4th Edition of the Clinical Cases Contest related to the non-surgical clinical management of non-surgical clinical management of renal lithiasis

Official template

Title: Recurrent prostatic cell encrusting lithiasis after Holmium laser enucleation of the prostate (HoLEP). Gradual resolution with urinary pH acidification.

Authors: Carmina Muñoz Bastidas, Luis Labairu Huerta, Andrés Calva López

Key words: prostatic cell calcification, Brushite, urinary pH, urinary acidification.

1. Abstract

Dystrophic calcification of the prostatic cell after HoLEP is a rare complication, but with a great impact on the patient's quality of life that poses a diagnostic and therapeutic challenge. We present the case of a 57-year-old man who after HoLEP presented with disabling voiding pain and urinary retention secondary to recurrent calcifications of the prostatic cell due to calcium phosphate dihydrate lithiasis (Brushite) which resolved after 5 endoscopic surgical interventions and strict medical treatment with thiazides, dietary modifications and Lit-Control® pH Down; as well as daily monitoring of urinary pH with an electronic device to maintain acid pH.

2. Introduction

Prostatic cell calcification after endoscopic treatment of benign prostatic hyperplasia is a very rare complication, with few reports in the literature after transurethral resection of the prostate (TURP) and KTP laser photovaporisation of the prostate, and much less frequently after Holmium laser enucleation of the prostate (HoLEP), with only 8 cases reported[1]. This is possibly due to the fact that the Holmium: YAG laser has a limited penetrability of 0.4 mm and minimal thermal energy diffusion, resulting in less tissue damage[1,2].

Calcifications are formed by crystal deposits in damaged tissue during the healing process, favoured by the lithogenic characteristics of urine[1]. Hypercalciuria, urinary pH above 6.5, low citrate excretion and insufficient hydration are risk factors associated with the formation of Brushite stones, which are characterised by rapid growth and high recurrence rate, posing a therapeutic challenge[3,4].

In addition to complete surgical removal of lithiasis, hygienic and dietary modifications, abundant fluid intake, diet and specific pharmacological treatment according to the composition of the lithiasis and the results of the metabolic study are essential[5]. Accurate urinary pH monitoring at home is an important tool to adjust treatments appropriately and improve patient adherence[6]. New electronic devices appear to be the best option for accurate pH measurement, which can be linked to a smart device via Bluetooth and synchronised with apps to record water intake, urinary pH and dietary supplement intake[7].

We present the case of a patient with dystrophic calcifications of the prostatic cell after HoLEP who recurred after several surgical treatments despite complete removal of the lithiasis, which gradually resolved after strict medical treatment.

3. Description of the clinical case:

a. Relevant background

A 57-year-old man came to our centre with a bladder catheter due to acute urinary retention and long-standing lower urinary tract symptoms refractory to medical treatment. Tests revealed: prostate volume of 40cc, IPSS 28, IQL 5, total PSA 1.6ng/mL and negative urine culture. An expert urologist performed a Holmium laser enucleation of the prostate with a bilobular technique (26Fr Storz resectoscope and nephroscope, Lumenis Moses Pulse 120H laser, Drill-cut morcellator), the surgery was uneventful and the anatomopathological study of 30g of morcellated tissue showed benign prostatic hyperplasia.

The patient was discharged after 48 hours following favourable removal of the bladder catheter. He presented irritative symptoms in the immediate postoperative period, usual in these cases, but they were abnormally persistent, progressing to disabling pelvic and urethral pain and mixed voiding syndrome that was difficult to control and required antimuscarinics, second-stage analgesics and coadjuvants.

b. Diagnostic support studies and results

Urine infection was ruled out with several negative cultures and blood tests were repeatedly normal. Urinalysis reported a pH of 7.8 with no abnormal sediment. Six months after surgery, an obstructive curve flowmetry and flexible urethrocystoscopy revealed an anterior urethra of good calibre and the prostatic cell completely occupied by multiple spiculated lithiasis that did not allow entry into the bladder (Figure 1).

c. Diagnosis

Dystrophic calcifications of prostatic cell.

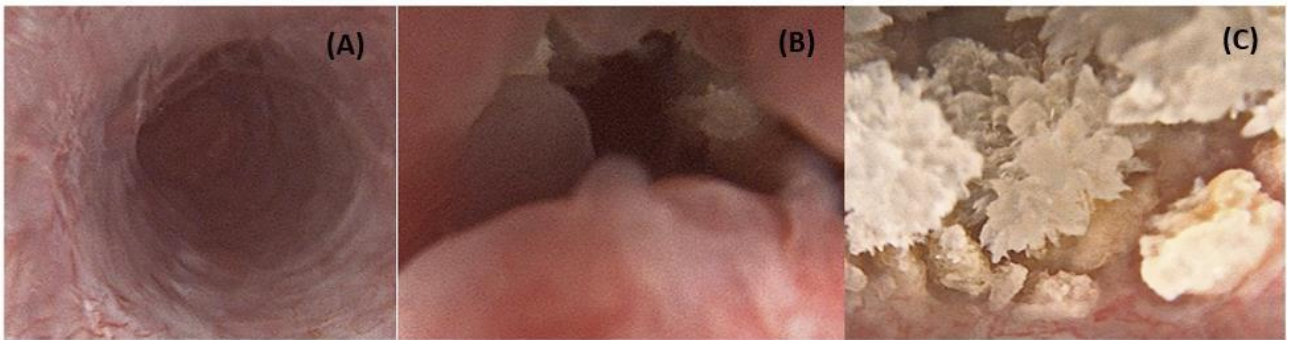

Figure 1. Urethrocystoscopy: (a) Anterior urethra (b) Veru montanum (c) Prostatic cell

d. Treatment

We performed an endoscopic examination under general anaesthesia and complete Holmium laser pulverisation of the lithiasis, which was firmly embedded in the mucosa. Fragments of the lithiasis and a sample of prostate tissue were sent for analysis, which reported prostatic hyperplasia with dystrophic calcifications and Brushite lithiasis.

The patient was discharged without a bladder catheter after 24 hours with comfortable urination and despite negative cultures, antibiotic treatment and hygienic-dietary modifications were prescribed: increased water intake and a balanced diet.

e. Evolution and follow-up

Two months later, he returned to the clinic with difficulty in urinating and incapacitating pain during urination. New tests were performed: negative urine culture, urinary pH of 8, blood tests with no abnormalities, and a CT-urethrography showed a prostate with multiple calcifications, with no other abnormalities in the urinary tract (Figure 2). The metabolic study showed hypercalciuria (CaU 481mg/24h) as the only finding. A further endoscopic examination in the operating theatre revealed a prostate cell occupied by calcifications of the same appearance, which were pulverised with Holmium with subsequent bipolar resection of the prostatic remnant (Figure 3).

Figure 2. Uro-CT: Prostate calcification

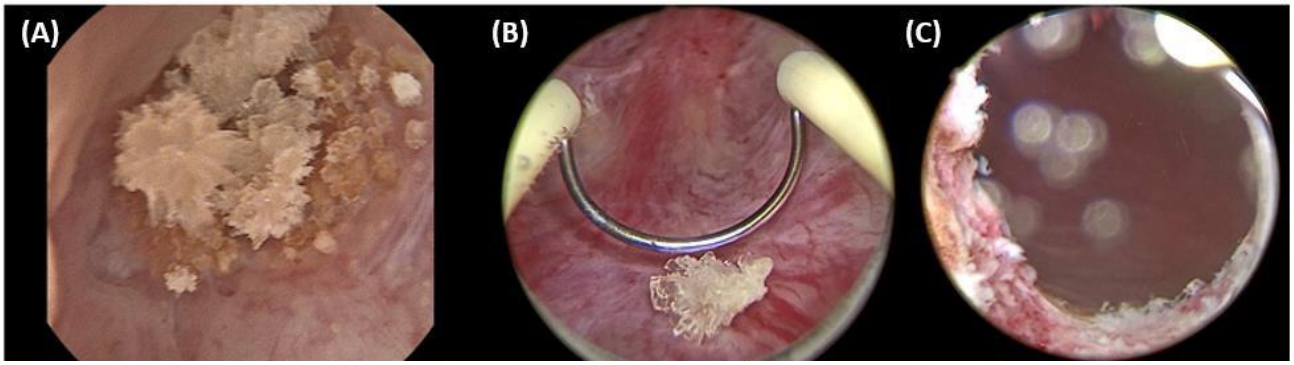

Figure 3. Cystoscopy (a) Calcified prostatic cell (b) TUR of the bladder neck and cell (c) Open neck.

After the operation, preventive medical treatment was added with thiazide diuretics to reduce renal calcium excretion and Lit-Control® pH Down to acidify the urine.

In the following 12 months, the calcifications recurred, although less and less severe, requiring 3 surgical interventions, and the pH remained above 6.5 despite 2 capsules a day of Lit-Control® pH Down.

After the last admission, a specific diet, maintenance of the thiazide diuretic and Lit-Control® pH Down, as well as daily urinary pH monitoring with an electronic device instead of test strips are recommended. In addition, the use of the myLit-Control® App is suggested to quantify water intake and urinary pH and, based on the records, to modify the dosage of supplements and also to improve adherence to the hygienic-dietary recommendations.

f. Clinical results

In the last 5 months, after close follow-up, the urinary pH has remained below 6.5 in most measurements, urinary symptoms have improved and there has been a significant improvement in pain, which has allowed him to resume his daily activities. At the last consultation, the patient reported a decrease in voiding calibre and a cystoscopy was performed under general anaesthesia, finding sclerosis of the bladder neck which was

resected until healthy tissue was observed, which was to be expected due to previous manipulations and the total absence of lithiasis in the prostatic cell (Figure 4).

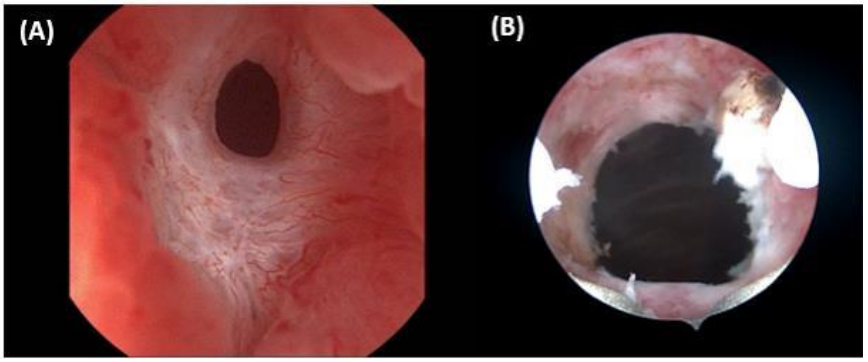

Figure 4. Cystoscopy. Sclerosis of the bladder neck and absence of lithiasis.

4. Discussion

Prostatic cell calcification following endoscopic surgery for prostatic hyperplasia is a very rare complication. A few case reports have been published over the years in patients undergoing TURP or KTP laser surgery[2,8,9]. Although the cause remains unclear, several hypotheses have been proposed including urinary stasis, necrotic tissue debris that generates inflammation and serves as a nidus for lithiasis formation, as well as metabolic conditions[9,10]. The low penetrability of the Holmium:YAG laser and its minimal thermal energy diffusion minimise tissue damage compared to other endoscopic methods; however, it is not exempt from this complication.

In our literature review we found only one publication of a series of 8 cases of prostatic cell calcification after HoLEP in a cohort of 877 patients, one of them with Brushite lithiasis[1] and with a clinical course similar to that of our patient. The diagnosis is complex, as the symptoms may be confused with other more common pathologies such as bladder hyperactivity, voiding problems, urinary tract infections or chronic pelvic pain.

The persistence of irritative symptoms after prostate surgery, especially urethral pain and irritative symptomatology, which does not improve with conventional treatment, requires an exhaustive study with cystoscopy, since calcification of the prostatic cell severely affects the patient's quality of life.

Treatment of urolithiasis requires a combined approach of surgical and medical treatment specific to the composition of the urolithiasis[5]. Previous studies have statistically significantly associated hypercalciuria, elevated urinary pH, low citrate excretion and inadequate hydration with Brushite stone formation[4]. Siener et al (2023) examined the patient profile and the impact of diet on the risk of Brushite stone formation under controlled conditions, demonstrating that urinary pH greater than 6.5 is the most frequent risk factor and that relative Brushite supersaturation decreased significantly under a balanced mixed diet compared to the usual diet, mainly due to the significant reduction in urinary calcium, phosphate and oxalate excretion[3]. Brushite stones represent a significant therapeutic challenge due to their rapid growth and high recurrence rate requiring an intensive treatment approach[4].

Patients receiving dietary and pharmacological therapies to maintain urinary pH in the non-lithogenic range may require continuous urine pH monitoring to assess adherence to treatment and determine the need for treatment adjustments. The Lit-Control® pH Meter (Devicare SL, Barcelona, Spain) connects to a smartphone via Bluetooth and synchronises with an app available for iOS and Android13. Studies have suggested high usability and acceptability, with 85% of patients reporting good adherence to using the device to record urinary pH and 97% of patients reporting high satisfaction with the app[6,13].

In the case of our patient, the initial management was surgical removal of the lithiasis, antibiotic treatment and hygienic-dietary modifications. However, despite these measures, recurrence of calcifications was observed, together with a persistent elevated urinary pH, which favours the formation of calcium phosphate dihydrate lithiasis5. Significant improvement was achieved by implementing a medical strategy focused on reducing renal calcium excretion with thiazides, a strict diet and urinary pH acidification with Lit-Control® pH Down. Home monitoring of urinary pH became an essential component of the management and probably the use of the myLit-Control® App facilitated follow-up, treatment adjustment and patient adherence to hygienic-dietary modifications.

Despite the therapeutic success in terms of pain and calcifications, certain complications persist such as sclerosis of the bladder neck, resulting from multiple urethral instrumentations, which also has a high risk of recurrence and will probably become our next therapeutic challenge in this clinical case.

5. Conclusions and recommendations

In conclusion, lithiasis formation in the prostatic cell after HoLEP is a rare but possible complication. Diagnosis requires a high level of suspicion, especially in patients with unexplained urethral pain. It is a difficult pathology to manage because of the high recurrence rate and may require a comprehensive approach including surgical interventions, specific medical treatment and continuous and accurate urinary pH monitoring. Although this approach showed promising results in reducing recurrences, it is important to recognise the limitations of this case report and the need for future studies.

6. Bibliographical references (*of special interest, **of extraordinary interest)

1. ** Lee YJ, Oh SJ. Calculi in the Prostatic Surgical Bed as a Complication after Holmium Laser Enucleation of the Prostate. *Endourology and stone disease.* doi: 10.22037/uj.v0i0.3965

2. Urushibara M, Shimizu Y, Matsumoto Y, Okumura T, Nagata M, Ishizaka K. Gradual resolution over time of recurrent dystrophic calcification after bipolar transurethral resection of the prostate: A case report. *Urol Case Rep*. 2023;47. doi:10.1016/j.eucr.2023.102369

3. ** Siener R, Pitzer MS, Speller J, Hesse A. Risk Profile of Patients with Brushite Stone Disease and the Impact of Diet. *Nutrients*. 2023;15(18). doi:10.3390/nu15184092

4. Pak CYC, Rodgers K, Poindexter JR, Sakhaee K. New Methods of Assessing Crystal Growth and Saturation of Brushite in Whole Urine: Effect of pH, Calcium and Citrate. *Journal of Urology*. 2008;180(4):1532-1537. doi:10.1016/j.juro.2008.06.011

5. * *Urolithiasis EAU Guidelines On*.; 2023.

6. De Coninck V, Keller EX, Rodríguez-Monsalve M, et al. Evaluation of a portable urinary pH meter and reagent strips. *J Endourol*. 2018;32(7):647-652. doi:10.1089/end.2018.0202

7. ** Ungerer GN, Winoker JS, Healy KA, Shah O, Koo K. Mobile and eHealth technologies in the management and prevention of nephrolithiasis: A systematic review. *Actas Urol Esp*. Published online 2023. doi:10.1016/j.acuro.2023.04.008

8. Jeon SW, Park YK, Chang SG. Dystrophic calcification and stone formation on the entire bladder neck after Potassium-titanyl phosphate laser vaporization for the prostate: A case report. *J Korean Med Sci*. 2009;24(4):741-743. doi:10.3346/jkms.2009.24.4.741

9. Thomas J, Khelif A, Arulanantham S, Lemaitre J, Lalive d'Epinay JE. Discovery of primary hyperparathyroidism following an endoscopic resection of the prostate: case report. *J Surg Case Rep*. 2022;2022(5). doi:10.1093/jscr/rjac247

10** Sanz-Gómez I, Angerri O, Baboudjian M, et al. Role, Cost, and Availably of Urinary pH Monitoring for Kidney Stone Disease—A Systematic Review of the Literature. *Curr Urol Rep*. 2023;24(8):381-388. doi:10.1007/s11934-023-01166-5