BRIEF REPORT

Prostatic Arterial Embolization for Control of Hematuria in Patients with Advanced Prostate Cancer

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ABSTRACT

Nine patients with advanced prostate cancer (stage T4) underwent prostatic arterial embolization (PAE) for refractory prostatic hematuria. Angiograms showed prostatic neovascularity in all cases, and complete PAE was achieved in 8 cases (89% technical success rate). Gross hematuria ceased after PAE in 6 cases, translating to a 67% clinical success rate. There were no PAE-related complications. At 3-month follow-up, 2 cases showed recurrent hematuria, 4 patients had died from PAE-unrelated etiologies, and only 3 patients survived and were without gross hematuria. PAE could represent an alternative option for patients with advanced prostate cancer to control hematuria.

ABBREVIATIONS

BPH = benign prostatic hyperplasia, PAE = prostatic artery embolization, TNM = tumor/node/metastasis [staging]

Prostatic hematuria that is usually associated with benign prostatic hyperplasia (BPH) or prostate cancer can be a clinical challenge. It can be managed by continuous bladder irrigation, bladder instillations, or cystoscopic treatments in more advanced cases (1). When all these measures have failed, prostatic artery embolization (PAE) could be indicated (2–9).

Most previous reports concerning PAE have focused on improving lower urinary tract symptoms in cases with BPH (2,7,8). The literature concerning the use of PAE for control of hematuria in patients with advanced prostate cancer is still limited (3–6,9). The purpose of the present retrospective study was to investigate the feasibility of PAE in advanced prostate cancer–related refractory hematuria.

MATERIALS AND METHODS

An institutionally approved retrospective review was performed on nine patients (mean age, 71.9 y) who underwent PAE for advanced prostate cancer–related refractory hematuria between 2012 and 2015. Patient informed consent was waived.

None of the nine patients had shown a response to conventional treatment, including bladder irrigation or cystoscopy, and they were referred for PAE treatment. All were diagnosed with stage IV prostate cancer with bladder invasion. The median Gleason score was 9 (range, 7–10). One patient (case 2; Table) had locally recurrent prostate cancer at the bladder neck after treatment with total prostatectomy 7 years before PAE treatment.

Internal iliac artery angiograms were obtained by using a 5-F Cobra catheter (Cook, Bloomington, Indiana). The hypervascular enhancement in the corresponding area of the prostatic fossa on the angiogram was interpreted as prostatic neovascularity. Based on the angiographic findings, the tumor feeding vessels were superselectively catheterized with a 2.7-F coaxial microcatheter (Progreat; Terumo, Tokyo, Japan) and were subsequently embolized.
<table>
<thead>
<tr>
<th>Case No./Age (y)</th>
<th>Tumor Stage</th>
<th>Chief Symptom</th>
<th>Coagulation Parameters*</th>
<th>ECOG</th>
<th>Angiographic Findings</th>
<th>Right</th>
<th>Embolized Target Artery</th>
<th>Embolic Agent</th>
<th>Technical Success</th>
<th>Hb Level pre/post (g/dL)†</th>
<th>Units pRBCs†</th>
<th>Residual Hematuria (d)</th>
<th>Retained Catheter (d)</th>
<th>Clinical Success</th>
<th>Prognoses at 3-mo follow-up</th>
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<tr>
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<td>IV (T4N1M1)</td>
<td>Hematuria</td>
<td>WNL</td>
<td>3</td>
<td>PN</td>
<td>–</td>
<td>OA, PA, VA, Anterior division of IIA‡</td>
<td>Gelfoam</td>
<td>Yes</td>
<td>8.2/9.6</td>
<td>6/2</td>
<td>2</td>
<td>–</td>
<td>Yes</td>
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<td>PN</td>
<td>VA</td>
<td>VA</td>
<td>PVA (both); Microcoils (left)</td>
<td>Yes</td>
<td>7.5/10.7</td>
<td>2/0</td>
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<td>–</td>
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<td>PN, CE</td>
<td>PA</td>
<td>PA</td>
<td>PVA, Gelfoam</td>
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<td>13.6/11.6</td>
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<td>10</td>
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<td>PAs</td>
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<td>PVA (45–150 μm)</td>
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<td>PN</td>
<td>PA</td>
<td>PA</td>
<td>PVA (45–150 μm)</td>
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<td>2</td>
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<td>9/3</td>
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CE = contrast extravasation; ECOG = Eastern Cooperative Oncology Group; Hb = hemoglobin; IIA = internal iliac artery; INR = International Normalized Ratio; IPA = internal pudendal artery; OA = obturator artery; PA = prostatic artery; PN = prostatic neovascularity; pRBCs = packed red blood cells; PVA = polyvinyl alcohol; VD = voiding difficulty; WNL = within normal limits.

*Coagulopathy was considered to represent an International Normalized Ratio > 1.3 or platelet count < 80,000/μL.
†Measurements given as pretreatment/posttreatment. Hemoglobin levels were measured within 1 week before and after PAE.
‡Anterior division of IIA except superior gluteal artery.

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until blood flow stasis occurred. Selection of embolic agents was dependent on operator preference and included polyvinyl alcohol particles (Contour; Boston Scientific, Marlborough, Massachusetts), gelatin sponge particles (Spongostan; Johnson & Johnson, Gauteng, South Africa), and microcoils (Cook). If a postembolization internal iliac angiogram revealed residual prostatic enhancement, the same procedure was repeated to occlude the additional arteries feeding the tumor.

Technical success was defined as elimination of all prostatic neovascularity by PAE (3,5). Clinical success was defined as cessation of gross hemostasis within 1 week after PAE (4,6,9). Patient data, PAE treatments, and patient prognoses at 3-month follow-up were collected.

RESULTS

Patient data, PAE treatments, and patient prognoses are summarized in the Table. Among the nine cases, eight received a complete embolization procedure, including seven cases with bilateral PAE and one case (case 8) with only right-sided PAE. Figure 1 shows the complete bilateral PAE procedure in case 3. Patient 8 had received an aortoiliac stent graft years earlier, and the aortogram showed occlusion of the left internal iliac artery at its origin; therefore, prostatic neovascularity was supplied only by right-sided feeder vessels and there was no left-sided prostatic neovascularity (not shown). One case (case 1) received an incomplete embolization procedure with left-sided PAE only because the right-sided minimal prostatic neovascularity was supplied by multiple fine feeder vessels, which were too small to undergo superselective catheterization (Fig 2). The technical success rate (ie, complete embolization) was 89%.

Based on pre-PAE internal iliac angiograms, prostatic neovascularity was observed in all patients, and contrast medium extravasation was observed in only one case (case 3; Fig 1). There was no PAE-related complication (eg, buttock or perineal pain, bladder necrosis, gluteal paresis, or skin necrosis) in any of the cases according to medical records.

After PAE, gross hematuria was alleviated in six of nine patients (67%). Hematuria subsided on day 0 in one case (case 8), day 1 in one case (case 4), day 2 in three cases (cases 1, 2, and 5), and day 3 in one case (case 3), with an overall clinical success rate of 67%. Although hematuria was less severe after complete PAE in cases 6 and 7, mild residual hematuria lasted for 12 and 26 days, respectively, and neither case was considered a clinical success. Both patients received continued supportive treatment before complete hemostasis was achieved, and vital signs and hemoglobin levels were maintained. Another case of clinical failure (case 9) occurred in a patient whose prostate tumor volume was more than 1,000 mL based on computed tomography (CT; estimated based on the ellipsoid formula width \times height \times length \times \pi/6) and had residual hematuria after complete PAE. He died from poorly controlled urosepsis on post-PAE day 17.

Seven patients received blood transfusions based on clinical symptoms during hospitalization. After PAE, despite residual hematuria, three cases (cases 2, 4, and 6) did not require further blood transfusion therapy. In contrast, three cases (cases 1, 7 and 8) still continued to receive blood transfusions, which were tapered off within 1 week; one case (case 9) showed a poor response to PAE, and the patient received blood transfusions.

Four patients with symptoms of voiding difficulty received bladder catheterization procedures during hospitalization. After PAE, two of these patients (cases 3 and 8) recovered spontaneous urination on post-PAE days 3 and 2, respectively. One of four cases (case 4) had persistent difficulty voiding and underwent transurethral resection of the prostate before the successful withdrawal of bladder catheterization on post-PAE day 10; one patient (case 6) continued to receive catheterization therapy until discharge.

At 3-month follow-up, two patients (cases 1 and 5) experienced recurrent gross hematuria on post-PAE days 34 and 24, respectively. Both received supportive treatment, with no further requirement for a repeat PAE procedure. Three patients (case 2, 7, and 9) died of urosepsis on post-PAE days 68, 74, and 17, respectively. One patient (case 8) died of cardiogenic pulmonary edema on post-PAE day 50. After excluding cases of early (< 3 mo) death or persistent/recurrent gross hematuria, only three patients (cases 3, 4, and 6) survived more than 3 months and were free from gross hematuria after PAE.

DISCUSSION

Transcatheter arterial embolization has been used to treat refractory hematuria in patients with pelvic cancer (3–6,9). Nabi et al (3), in their study of six cases in 2003, reported that the hematuria in two of their three cases with prostate cancer (tumor/node/metastasis [TNM] stage T3N2M0, M1, and T3N0M1, respectively) was completely controlled by the first attempted embolization. Rastinehad et al (4), in their study of eight cases in 2008, reported successful treatment of gross hematuria in all six cases of prostate cancer (one stage T1c, one stage T2a, two stage T3, and two stage T4). They also reported one case with recurrent hematuria 14 months later (attributed to recurrent tumor) and another case with stage T4 cancer in which a rectovesical fistula developed 1 month later. Prasad et al (5), in their study of 11 cases in 2009, reported successful treatment of gross hematuria by using superselective embolization in all four cases.
involving prostate cancer (stage not reported), with no further management required. They also reported that two of those cases had recurrent hematuria at 84 and 11 days after embolization, respectively. Delgal et al (6), in their study of 20 cases in 2010, reported successful treatment of gross hematuria in both cases with prostate cancer (stage T2N0M0 and T3bN0M1, respectively) within a few days. Korkmaz et al (9), in their study of 18 cases from 2015, reported successful treatment of gross hematuria within 3 days in all six cases with prostate cancer (stage not reported).

Although embolization for prostatic hematuria control has already been described (3–6,9), the efficacy of the therapy is still difficult to assess because all published
reports of which we are aware were limited by small case numbers and heterogeneous cancer staging. The present study focused on only patients with prostate cancer and found that PAE had a high technical success rate (89%) and a moderate effect on hemostasis (ie, a 67% clinical success rate). The effect on hemostasis was slightly lower compared with previous reports, probably because of the relatively late stage of cancer (all locally advanced tumors, stage T4) and complex collateral vessels in the present study.

Prostate cancer–related hematuria results from tumor causing bleeding into the prostatic urethra or tumor invading the bladder. As prostate cancers progress, extracapsular neovascular anastomoses to collateral vessels within the pelvis usually develop (10). Selective prostatic angiograms help to determine the complex

**Figure 2.** Images from an 81-year-old man who presented with intractable hematuria caused by advanced prostate cancer (case 1; Table). Early- (a) and late-phase (b) images of a left internal iliac arteriogram show a hyperemic prostate gland supplied by the left vesical (short arrows, a), prostatic (arrowheads, a), and obturator (long arrows, a) arteries and prostatic neovascularity (black asterisks, a,b) within the prostate gland and urinary bladder. Note the midline-crossing prostatic neovascularity on the right side of the prostate gland (white asterisk, b). (c) Right internal iliac arteriogram shows multiple fine feeder vessel (arrows) to the faint prostatic neovascularity. Embolization on the right side was not performed because of difficulty in superselection of these fine feeder vessels. (d) Left internal iliac arteriogram shows no further prostatic enhancement after embolization of the left-sided feeder vessels with the use of gelatin sponge particles. The hematuria was controlled.
prostatic vascular anatomy and to identify prostatic neovascularity before embolization (4,11). The incidence of postembolization ischemia of pelvic structures is lower when selective technique is employed compared with nonselective technique (7,12). In our hospital, the selective PAE technique is preferred for the prostate gland, with no procedure-related ischemia. If the target arteries cannot be selectively catheterized, it may be appropriate to “steer” the polyvinyl alcohol particles into tumor feeding vessels after microcoil blockade at the orifice of distal nontarget arteries (5). However, selective catheterization that is too advanced may miss some feeding arteries from unexpected collateral vessels and reduce or delay the effect on hemostasis. Therefore, a balance should be sought between the use of the two techniques (selective vs nonselective).

An earlier study (13) suggested a higher risk of recurrent pelvic bleeding after unilateral embolization, as recurrent bleeding is probably caused by rich collateral blood supply to the internal iliac artery from the contralateral internal iliac, inferior mesenteric, external iliac, and femoral arteries (13). To prevent recurrent bleeding, embolization with the use of particles is suggested bilaterally regardless of whether the bleeding site is detectable on the angiocardiogram (3–5). However, in the present study, recent gross hematuria occurred in cases of unilateral (case 1) and bilateral (case 5) embolization. Bilateral embolization with the use of particles cannot ensure complete prevention of recurrent bleeding in cases with advanced prostate cancer. Prasad et al (5) also reported a similar case with locally advanced prostate cancer in which bleeding recurred 84 days after bilateral embolization.

Carnevale et al (8), in a study of cases with BPH, reported that PAE was effective in relieving lower urinary tract symptoms as well as providing significant volume reduction of the prostate. In the present study, two cases (cases 3 and 8) with voiding difficulty recovered spontaneous urination soon after PAE. The additional advantage of PAE for patients with prostate cancer in relieving lower urinary tract symptoms is rarely mentioned in the published literature. Blood clot–induced voiding difficulty was considered in two of the present cases because both showed a good response to PAE with regard to hematuria control. However, another case (case 4) had persistent voiding difficulty and underwent transurethral prostate resection surgery despite PAE having controlled his hematuria. The mass effect from advanced tumor rather than urethral obstruction by blood clots may be responsible for the difficulty in voiding. The relation between lower urinary tract symptoms and PAE in patients with advanced prostate cancer requires further investigation in larger patient cohorts with an appropriately rigorous study design.

Urosepsis occurs in approximately one fourth of all patients with sepsis and carries a high risk in cases with congenital or acquired genitourinary abnormalities (14). Although PAE was attempted to control prostate cancer–related hematuria, three patients had died of urosepsis by 3-month follow-up. The medical records were reviewed, and sepsis was attributed to the comorbidity of advanced prostate cancer rather than a complication of the PAE procedures. Therefore, post-PAE care is critical. However, a detailed discussion concerning antimicrobial therapy for urosepsis is beyond the scope of the present study.

The present study has several limitations, including its small sample size. In addition, because of its retrospective nature, some data were incomplete including objective quantification of lower urinary tract symptoms, the exact time point at which hemoglobin levels were measured, and a lack of rigid criteria regarding blood transfusions. In addition, the embolic agents and embolized target arteries were heterogeneous. Therefore, it cannot be evaluated whether procedural differences influenced treatment outcomes. Finally, cone-beam CT can be used to evaluate PAE in patients with BPH because it can potentially mitigate the risk of nontarget embolization or identify a duplicated prostatic arterial supply or contralateral perfusion (15). However, the benefit of cone-beam CT for hematuria control was not demonstrated in the present study because PAE was performed based on angiography alone.

In conclusion, PAE had a high success rate and a moderate effect on hemostasis without obvious technique–related complications in patients with advanced prostate cancer.

REFERENCES


