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Oncology

The Kilogland: Giant prostatic hyperplasia with incidental prostate adenocarcinoma

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ABSTRACT

A 74-year-old man with PSA of 21.1 ng/mL, eGFR of 13 mL/min/1.73 m 2 (stage 4 renal disease), and an 889 mL prostate (MRI; transrectal ultrasound estimated 1000 mL) underwent robotic simple prostatectomy for severe lower urinary tract symptoms, including nocturia and recurrent urinary retention. Adenoma dissection, bladder re-anastomosis, and morcellation resulted in 500 mL blood loss and one transfusion. Pathology revealed stromal/glandular hyperplasia and incidental Gleason 8 (3 + 5) adenocarcinoma (<2 % of tissue, no invasion). At six months, PSA was 0.25 ng/mL, with good continence. This case highlights successful robotic management of massive BPH with incidental malignancy.

1. Introduction

Benign prostatic hyperplasia (BPH) presents in approximately half of patients 60 years or older with 25–50 % of men of these men reporting progressive lower urinary tract symptoms. ^{1,2} In extremely rare cases patients may develop a condition known as giant BPH (GPH), defined as a prostate hyperplasia weighing over 500mL. ³ For comparison, the average prostate in men with BPH recognized from autopsy is 33mL, with less than 4 % of men over the age of 70 exceeding values over 100mL. ⁴ Guidelines provide clear guidance regarding surgical treatment options for patients with prostates >100ml volumes. However, treatment options for patients with giant prostate volumes are poorly characterized and largely the subject of case reports. Here we report a case of a patient with GPH successfully managed with minimally invasive robotic techniques and incidentally identified high risk prostate cancer.

2. Case presentation

A 74-year-old man was referred to our facility with foley catheter dependent acute urinary retention and a history of severe lower urinary tract symptoms including nocturia 4 times per night, weak stream, straining to void, and double voiding, with an International Prostate

Symptom Score (IPSS) of 17. He had no hematuria or urinary incontinence. The patient's medical history included a history of deep vein thrombosis, congestive heart failure, and chronic kidney disease. Preoperative digital rectal exam was remarkable for a very large prostate estimated at greater than 200mL volume with no palpable nodules. Abdominal exam demonstrated a large palpable midline mass superior to the pubic symphysis extending to the level of the umbilicus. Laboratory analyses demonstrated a prostate specific antigen of 21.1 ng/mL and EGFR of 13 mL/min/1.73 m².

Diagnostic transrectal ultrasound identified a very large prostate with a calculated volume of 1002mL prostate. Renal ultrasound demonstrated a renal cyst, bilateral hydronephrosis, a trabeculated, thickened bladder wall, and a postvoid residual volume greater than 2 L. Pelvic ultrasonography showed a very large intravesical mass originating from the prostate representing the median lobe of the prostate. A foley catheter was placed to alleviate his urinary obstruction and the patient underwent further workup. Preoperative prostate MRI indicated a significant median lobe hypertrophy displacing the bladder and the rectum (Fig. 1 The prostate volume was calculated as 889 mL using MRI measurements (approximate dimensions: 13 cm \times 11 cm \times 12 cm) and ellipsoid method, and a PI-RADS 2 score was assigned. MRI demonstrated no adenopathy, bone abnormalities or other soft tissue

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abnormalities beyond the prostate. PSA density was $0.03~\text{ng/mL}^2$. Prostate biopsy was discussed but ultimately not performed due to the patient's low PSAD and low PIRADS score. In the subsequent weeks the patient was started on tamsulosin 0.4mg PO daily and finasteride 5mg PO daily but failed several trials of void.

After consultation and discussion of the treatment options, a mutliport suprapubic robot-assisted simple prostatectomy (RASP) was planned using the Xi DaVinci System. The urachus was incised, and the bladder was dropped to enter the space of Retzius. We created a transverse incision in the anterior dome of the bladder, 1.5-2 cm from the bladder neck, allowing entry into the bladder and visualization of an enormous prostate median lobe along bi-lobar hyperplasia. Both ureteral orifices were identified and displaced in a posterior and cephalad direction by the prostate. A retraction stitch was placed through the median lobe and the adenoma was circumferentially mobilized and separated from the peripheral zone. A combination of blunt dissection, monopolar electrocautery with robotic scissors and bipolar electrocautery with a vessel sealer were used to circumferentially mobilize the transition zone of the prostate. Once the prostate adenoma was removed the bladder neck was anastomosed to the urethra with a double-armed CovidienTM V-LocTM 3-0 suture. The surgical specimen was placed into a Endo CatchTM laparoscopic bag and then morcellated within the bag using the LiNATM Xcise cordless laparoscopic morcellator (Fig. 2). After confirming hemostasis, a 20-French 3-way Foley catheter was placed. The bladder was closed in two layers, and filled with 250 mL of saline, and no leaks were observed. The duration of the procedure was 340 minutes with no perioperative complications. The estimated blood loss was 500mL and one unit of blood was transfused. The patient was placed in overnight observation with continuous bladder irrigation (CBI). On postoperative day (POD) 1 CBI was stopped due to minimal bleeding and the patient was discharged on POD 1. On POD 7 the patient was presented to the clinic with bloodless urine. A trial of void was performed and he successfully voided.

Postoperative pathology indicated two foci of incidental Gleason 3+5=8 prostate adenocarcinoma comprising less than 2 % of the total tissue specimen, with largest foci measuring 9.5mm. An assessment of margin status was not possible due to specimen morcellation. Perineural and angiolymphatic vascular invasion were not identified. Tumor immunohistochemistry showed stromal and glandular hyperplasia (Fig. 3). Prostate tissue removed weighed 690 g. His case was presented at tumor board to address the management of the incidentally discovered Gleason 8 prostate cancer. PSA surveillance vs immediate adjuvant radiation, and transrectal ultrasound with prostate needle biopsies of the peripheral zone were suggested by the tumor board. The patient elected for PSA surveillance with treatment if PSA elevation occurred. On 10month follow-up, the patient was doing well with complete emptying, no incontinence, resolution of his urinary tract symptoms and no changes in erectile function. His six-month postoperative PSA was stable at 0.25 ng/mL and radiation therapy was not administered.



Fig. 2. Morcellated surgical specimen illustrating the GPH removed by robotic simple prostatectomy.

3. Discussion

The optimal means of management of benign prostatic hyperplasia are undefined. The current guidelines from the American Urological Association recommend an endoscopic approach for treating small (\leq 30 mL) and medium-sized (31–80 mL) prostates, while suggesting simple prostatectomy for large prostates (\geq 81 mL). These size categories are essential for guiding the management and treatment options for patients with BPH, including pharmacotherapy and surgical interventions. No guidance is provided for cases of giant prostatic hyperplasia.

This case represented an interesting opportunity to employ modern surgical tools and strategies for the management of GPH. Historically, open simple prostatectomy was favored in cases of GPH, however it is associated with high rates of hemorrhage. In one series of 8 patients with a prostate mass of greater than 700 g, the open simple prostatectomy resulted in mortality from hemorrhage in 3 of 8 patients. Conversely, only one case of a robotic simple prostatectomy for GPH over 700 g has been reported with no complications. Here we report the second case of a successful simple robotic prostatectomy without complication. While data is limited, RASP allows for excellent visualization of the prostatic adenoma to aid dissection and cauterization of bleeding, urethra sparing, pneumoperitoneum to limit intraoperative hemorrhage and the potential for bladder mucosal advancement to help further limit the risk of post operative bleeding.

When we conducted a literature search on online databases such as PubMed®, we found no published cases of aquablation or holmium enucleation of the prostate for prostates of such volumes. Similarly, prostate artery embolization has been studied in the treatment of BPH,

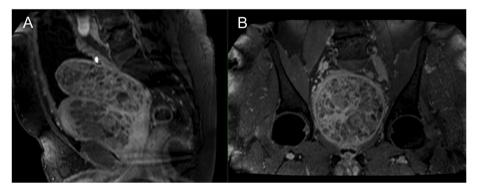
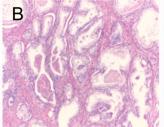


Fig. 1. Preoperative MRI demonstrating a giant prostate A). Sagittal view B). Axial view.



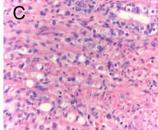


Fig. 3. The specimen consisted of 690 g of rubbery prostatic tissue (A). Microscopic evaluation demonstrated changes of diffuse stromal and glandular hyperplasia (B). Two foci of prostatic adenocarcinoma were identified, the largest of which measure 9.5 mm. The carcinoma shows features of Gleason patterns 3 and 5 (C), for a score of 8/10, Grade Group IV.

however studies addressing outcomes among men with very large prostate volumes are absent from the literature. In one series, Somwaru et al. reported prostate artery embolization led to favorable improvements in IPSS scores, with the average score decreasing from 26.5 to 10 at 24 months, with limited adverse effects among patients with an average prostate volume of 300 ml following prostate artery embolization. Similarly, there are no case reports of prostate artery embolization followed by staged robotic simple prostatectomy within this patient population. The absence of published series highlights the need for case reports in this extremely rare population.

The etiology and pathophysiology of GPH is not well understood. There are a myriad of factors that have been implicated in prostate grow including the overexpression of oncogenes including Ras and c-erbB-2 promoting cell proliferation, and decreased expression of cell cycle regulators like TP53 via a deletion or point mutation.^{7,8} Although these genes can be heterogeneously expressed in both BPH and prostate cancer, genetic differences due exist in both pathologies. A study conducted by Ahana et al. identified significant differences in the expression of apoptotic genes between patients with prostate cancer and those with BPH. Notably, BCL-2, a gene known to inhibit apoptosis, was found to be expressed 18-fold higher in prostate cancer patients compared to those with BPH. In contrast, BPH patients exhibited elevated levels of BALR2 lncRNA, a noncoding RNA that plays a dual role in promoting cell proliferation and inhibiting apoptosis. BALR2 upregulates CDK6, a key regulator of the cell cycle, and suppresses pro-apoptotic proteins like BIM, further contributing to its anti-apoptotic effects.

Furthermore, there is a gap in knowledge about the possible association of BPH and prostate cancer. Studies show patients with larger prostates (>80 g) diagnosed with prostate cancer tend to have lower Gleason scores, reduced extraprostatic extension, and fewer positive surgical margins compared to those with smaller prostates. 10-12 For instance, larger prostate volumes may be associated with a higher incidence of well-differentiated tumors and a lower likelihood of pathological upgrading after radical prostatectomy. 12 There may be a possible genetic linkage between BPH and prostate cancer as mutations in genes such as HBOX13, a protein which in its wild-type form represses androgen receptors, can increase the risk for prostate cancer in patients with BPH. 13 A study involving over 200 patients with BPH and prostate cancer investigated CYP17, a gene critical for sex hormone synthesis. ¹⁴ The researchers identified two alleles, A1 and A2, both of which are associated with an increased risk of developing BPH and prostate cancer. Notably, patients carrying two copies of the A1 allele exhibited the highest risk for both BPH and prostatic malignancy, compared to patients with one copy of each allele or two copies of A2, highlighting the potential role of CYP17 variants in the pathogenesis of these conditions.

In addition to the surgical challenge associated with this case, this case represents an atypical management strategy of subtotal prostatectomy (i.e. robotic simple prostatectomy) for prostate cancer isolated to the transition zone of the prostate. The AUA guidelines recommend procedures like transurethral resection of the prostate (TURP), holmium

laser enucleation of the prostate (HoLEP), or open prostatectomy for large prostates (>80 g). In this case, a robotic-assisted simple prostatectomy (RASP) was chosen, aligning with AUA guidelines for glands ≥100 mL. RASP is less invasive than open surgery and reduces hospital stay and blood loss. 15 The resection of the adenoma resulted in the incidental detection of high-grade prostate cancer and a dramatic PSA decline. Prior series have demonstrated incidental treatment of prostate following simple prostatectomy. In Ramos-Carpinteyro et al. reported 5 % of patients undergoing single-port prostatectomy were found to have incidental prostate cancer with 45 % of these patients having grade group 2 or higher prostate cancers. 16 The majority of patients were managed with surveillance for a short-term follow-up period of 17 months with low rates of adjuvant therapy, with only one patient with Gleason Grade Group 4 undergoing definitive therapy. Additional data is needed to evaluate the value of simple prostatectomy in patients with disease localized to the transition zone, but this case provides an interesting anecdote of a patient demonstrating an incidental prostate cancer during the treatment of a GPH.

4. Limitations

Despite the treatment success reported here, providers should take caution before generalizing these results. Though we encountered no surgical complications, this singular case represents anecdotal evidence and cannot be used in isolation to estimate the risks and benefits of taking a similar surgical approach. Similarly, this patient has a relatively short follow up limiting our ability to assess the oncologic control of his prostate cancer. We successfully demonstrate the use of robotic simple prostatectomy for GPH, while cautioning providers inexperienced in this technique.

5. Conclusion

GPH is a rare phenomenon which can be managed through minimal invasive robotic simple prostatectomy. While rare, giant prostatic hyperplasia can co-present with prostate cancer even in the context of a low PSA density and low PIRADS score. Concurrent GPH and prostate cancer is an extremely rare possibility presented here. Here we present a case documenting management of these conditions in the same patient.

CRediT authorship contribution statement

Rushil Rawal: Writing – review & editing, Writing – original draft, Data curation. Joshua Davood: Writing – review & editing. John Heard: Writing – review & editing, Conceptualization. Peris Castaneda: Writing – review & editing, Conceptualization. Hyung Kim: Supervision, Conceptualization. Daniel Luthringer: Data curation. Michael Ahdoot: Writing – review & editing, Writing – original draft, Validation, Supervision.

Disclosures

None.

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