesthesia agent. However, due to fact that its use is associated with altered sensations and euphoria, it is also known as "Special K", a recreational drug that is used in nightclubs and by drug abusers. Shahani et al has reported lower urinary tract symptoms caused by eosinophilic infiltration in patients with ketamine-associated ulcerative cystitis [1]. In animal experiments with rats, intravenous ketamine produces a dose-dependent inhibition of the spinal cord neuronal responses evoked by urinary bladder distension and this can result in bladder and later kidney dysfunction [2]. Here, we presented a very unique case of a ketamine abuser with lower urinary tract symptoms that showed further progression to vesicoureteral reflux (VUR) and associated urinary tract infection.

CASE PRESENTATION AND MANAGEMENT

This 25 year-old female presented with bilateral dull flank pain for five days and micturition interval frequency of less than one hour for two years. Tracing her past history, she denied previous medical and surgical interventions but stated that she had used ketamine for four years. Urinalysis showed severe pyuria and hematuria and both the leukocyte and hamatocyte counts were more than 100 per high power field. A slightly elevated creatinine level of 1.21 mg/dl was noted. An excretory urography together with abdominal computed tomography showed dilatation of the bilateral renal pelvis, renal calyces and right proximal ureter, but the obstruction level could not be identified. She had received an excretory urography one year ago due to an episode of bilateral flank soreness, and mild left hydronephrosis has been noted. Comparing these two excretory urography datasets, progressive left hydronephrosis and a new onset of right hydronephrosis were noted. Cystoscopy revealed a small capacity bladder. A bilateral ureterorenoscopy examination showed patent ureters on both sides. Obstructive factors such as urolithiasis, tumor, or stricture segments were not found. Chronic cystitis, a small bladder capacity, and bilateral patent ureters with hydronephrosis were impressed. A renal scan yielded neither mechanical nor functional obstruction, but impaired left renal function was suggested. The glomerular filtration rates were 34.54 and 56.74 mL per minute for the left and right kidney respectively. Retrograde voiding cystography was conducted. During the contrast filling, the patient experienced strong voiding desire associated with a small bladder capacity, which was 50 mL. An X-ray of kidney, ureter, and bladder was taken immediately after filling and showed bilateral VUR. Under the impression of bilateral VUR due to a contracted bladder, intermittent self bladder catheterization and empirical antibiotics were pre-

scribed together with alpha-blockers to facilitate efficient bladder emptying. There were no further urinary tract infection episodes during the one-month follow-up.

DISCUSSION

VUR is a commonly encountered diagnosis in children. The incidence of VUR declines with age. About 65% of patients with VUR are younger than 7 years old and only 4.4% of patients are members of the adult population. Female are twice as likely as males to have VUR among the pediatric population [3]. However, VUR is still found in 10% of patients with end stage renal disease. In adults, the estimated female to male ratio can be up to 5:1. Patients who have received renal transplantation or cystectomy with ileal conduit, pregnant patients, and patients with a neurogenic bladder more often have VUR. The incidence of male VUR rises in the 60-70 year old age group due to bladder outlet obstruction [4]. In summary, voiding dysfunction due to neurogenic etiologies or obstruction, a shortening of the ureter due to surgical intervention, and the presence of chronic irritation caused by infection or hormonal changes may all contribute to the development of secondary VUR. The patient described in this case report denied a previous history of urinary tract infection and having VUR during childhood. Her lower urinary symptoms, which included frequency, dysuria, and microscopic hematuria, occurred after two years of non-medical daily usage of ketamine and had gradually progressed with time. The severity of her VUR also showed a correlation with prolonged ketamine use. To our knowledge, our patient is the first case to be documented with lower urinary tract symptoms and VUR that is associated with the recreational use of ketamine.

Ketamine (K) was synthesized as a dissociative anesthetic drug in 1970s [5]. Since the early 1980s, it has become widely used for non-medical, recreational purposes in night clubs and at dance parties. The street names for the drug include Vitamin K and Special K [6]. The psychological effects of ketamine include mind alteration, increased empathy and insights, the revelation of old memories, and near-death experiences [5]. Some recreational users have even described buzzing, ringing, whistling sounds, a sense of traveling through a dark tunnel into a light at high speed, and intense visions [1]. Although ketamine-related mortality is rare, there are many possible negative physical effects of ketamine, including increased heart rate, increased respiratory rate, convulsions, nausea, vomiting, difficulty with walking and balance, numbness, slurred speech, dizziness, visual problems, nausea, headache, spasms, twitching, anxiety, panic attacks, flashbacks, persistent perceptual changes, mania, depression, insomnia, and possible damage to brain as indicated by rat model studies [1,6].

Shanani et al were the first group to investigate the effects of recreational ketamine usage on the genitourinary system. They ob-

Clinical pearls — Genitourinary tract image

tained detailed histories, physical examinations, urinalysis, urine cultures, urine cytology, cystoscopic biopsies, and computed tomography from nine patients who indicated that they used ketamine chronically. The subjective lower urinary symptoms were severe dysuria, frequency, urgency, and gross haematuria. Cystoscopic biopsy showed eosinophil predominant active cystitis and a new clinical entity named "ketamine-associated ulcerative cystitis" was proposed. The mechanism is still unclear [1]. In Hong-Kong, Chu et al also demonstrated the presence of similar lower urinary tract symptoms among ten recreational ketamine users [7]. Their functional bladder capacities ranged from 30-100 mL. Seven of the ten patients had detrusor overactivity with urine leakage when the bladder was filled to 30-50 mL. Hydronephrosis and renal impairment were noticed in half of these patients. Chu et al suggested that damage to neurons or the spinal cord by ketamine might be the cause of the bladder dysfunction. However, since ketamine metabolites are excreted in urine, it is also possible that ketamine and its metabolites might directly damage the bladder mucosa. Although there is limited experience treating ketamine associated cystitis, it has been indicated that pentosan polysulfate may be able to partially relieve the lower urinary symptoms. Cessation of ketamine usage is the key point of avoiding disease progression [1]. These previous reports have documented that the long term use of ketamine does seem to cause fibrosis and thickening of bladder wall and result in a small bladder capacity. Our case supports the hypothesis that a dysfunction bladder due to ketamine use could finally lead to renal impairment due to VUR. As recreational drug usage is a growing public health issue, urologists should also be aware of these new entities and the genitourinary problems that are associated with such activities.

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Fig. 1. Bilateral hydronephrosis with obstruction at the upper ureter (arrows).

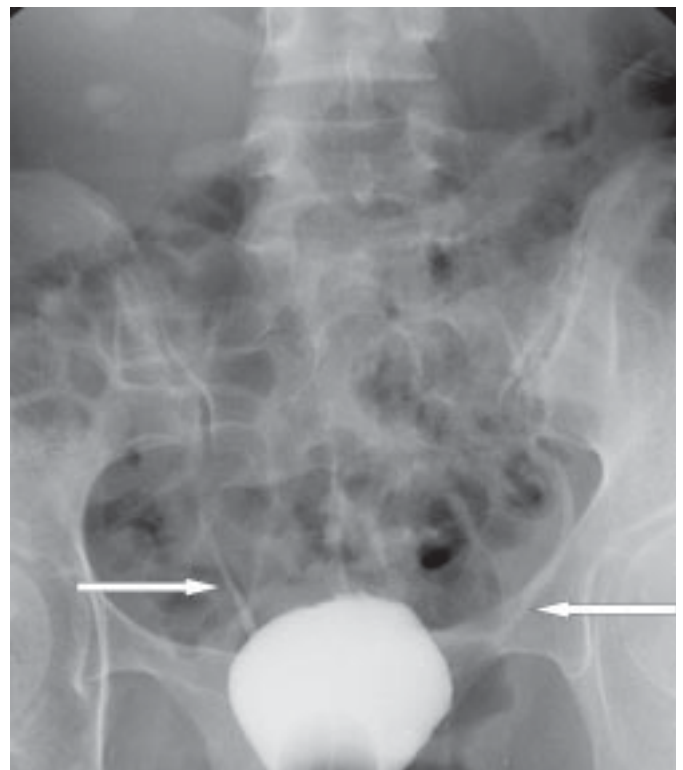


Fig. 2. Bilateral vesico-ureteral reflux (arrows) shown by voiding cystourethrography.