

Robotic Prostatectomy in a Patient with Hemophilia

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ABSTRACT

Given the rich blood supply to the prostate and the adjacent Santorini's plexus, radical prostatectomy is associated with significant blood loss even in patients with normal coagulation profiles. In patients with hemophilia, any surgical procedure carries a risk of significant hemorrhage due to a deficiency of factors in the coagulation cascade. For these reasons, hemophiliac patients have often been encouraged to undergo radiation or other forms of nonsurgical treatment for clinically localized prostate cancer. However, the decreased blood loss associated with a laparoscopic/robotic approach and appropriate perioperative factor transfusions can minimize the risk of hemorrhage during robotic-assisted radical prostatectomy. We present the case report of a successful robotic-assisted laparoscopic prostatectomy in a patient with mild hemophilia A, with an estimated blood loss for the procedure of 20mL. We will focus on the perioperative management of the patient's factor replacement.

Key Words: Prostatic neoplasm, Prostatectomy, Hemophilia A, Robotic.

INTRODUCTION

Better hematological management has reduced bleeding complications in patients with acquired or congenital bleeding disorders who have undergone surgery. Successful open subtotal and transurethral prostatectomy has previously been described in patients with known hemorrhagic disorders after appropriate perioperative preparation.¹ One case report of a successful extraperitoneal laparoscopic radical prostatectomy has been described in a patient with hemophilia B (factor IX deficiency).² We present the first report to date of a successful transperitoneal robotic-assisted laparoscopic prostatectomy (RALP) in a patient with hemophilia A (factor VIII deficiency).

CASE REPORT

The patient was a 69-year-old white male with mild hemophilia A, who was diagnosed with clinically localized prostate cancer following evaluation for an abnormal digital rectal examination (T2a nodule). His PSA was 1.3. He underwent a prostate biopsy with periprocedural intranasal 1-deamino 8-D arginine vasopressin (dDAVP) and oral aminocaproic acid without bleeding complications, which revealed Gleason 3+4 =7 prostate cancer in 15% of one core. Prostate volume on ultrasound was 30mL. Aside from the hemophilia, the patient's past medical history is significant for lower urinary tract symptoms managed with alpha-blockers and morbid obesity, with a body mass index of 38. He had a prior surgical history of a left hip replacement in 1998, which was managed without bleeding complications following factor VIII replacement. All treatment options were discussed, the patient sought numerous opinions from urologists and radiation oncologists, and the patient opted for RALP.

Surgical Management

The patient underwent successful RALP with bilateral pelvic lymphadenectomy and bilateral nerve sparing with no bleeding complications and an estimated blood loss of 20mL. No hemostatic agents, such as Surgicel (Ethicon, Somerville, NJ) or Floseal (Baxter, Deerfield IL), were used during the procedure. He remained hospitalized

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until postoperative day (POD) 4 for careful hematologic monitoring and product administration. A small hematoma was noted at his Jackson-Pratt drain site on POD 4, but he was hemodynamically stable and asymptomatic. The Foley catheter was removed on POD 10. Final histopathology was pT2cN0, Gleason 3+4=7 with negative surgical margins and 10 negative lymph nodes.

He had very mild hematuria intermittently following catheter removal, but voided well until POD 28, when he developed gross hematuria and clot urinary retention. Following a failed attempt at Foley catheter placement, he was admitted. Cystourethroscopy was performed that revealed a small clot at the widely patent bladder neck and a slowly bleeding area at the level of the urethrovaginal anastomosis. This area was fulgurated, no further bleeding was identified, and a Foley catheter was placed. No further hematuria was noted, and he passed a trial of void 3 days later. Since then, no further complications have developed, and his PSA is undetectable.

Hematologic Management

Baseline factor VIII levels were 8% to 14% (normal range, 50% to 150%), with a response of >50% with dDAVP. This is consistent with mild hemophilia A. The goal was to keep his factor VIII levels above 100% during surgery and above 30% for 14 days postoperatively. On the morning of surgery, he received 20ug of intravenous dDAVP and 2720 IU of intravenous concentrated factor VIII with von Willebrand factor (Alphanate). His postoperative factor VIII level was 87%, and his hemoglobin was 13.9g/dL. Postoperatively, he received 2720IU of Alphanate every 12 hours for 3 days; in the 24 hours prior to discharge, he received 2 doses of 4080 IU. He also received 20ug of intravenous dDAVP daily for the first 2 postoperative days. Hemoglobin on POD one was 13.2; it reached a nadir of 13.0 on POD 3. His factor VIII level remained between 84% and 120% throughout his hospital course and peaked at 190% immediately prior to discharge.

Following discharge, he received infusions of 4080 IU of Alphanate daily for 7 days, then 2720 IU daily for another 7 days. An outpatient factor VIII level was drawn on POD 7, which at 66% was within the target range. At the time of readmission for gross hematuria on POD 28, his factor VIII level had dropped to 24% but his hemoglobin was 15.0. Prior to his cystourethroscopy, he received intranasal dDAVP. He then received 4080 IU every 12 hours for 2 doses, and his factor VIII level responded to 74%.

DISCUSSION

Open radical retropubic prostatectomy carries a high risk of intraoperative blood loss due to its rich blood supply and anatomic location deep in the pelvis and adjacent to Santorini's plexus. However, the tamponade provided by pneumoperitoneum and better visualization of vascular structures offered by the laparoscopic approach has substantially decreased the average blood loss during robotic radical prostatectomy.^{3,4} The widespread availability and appropriate use of coagulant factors has also improved the perioperative management of hemophilic patients undergoing surgery.⁵ However, persistent concern regarding intraoperative hemorrhage has led many urologists to consider radiation or other forms of primary prostate cancer treatment in patients with hemophilia.

Our patient was extremely well informed about prostate cancer and its various treatment options. He had no interest in active surveillance. He sought opinions from several open surgeons who felt that his risk of intraoperative hemorrhage was too great to undergo open radical retropubic prostatectomy, and recommended radiation therapy. Radiation oncologists felt that he was an appropriate candidate for intensity modulated radiation therapy. However, the patient was concerned that his bothersome preoperative voiding symptoms would worsen following radiation therapy. He was most interested in undergoing radical prostatectomy. A lengthy discussion was held with him regarding the risks and benefits of surgery, including the need for factor administration and longer postoperative monitoring than usual, and he was accepting of the risks. Considering that he had previously undergone successful orthopedic surgery without bleeding complications, he was confident that he could avoid significant morbidity following prostatectomy.

A multidisciplinary approach involving the urology, hematology, and anesthesia teams was used to coordinate his care. As there had been no reported experience with the management of hemophilia A in this situation, the hematologic decisions were empiric, based on experience with orthopedic and other open surgeries. It is recommended that patients undergoing surgery have factor VIII levels between 80% to 100% at the time of surgery and be maintained above 30% for at least 10 days to 14 days after surgery.^{5,6}

Patients with mild hemophilia A synthesize functional factor VIII, but at levels too low to be therapeutic. Such patients respond to dDAVP, which releases factor VIII and von Willebrand factor (vWF) from platelets, increasing

their serum concentration by up to 50%.⁵ In contrast, patients with severe hemophilia do not produce any functional factor VIII, and thus do not respond to dDAVP. In addition to dDAVP, purified factor VIII is available for intravenous infusion. This is usually necessary to achieve the factor VIII levels required in the perioperative period. Alternatively, cryoprecipitate can be utilized; however, it can require as much as 15 units to 20 units for effective replacement.⁶

One risk of factor replacement, however, is the development of antibodies to factor VIII, known as inhibitors, which functionally inhibit it. After the patient develops such inhibitors, it is much more difficult to control future bleeding episodes, as transfused factor VIII is less effective. The use of vWF in addition to concentrated human factor VIII has been reported to reduce the risk of inhibitor development, which was the rationale for using Alphanate in our patient.⁷

His postoperative factor replacement regimen remains a topic of debate. During his postoperative prophylactic Alphanate replacement, he did not have any bleeding issues. Potentially, this was overcautious and unnecessary; perhaps he could have been managed with purified factor VIII alone or simply intranasal dDAVP. Clearly, when he had a bleeding complication on POD 28, his factor VIII level was subtherapeutic. It is unknown whether this complication could have been prevented by maintaining his factor VIII level above 30% at that time.

Kernoff⁸ reported several cases of suprapubic or transurethral prostatectomies in which there were extensive blood loss and massive blood requirements. Following the development and availability of factor concentrates, similar procedures had improved rates of intraoperative hemorrhage and the postoperative course.^{9,10} Goldsmith¹ later described a successful perioperative management plan in hemophiliac patients who underwent subtotal prostatectomy. However, given the effective medical treatments for benign prostatic hyperplasia that were subsequently developed, the need for surgical intervention in such patients largely disappeared. With the growing acceptance of laparoscopic radical prostatectomy, this procedure is now feasible in patients with hemophilia.²

This case demonstrates that with a multidisciplinary approach, RALP can successfully be performed in patients with hemophilia A. The patient was observed in the hos-

pital for 3 days longer than the standard one night stay, and there was a Clavien grade III bleeding complication at POD 28 that required surgical intervention.¹¹ It is possible that this could have been avoided by longer home use of intranasal dDAVP or intravenous factor VIII. We will use this information as we work toward establishing a protocol for the postoperative management of persons with hemophilia undergoing RALP.

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