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Ketamine Induced Cystitis: An Important Differential Diagnosis in Patients Presenting with Recurrent Lower Urinary Tract Symptoms

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Abstract

The usage of Ketamine ("Special K", "Vitamin K") and its derivative, PCP ("angel dust") particularly amongst the younger 16–25-year-old demographic, has dramatically risen in the past decade in the United States. Its effects on the urinary system have only recently been elucidated through publication of a limited number of case reports. This clinical diagnosis, termed ketamine induced cystitis, or ketamine bladder syndrome, is characterized by bladder pain and urinary frequency that occurs with long-standing ketamine use. It is of importance to have awareness of this condition with a high degree of clinical suspicion for early diagnosis and multidisciplinary treatment as it can produce rather debilitating symptoms in those complaining of lower urinary tract symptoms. We report a case of ketamine-induced cystitis in a 23-year-old female with recurrent lower urinary tract symptoms, and discuss the diagnosis, pathology, and management for physicians who may encounter this disease in their practice.

Keywords: Cystitis; Ketamine; Urinary Tract Infection

Introduction

Ketamine, a phencyclidine derivative, is a unique disassociate anesthetic that produce significant analgesia and amnesia [2]. Prior to ketamine, in the 1940's, phencyclidine (PCP) was synthesized; a hallucinogen that remains in use for recreational purposes [1]. When PCP was given to animals, it was found to have a calming effect, suggesting a "dissociative anesthesia" property [2]. Due to this effect, PCP went to clinical trials for its function as an anesthetic [2]. PCP was relatively safe because higher doses were not fatal, but people came out of PCP anesthesia in a psychotic state [5]. Ultimately, it was never approved for use as an anesthetic but the desire remained for recreational use due to its rapid anesthetic effect without the potential danger of overdose [2]. Due to this, various drug companies began to synthesize different analogs of PCP. This has led to the discovery of ketamine, known as Ketalar, in the early 1970s, which had similar properties as PCP, but was much shorter acting without the after effects of psychosis [5]. Ketamine had been synthesized as the Vietnam War was going on. It was used by medics to quickly put individuals under anesthesia safely [5]. There have been very few deaths associated with ketamine overdose [5]. It was during this time that the recreational use of Ketamine had followed. While the full mechanism has not been fully elucidated, it is speculated that it involves an antagonistic action at NMDA (N-methyl-D-aspartate) receptors throughout the central and peripheral nervous system [4,5]. Ketamine is the only anesthetic available which has analgesic, hypnotic, and amnestic effects [4].

Additionally, there has been a rising phenomenon demonstrating ketamines association with lower urinary tract symptoms including dysuria, urgency, nocturia, decreased bladder capacity, and increased urinary frequency consistent with chronic ulcerative cystitis [2]. The mechanism of action is not fully known, but there are thoughts that accumulations of ketamine's metabolites may produce an autoimmune or inflammatory response within the bladder wall [4]. Here, we discuss the pathology, diagnosis, and management of ketamine-induced cystitis with a patient case and available literature regarding the impact of ketamine abuse.

Case Presentation

A 23-year-old female presented to the emergency department (ED) with a complaint of suprapubic pain, dysuria, hematuria, and pelvic pain. Upon chart review, it appeared that that she was seen in our ED multiple times in the past 2 months for a similar complaint. Additionally, she stated that she had been seen at multiple hospitals within the area and was unable to find the cause of her symptoms or able to obtain relief in her symptoms. There was no history of fever, vaginal bleeding, recent sexual activity, or abdominal pain. She had stated that she had attempted a full course of nitrofurantoin and trimethoprim-sulfamethoxazole without relief. Upon further history she endorses ketamine usage for the past 12 months, both intravenously and intramuscularly, with most recent use a few days prior to her presentation in our ED. She had Pelvic exam demonstrated no obvious lesion, rash, injury, discharge or cervical motion tenderness.

Urine analysis showed no leukocytosis (2 white blood cells per high power field), no bacteria, no nitrites, and hematuria (43 red blood cells per high power field). Her serum urea level was 15 mg/dL, and creatinine level at 0.67 mg/dL. Urine culture did not grow any organisms after 6 weeks of culture. Chlamydia, gonorrhea, and trichomonas vaginal swabs were negative as well.

Ultrasound was initially applied to evaluate for bladder wall thickness, which did show slight enlargement of the bladder wall. However, there were no findings of hydronephrosis. Given the non-specific findings on ultrasound, patient then proceeded to have further imaging which included a computerized tomography scan of her abdomen and pelvis without contrast. CT abdominal/pelvis without contrast demonstrated no hydronephrosis or stones in the collecting system. However, it did show mild bladder wall thickening, which was not present on imaging 2 months prior (figure 1). Cystoscopy performed 2 months later demonstrated diffusely inflamed bladder mucosa. Bladder biopsies of posterior wall of bladder revealed chronic inflammation of the urothelial epithelium, consistent with cystitis. No dysplasia, malignancy, or granuloma was seen. Cystogram demonstrated normal bladder capacity. Bilateral retrograde pyelogram showed no filling defects and efflux of urine were noted from bilateral ureteric orifices. Findings were given to patient that her lower urinary tract symptoms were likely due to ketamine use. There is no single best treatment other than ceasing use of ketamine. Patient agrees to stop ketamine use. She was given 50mg hydroxyzine to use once nightly, Ditropan 10mg XL, and pentosoan polysulfate 100mg TID. At one month follow up, she stated her symptoms have nearly resolved.

At six months of follow up, she did indicate there was moderate improvement in her symptoms but did have a few flares upon relapse with ketamine. Urine analysis demonstrated 6-10 white blood cells per high power field, 40-60 red blood cells per high power field, no bacteria, nitrites, or leukocyte esterase. Her renal profile remained normal. Intravesicle instillation was provided to the patient as an alternative treatment which she declined.

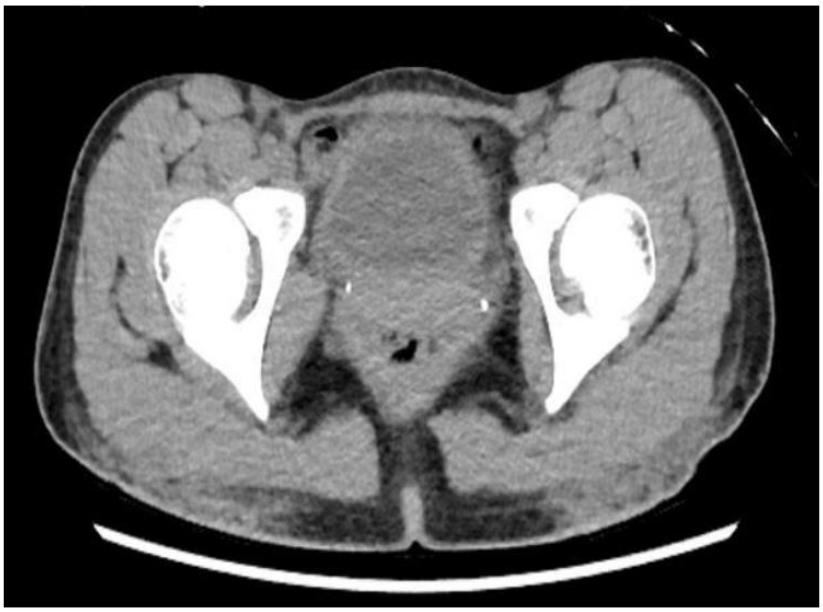

Figure 1: Axial slice of abdominal/pelvic CT highlighting mild bladder wall thickening

Discussion

Since the early 1990's, it has been abused as a recreational drug due to its variety of addictive effects, especially in nightclubs [1]. Long-standing ketamine, defined as use of ketamine for at least 2 years at a frequency of three or more times a week, has been associated with lower urinary tract symptoms consistent with chronic ulcerative cystitis [4]. These symptoms can include dysuria, increased urinary frequency, urge incontinence, nocturia, bladder pain, decreased bladder capacity, and eosinophil infiltration [2]. Urine culture usually fails to yield any microbiology in ketamine cystitis with bladder pain alone [3]. The mechanism of ketamine-induced injury isn't fully known but may have to do with accumulation of a increased concentration of ketamine and/or it's metabolites producing an inflammatory response within the urothelial cells of the bladder wall [1]. The intensity of symptoms correlated with frequency and amount of ketamine use [1]. Early detection aims at symptom resolution and to ultimately prevent renal function deterioration which is dependent on duration and amount of ketamine abuse. Studies have shown that use of anticholinergic agents or antibiotics have failed in symptom resolution caused by chronic ketamine usage [2]. The best treatment is stopping ketamine use [2,3]. Ketamine-induced cystitis is a new clinical entity that is becoming an increasing burden on our healthcare system due to increased ketamine abuse especially amongst the younger population. Healthcare providers, especially those in the emergency medicine setting, should be aware of this differential in a young patient with recurrent lower urinary tract symptoms in conjunction with unremarkable findings on the urine analysis.

Conclusion

We report a case of ketamine-induced cystitis seen in a 23-year-old female with recurrent lower urinary tract symptoms with unremarkable urine analysis findings and refractory to antibiotic usage. Diagnosis was mostly made based on clinical findings and proper test to rule out other possible differential diagnosis. Follow-ups were scheduled to monitor the progress of the patient.

It is of significant importance that medical providers ask specifically about recreational drug consumption in a young patient presenting with recurrent or persistent unexplained lower urinary tract symptoms. There should be a low threshold to provide prompt referral to a urologist in those with recurrent lower urinary tract symptoms with negative urine culture and/or poor response to antibiotics. Lastly, the importance of discontinuing ketamine use in those with a positive history of ketamine use should be stressed for symptom resolution and to prevent significant and irreversible damage.

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