

Prostate Brachytherapy seed migration to the Bladder presenting with Gross Hematuria

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ABSTRACT

We present the radiologic findings in a case of prostate brachytherapy seed migration to the bladder presenting as gross hematuria. While prostate brachytherapy seed implantation is considered a relatively safe procedure, migration is not uncommon; however, it is usually clinically silent and the seeds most commonly migrate to the lungs through the venous circulation via the periprostatic venous plexus. Our case illustrates that local erosion is possible, can be symptomatic, and therefore must be considered when evaluating select patients.

CASE REPORT

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A 74 year-old male presented for a four-phase renal protocol CTA of the abdomen to evaluate persistent gross hematuria. Relevant past medical history included melanoma in remission and prostate cancer diagnosed in 2003. Patient was diagnosed with prostate cancer after noting increased frequency and PSA level of 4 ng/ml which prompted prostate biopsy that revealed (Gleason 3+3) prostate carcinoma. He underwent brachytherapy with ultrasound-guided I-125 (coated) seed implantation at the time of diagnosis in 2003. Prostate-specific antigen (PSA) levels subsequently normalized to <0.01 ng/ml. In 2013 (ten years after the initial presentation), he presented with rapidly elevating PSA (from 2.1 ng/ml to 4 ng/ml within 5 months interval) and hematuria, raising suspicion for local recurrence. Of note, interim imaging for the patient included CT of the pelvis revealing anteriorly placed prostatic seeds. Cystoscopy was performed at the time of presentation and revealed a tumor arising from the prostate at the bladder neck. Six months later, he underwent transurethral resection of the prostate, bladder neck biopsy was obtained and pathology reported prostatic adenocarcinoma (Gleason 4+5) invading the lamina propria but sparing the muscularis propria. His PSA normalized to less than 1 ng/ml but his hematuria persisted. Given the degree of hematuria,

palliative external beam radiation therapy was initiated for four weeks but was ineffective in alleviating his symptoms and hematuria persisted. A four-phase renal protocol CTA of the abdomen was ordered to better evaluate the bladder, where a hyperdense linear structure with an appearance similar to the prostate brachytherapy seeds was noted within the bladder lumen raising suspicion for hematuria subsequent to foreign body induced cystitis (Figure 1). One month later, the patient underwent cystoscopy, prostatic urethral atrophy was noted with no bladder neck contracture and normal bladder mucosa, upon passing the bladder neck, a brachytherapy seed was clearly noted in the bladder which was removed and surrounding bleeding vessels were cauterized, pathology report indicated the removal of one small rod like fragment of silver gray metal measuring approximately 0.4 X 0.1 X 0.1 cm. The patient's hematuria improved significantly on subsequent follow-up visits.

DISCUSSION

Etiology & Demographics:

Prostate cancer is the most frequently diagnosed non-skin cancer in males in the United States, with a lifetime risk of 15.9% [1]. Several management methods for prostate cancer

have evolved over years, including radical prostatectomy, radiation therapy (external beam and brachytherapy), and active surveillance, with management decisions determined by patient's preference, clinical status, cancer stage and resource availability [2]. Brachytherapy via radioactive seed implantation was first used in 1960. At that time, Iodine 125 seeds were only placed intraoperatively in patients undergoing lymphadenectomy. It was officially introduced as a treatment for localized prostate cancer in 1980. Currently, the technique involves prostatic volumetry via transrectal ultrasound to determine the number, type (Iodine 125 or Palladium 103) and radiation emission dose of the seeds, which are then implanted transperineally under ultrasound or MRI guidance [2]. Seed migration is considered a relatively common complication with studies showing that incidence of seed migration per patient ranged between 25-55% [3, 4].

Clinical & Imaging findings:

Prostate brachytherapy is considered a minor procedure with a high success rate and minimal complications. Short-term complications arise in several hours to several weeks and most commonly include urinary urgency, frequency, retention and incontinence. Long-term complications such as erectile dysfunction, rectal toxicity and urethral stricture, often require over a year to ensue [5]. Seed migration is considered a relatively common complication; however, it is underreported because most cases of seed migration are clinically silent. They rarely cause symptoms at the ectopic site and do not appreciably affect the post-implant dosimetry or efficacy of the procedure (given the low percentage of migrated seeds relative to the total seeds implanted) [6]. The most common site of migration is the lung; it is thought that seeds follow the venous circulation, passing from the periprostatic venous plexus through the inferior vena cava into the pulmonary arterioles. However, seeds can reach the arterial circulation and end up in virtually any anatomical location if a patent foramen ovale, pulmonary arteriovenous shunt, or other right-to-left shunt is present [7].

Several investigators have attempted to quantify and characterize seed migration. Sugawara et al investigated the incidence of Iodine 125 seed migration to the chest, abdomen, and pelvis in 267 prostate cancer patients and found a 25% per-patient (0.46% per-seed) incidence of migration; the vast majority of these (20% of all patients) had migration to the chest with only 2.2% and 5.6% of patients demonstrating migration to the abdomen or pelvis, respectively. All patients were asymptomatic, and no seeds were reported in the bladder [3]. Eshleman et al found that 55% of 100 patients undergoing prostate brachytherapy had evidence of seed migration to the chest on subsequent chest x-rays; they also found no clinical dosimetric consequences [4]. The differences in migration rates between the studies could be related to several factors, such as the technical experience [6] and the type of seeds used (coated versus uncoated) as the fixity of I125 seeds embedded in a vicryl suture (coated) is higher compared to uncoated I125 seeds. The migration rate in coated seeds is less than the migration rate in uncoated seeds [8]. In other series, Stutz et al. reported that seeds loss in the urinary tract is common with up to 29.7 % of patients experiencing this event in the post implantation period (while in the recovery room) and loss of

0.58% of seeds activity was reported. Seeds were found in the urine or in the bladder through cystoscopy immediately following the implantation procedure. However, the route of seed migration to the urinary tract or any potential clinical manifestations has not been discussed. Furthermore, percentage of seeds recovered in the urinary tract following patients discharge was insignificant. Potential causes as discussed were technical inexperience and difficulty delineating the prostate/bladder interface on axial imaging [9].

While most systematic investigations have shown that seed migration is rarely symptomatic, several case reports have described unusual sites with consequent clinical impact, including migration to the left testicular vein presenting with testicular pain [7], to the vertebral venous plexus and then renal artery resulting in nerve root compression [6], to right coronary artery with subsequent myocardial infarction [10], and to the right ventricle with subsequent fatal arrhythmia [11]. Interestingly, all of these case series and reports implicated transvenous migration from the periprostatic plexus to the target organ; however, the close proximity to the bladder, erosion seen on cystoscopy, and persistent hematuria in our case suggests direct erosion into the bladder wall.

Migrated seeds can be identified with plain radiography or computed tomography; they present as small linear hyperdensities simulating the intraprostatic seeds. Identification can be difficult given their small size; in our case, multiplanar and 3-D reconstructions greatly aided localization and diagnostic certainty.

Treatment & Prognosis:

As indicated previously, prostate brachytherapy seed migration is a very common entity. However, it is underestimated as it rarely causes any clinical manifestations and the number of migrated seeds is relatively small compared to the number of implanted seeds, in this majority of cases, no additional management of clinically "silent" cases is required [6]. On the other hand, when a patient presents with clinical symptoms that could be attributed to a migrated seed, management is considered on case by case basis depending on the site of migration and clinical consequences of the migrated seeds [6, 7, 10, 11]. In our case seed was removed through cystoscopy and patient's hematuria significantly improved on follow up visits.

Differential Diagnosis:

Gross hematuria in a patient with prostate cancer might result from wide spectrum of etiologies. Multiple factors contribute to hematuria in those patients including the carcinoma itself, previous managements or local recurrence. However, the frequency of this complication and exact management is not well addressed [12]. Local recurrence in our case would have presented on CT, MRI and ultrasound as a soft tissue extending into the bladder. It would present on PET as a hypermetabolic soft tissue. Our patient had undergone renal protocol four phase CTA of the abdomen which revealed no abnormal masses into the bladder. Local recurrence proved not to be the etiology of hematuria given the lack of improvement following TURP and palliative radiation therapy.

Appropriately located brachytherapy seeds are a very rare etiology of gross hematuria. The incidence of hematuria in patients who underwent brachytherapy was reported by Anderson et al as 1% [13]. They present on Plain radiographs or CT as small metallic density structures in their expected anatomic location within the prostate gland. On the other hand, they present on ultrasound as small echogenic foci with posterior shadowing within the prostate gland and on MR with signal voiding at the expected anatomic location within the prostate gland. Migrated seeds would present on the previous modalities with the exact same presentation but in an expected anatomic location. Improvement of symptoms after removal of the migrated seeds in our case despite presence of the previous appropriately located seeds could not be explained assuming the latter as a potential cause of the patient's hematuria.

Finally, gross hematuria in an old patient raises suspicion for primary bladder carcinoma [14]. Bladder cancer would present on CT and MRI as a small nodular enhancing soft tissue mass and on PET scan as hypermetabolic mass. In our case, however, CT findings and pathology reports did not indicate any primary bladder carcinoma.

TEACHING POINT

A high index of suspicion must be maintained when evaluating patients with persistent symptoms that could be attributable to prostate brachytherapy seed migration (Gross hematuria in our case resulting from a seed migration to the bladder). Migrated seeds are best appreciated on X-ray or CT images. Multiplanar and 3-D CT reconstructions greatly aid localization and diagnostic certainty.

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FIGURES



Figure 1: 74- year- old male with history of prostate cancer treated with brachytherapy presents with gross hematuria that was attributed to a migrated seed from the prostate to the bladder eroding the bladder mucosa.

Findings: Renal protocol contrast-enhanced CT through the bladder in venous (a and b) and delayed (c and d) phases show a small hyperdense structure measuring approximately 0.4 x 0.1 x 0.1 cm in the bladder lumen (arrows), surrounded by contrast material on delayed phase images. An intraluminal prostate brachytherapy seed was removed at cystoscopy. Normally localized prostate brachytherapy seeds can also be seen (arrowheads). A. Coronal. B. Sagittal. C. Axial. D. Coronal.

Technique: Renal protocol contrast enhanced CT (Siemens 64 slice scanner, 325 mA for venous, 275 mA for delayed, 120 kV, 3 mm slice thickness, 110 ml IV Visipaque).

Etiology	Migrated brachytherapy seed causing local erosion
Incidence	Unknown for this specific case but seed migration incidence overall varies between 26-55% amongst studies
Gender ratio	Only males
Age predilection	Unknown but prostate cancer prevalence is higher in old males.
Risk factors	Uncoated seeds, lack of experience of the medical professional introducing the seeds.
Treatment	Cystoscopy and seed removal
Prognosis	Very good after seed removal in regard to hematuria

Table 1: Summary table for prostate brachytherapy seed migration to the bladder.

Differential	Plain X-ray	CT	MRI	US	PET
Appropriately located brachytherapy seeds	Small metallic density structures in expected anatomic location inferior and posterior to the base of the bladder	Small metallic density structures in expected anatomic location within the prostate gland	Signal voids in expected anatomic location within the prostate gland	Small echogenic foci with posterior shadowing within the prostate gland	N/A
Migrated brachytherapy seed	Small metallic density structure in unexpected anatomic location	Small metallic density structure in unexpected anatomic location	Small metallic density structure in unexpected anatomic location	Small echogenic foci with posterior shadowing within the urinary bladder	N/A
Local recurrence	Occult on radiographs	Soft-tissue extending into the bladder	Soft-tissue extending into the bladder	Soft-tissue extending into the bladder	Hypermetabolic soft tissue extending into the bladder
Primary bladder neoplasm	Occult on radiograph	Nodular enhancing soft tissue mass	Nodular enhancing soft tissue mass	Nodular enhancing soft tissue mass	Hypermetabolic bladder mass

Table 2: Differential diagnosis for prostate cancer brachytherapy migrated seed causing local erosion and presenting with hematuria.

ABBREVIATIONS

3-D = 3 Dimensional
 CT = Computed tomography.
 MRI = Magnetic resonance imaging
 PET = Positron emission tomography.
 US = Ultrasound

KEYWORDS

Prostate cancer; brachytherapy; seed migration; hematuria; 3-D Computed tomography

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