Author’s response to reviews

Title: Dysuria due to benign prostatic hyperplasia of the median lobe with ketamine-associated uropathy in a young male

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Author’s response to reviews:

Response to Editor and Reviewers

Response to Editor:

We would like to sincerely express our great appreciation to you for your and the reviewers’ thoughtful and helpful comments on our manuscript. We have carefully made corrections according to your comments.

1. Language.

We truly apologize for the trouble caused by the poor English-language expression, and we thank you for pointing out these mistakes. The manuscript has been edited by a professional language editing service (Nature Research Editing Service, order number: S8D6G4QX3). The Nature Research Editing Service Certification is affiliated in cover letter. We sincerely hope that it is met with approval.

2. Ethics and consent to participate.

The case report was approved by the Human Ethics Committee of Xiangya Hospital of Central South University Ethics Committee. Written informed consent was obtained from the patient.

3. Consent for publication

Written informed consent was obtained for publication from the patient.

4. Abbreviations

Thank you very much for your kind reminder. We have listed all abbreviations after the conclusion section.

We are most grateful for your pointing out the existing problems in our manuscript carefully and patiently.
Response to Reviewer 1:

Thank you very much for your comments on our manuscript. We have studied the comments carefully, and we found that these comments were helpful for revising our paper; they also provided important guidance for our future research. We have made corrections according to your comments to the best of our ability.

1. The CT scan provided is suboptimal, any imaging to show the sagittal view and the size of the prostate.

Response: Thank you for your constructive suggestion. We have uploaded better CT images, and we hope that they are met with approval. The CT images provided by the patient were taken in another hospital, and we did not find a sagittal view among the images. Combining the CT results and the operative findings, we found that the auxetic median lobe of the prostate was a spherical mass of approximately 2-cm-diameter in size. (Case presentation section, line 8-13, page 5-6 in man text)

2. How many grams of tissue were resected for the median lobe?

Response: We appreciate your objective comment. The auxetic median lobe of the prostate was resected completely under the endoscope and then separated into small pieces to remove all resected prostate tissue through the urethra. We did not weigh all the resected prostate tissues after surgery due to the fact that a portion of the tissue was sent for rapid pathological examination to determine whether malignant tumours existed during the early surgical procedure.

Thank you for taking the time to review our manuscript. We would like to sincerely express our great appreciation again!

Response to Reviewer 2:

We would like to sincerely express our great appreciation to you for comments on our manuscript. We have studied comments carefully and found that those comments are very helpful for revising and improving our paper. Following is our point-to-point response to your kind comment which we hope meet with approval.

1. It is desirable that the authors further describe in the discussion the immutability arguments of ketamine in prostatic lesions. Are they the consequence of bladder injury? or are they due to the direct toxicity of ketamine metabolites?

Response: We really appreciate this valuable comment which improved our manuscript a lot. We have discussed the effect of ketamine in prostatic lesions furtherly as follows:

To our knowledge, there has been no case of BPH with ketamine-associated uropathy ever reported in young patients. The exact pathophysiology of ketamine-associated cystitis remains greatly unknown. An important theory is that ketamine and/or its metabolites accumulates at a high concentration in urine, leading to a direct toxic effect on the urothelium and resulting in significant inflammation. The nuclear factor-kappa B (NF-κB) pathway was found to be activated during inflammatory signalling of
ketamine-induced cystitis in the bladder in a rat model [1]. Furthermore, there exists a significant increase in pro-inflammatory cytokines, such as IL-1β, IL-2, IL-4, IL-6, IFN-γ, NGF, and COX-2, in bladder tissue in ketamine-associated cystitis [2, 3]. Similarly, although ageing and androgens are the two established risk factors in the progression of benign prostatic hyperplasia (BPH), the pathogenesis of BPH is still largely unresolved. Currently, increasing evidence indicates that inflammation is strongly involved in the aetiology and progression of BPH. Particularly, it has been identified that inflammatory cytokines, IL2, IL4, IL7, IL17, IFN-γ and their relevant receptors are upregulated in and that inflammatory cells infiltrate into BPH tissues [4-6]. Anti-inflammatory agent was proved to produce an antiproliferative effect during BPH by markedly decreased BPH-related upregulation of COX-2 protein expression [7]. It is possible that inflammation in the urinary tract due to the direct and indirect effects of ketamine stimulates the enlargement of the prostate. However, few studies have investigated the direct effect of ketamine or its metabolites on the prostate, and their relationship needs to be confirmed with further research.

2. Is it possible to know the doses of ketamine consumed by the patient?
Response: Thank you for your constructive suggestion. The patient reported that he used ketamine once weekly at first and then once every 2–3 days up to a maximum of approximately 10 g/day. (Case presentation section, paragraph 1, line 3-4, page 5 in man text). Thank you once again!

3. The discussion should include comparisons with other cases described in ketamine-induced uropathy literature associated with uretrohydroephrosis.
Response: We sincerely appreciate your constructive suggestions again. We have added comparisons between other cases and our case in discussion according to your comment as follows:

Ketamine-induced upper urinary tract lesions seem not to be paid enough attention due to a greater incidence of apparent lower urinary tract syndromes [8]. Hydronephrosis and ureteral wall thickening were reported most frequently in ketamine-induced upper urinary tract damage. According to clinical case summaries, the incidence of hydronephrosis (bilateral or unilateral) can be as high as 44.4% [9] or 51% [10]. Huang LK et al. [9] reported three patients with unilateral hydronephrosis and nine with bilateral hydronephrosis among twelve ketamine-induced uropathy patients with hydronephrosis. In addition, nine patients had ureteral wall thickening, and two had ureterovesical junction involvement. Bilateral upper ureteric narrow and mild bilateral hydronephrosis were detected in 3 patients in a 6-patients cases report [11]. Misra S et al. [12] reported that two of 34 patients had bilateral hydronephrosis with hydrourerets to the vesicoureteral junction. In another case of A 26-year-old man with ketamine abuse, bilateral hydronephrosis, obstructive nephropathy and kidney injury were detected in spite of no obstruction at the ureteric orifices [13]. Many other studies referred to bilateral or unilateral hydronephrosis in ketamine-related uropathy but did not report the ureteric or renal lesions [10, 14]. In our case, bilateral moderate hydronephrosis with hydrourerets to the vesicoureteral junction was detected, but ureteral wall thickening or ureteric narrow was not found. Therefore, obstruction due to BPH and bladder damage in anatomy and function may be the primary causes of hydronephrosis and hydrourerets in our case.

Reference


