

CYSTECTOMY INFORMATION BINDER

JAMES BUCHANAN BRADY UROLOGICAL INSTITUTE

WELCOME TO THE UROLOGY CLINIC AT THE JOHNS HOPKINS OUTPATIENT CENTER

This folder has been compiled to provide information for patients who come to the clinic for answers to the clinical diagnosis of bladder cancer.

- ❖ Clinical information which you should be prepared to provide for us includes:
 - CAT scan and MRI films
 - Pathology slides (glass slides from biopsy)
 - Medical Records
 - Referring doctors names and addresses

This folder includes:

- ❖ An outline of:
 - Diagnosis and treatment of bladder cancer
 - Types of bladder reconstruction
- ❖ Relevant articles
 - Local Recurrence and Survival Following Nerve Sparing Cystoprostatectomy for Bladder Cancer: 10 year follow-up
 - Detection of Bladder Recurrence by Microsatellite Analysis or Urine
- ❖ Information regarding the Cancer Information Service and the Cancer Counseling Center
- ❖ The bowel preparation for cystectomy and laparotomy patients

WE HOPE THE INFORMATION IN THIS FOLDER WILL BE A HELPFUL GUIDE DURING YOUR CONSULTATION AND AFTER YOU RETURN HOME



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DEPARTMENT OF UROLOGY:

Brady Urological Institute

The Brady Urological Institute of The Johns Hopkins Hospital is dedicated to providing state-of-the-art medical and surgical care in all aspects of adult and pediatric urology.

The clinical faculty, under the direction of the chairman, Dr. Alan Partin, represents international leaders in the areas of prostate cancer, bladder cancer, renal cell carcinoma, testicular cancer, reconstructive surgery, impotence, endourology, laparoscopic surgery, kidney and ureteral calculi, incontinence, hypospadias, bladder exstrophy, benign prostatic hyperplasia and bladder dysfunction.

The research faculty, under the guidance of Dr. Robert Getzenberg, represents international leaders in areas of molecular genetics, steroid receptors, nuclear matrix, DNA structure and function, telomeres, growth factors, tumor suppressors/oncogenes, cell adhesion molecules, nitric oxide, genitourinary neuroanatomy, gene therapy, novel chemotherapeutic approaches, smooth muscle physiology, tumor markers (PSA), cell motility, nuclear morphometry, video image analysis, surgical robotics, hereditary prostate disease, and chaos/complexity theory as it relates to genitourinary cancer.

<http://urology.jhu.edu>

Frequently used Herbal Supplements

HERBS	USE	SIDE EFFECTS
Cranberry Pills	Decrease UTI's	Chronic use may cause kidney stones
Saw Palmetto	Mild diuretic, reduce prostate swelling	GI upset, possible headaches
Lycopene	Lower incidence of some cancers, enhance immune function	None known
Green Tea	Cancer preventing	May deplete calcium
Chamomile Tea	Improve sleep , soothe sore throat	Avoid if taking blood thinners, allergy to daisies or pregnant
Cat's Claw	Strengthens GI system	Constipation or diarrhea Possible bleeding
Chondroitin	Osteoarthritis	GI upset, headache
Glucosamine	Osteoarthritis	GI upset, may increase insulin resistance, headache, drowsiness, skin reactions
Ginkgo	Improve memory, promote circulation	GI upset, headache, dizziness, do not take if taking blood thinners
Milk Thistle	Reduce cholesterol, prevent liver damage	Mild laxative, GI upset
Garlic	Lower blood pressure and cholesterol levels	Heartburn, nausea, may cause bleeding

We do not recommend the use of any herbal supplements.

*** IF YOU ARE SCHEDULED FOR SURGERY, PLEASE DISCONTINUE ALL HERBAL SUPPLEMENTS AT LEAST ONE WEEK PRIOR TO YOUR PROCEDURE.**

A study examining herbal therapy use among adults in the U.S. found almost 20% of adults use herbs for health treatment or promotion. More than half did not report this use to their medical professional.

Blood Thinners

The following prescription medications are blood thinners. These medications generally need to be stopped prior to your surgery. Please contact the doctor that prescribed these medications to find out what needs to be done prior to any procedure.

Usually these medications are discontinued about one week before your surgery. Your doctor may prescribe another medication in its place.

- Aspirin
- Coumadin or Warfarin
- Heparin
- Plavix
- Lovenox

The following are herbal supplements that also act as blood thinners. These also need to be discontinued.

- Fish Oil
- Garlic

Diagnosis and Treatment for Bladder Cancer

Invasive Bladder Cancer- bladder cancer which is invasive to the bladder wall, lymph nodes or present outside the bladder.

Information about Bladder Cancer in General:

- Is the second most commonly occurring genitourinary cancer in adults
- Incidence increases with age
- 54,000 new cases of bladder cancer per year in the USA

Diagnosis and Evaluation:

- Cystoscopy
- Trans-urethral Resection (TUR)
- Biopsy
- Intravenous Pyelogram (IVP)
- Urine testing/cytology

Treatment of Invasive Bladder Cancer:

- Complete cystectomy and cystoprostatectomy
 - Ileal-conduit diversion
 - Catheterizable pouch
 - Neobladder
- Comprehensive Medical Care
 - Multidisciplinary care
 - Physician experts in bladder cancer
 - Marburg Inpatient Nursing Unit-Nursing expertise in post-operative urological care
 - Enterostomal nurse follow-up
 - Social work follow-up/ Cancer Counseling Center
 - Johns Hopkins Oncology Center medical consultation-chemotherapy or radiation therapy

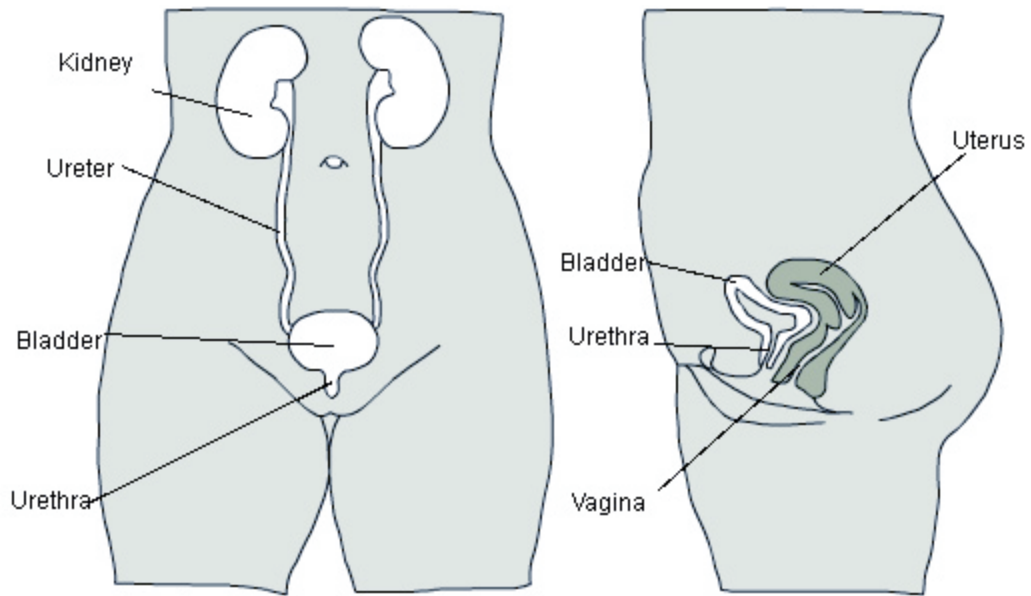
Exciting New Projects:

- Development of diagnostic urine testing to detect bladder cancer
- Surgical innovations in management of invasive bladder cancer
- Protocols for invasive bladder cancer
- Bladder sparing program

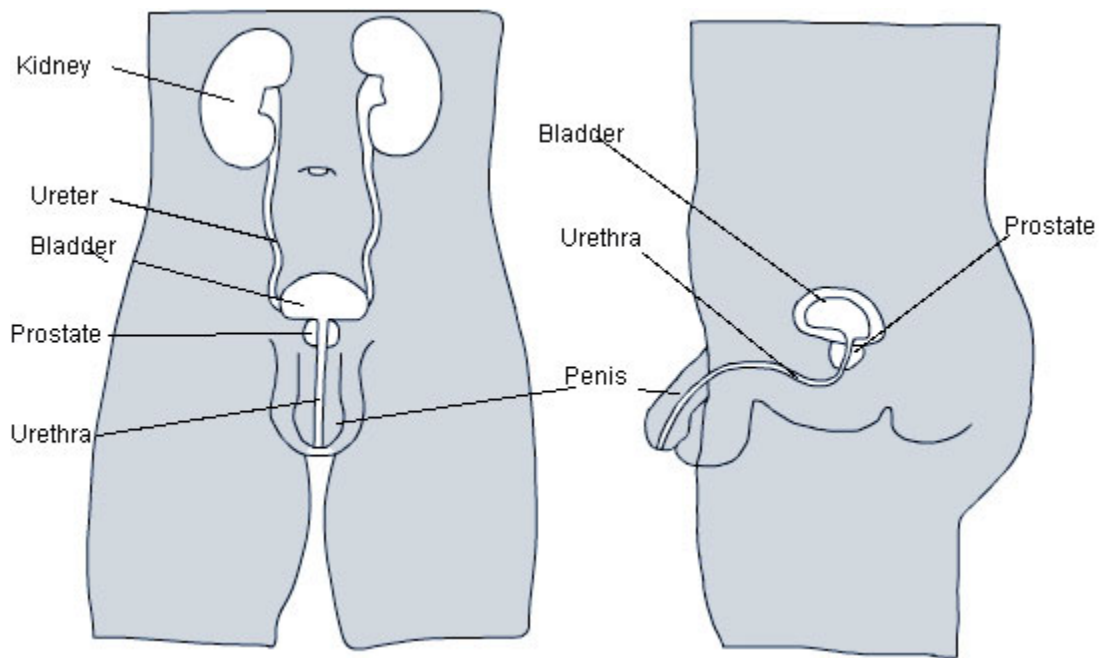
Basic Anatomy of the Genitourinary Tract

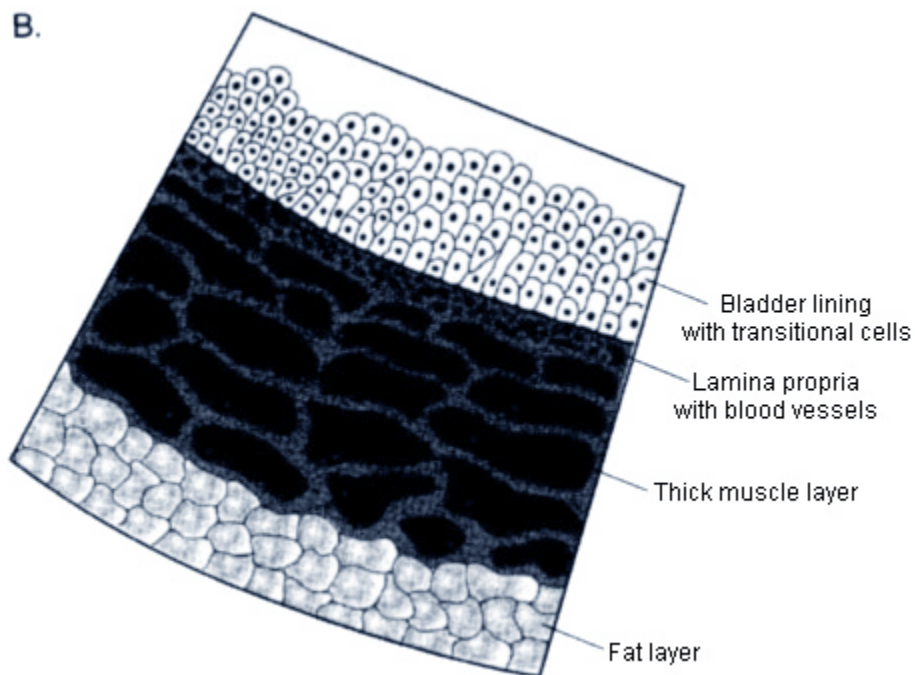
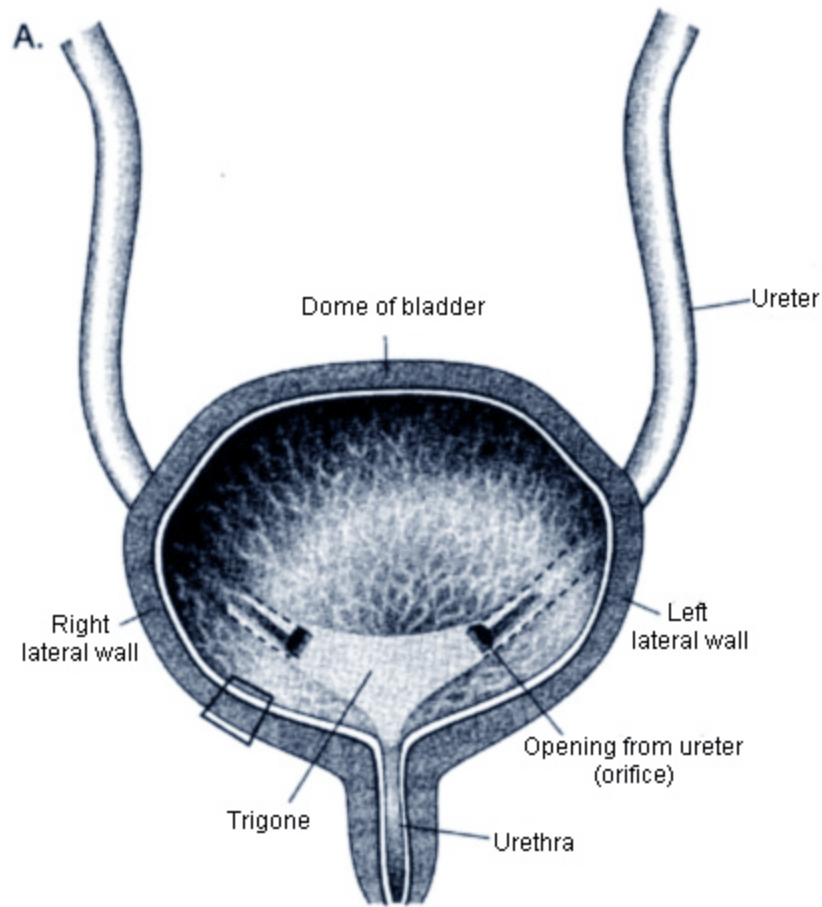
The urinary system's function is to filter blood and create urine as a waste by-product. Organs of the urinary system include kidneys, renal pelvis, ureters, bladder and urethra.

FEMALE



MALE





Upon examination specific "landmarks" are used to describe the location of any irregularities in the bladder. These are:

- trigone: a triangle-shaped region near the junction of the urethra and the bladder
- right and left lateral walls: walls on either side of the trigone
- posterior wall: back wall
- dome: roof of the bladder

Anatomy The urinary bladder is a muscular balloon-like structure that lies in the pelvis. The ureters connect to the bladder at the ureterovesical junction (vesical means bladder). The ureters enter the back of the bladder surface and tunnel into the substance of the bladder at its base which prevents back flow of urine. The bladder is a thick walled structure. The inner lining of the bladder has three to seven layers and is composed of transitional cells which are thick compared to the wall of the ureters. Urine exits the bladder through the urethra.

Function The bladder typically holds 400-500 ccs (about 1 pint) of urine. The bladder expands and contracts according to how much fluid it contains. The muscles of the bladder wall allow the bladder to forcefully contract when a person urinates. This contraction which empties the bladder is under complex neurologic control that involves participation of centers in both the brain and the spinal cord.

A CHECKLIST FOR PATIENTS:

What you need to have completed to have a cystectomy at Johns Hopkins Hospital

Outside pathology slides submitted to the Pathology Department at Johns Hopkins Hospital for review

Blood Work:

- CBC and Diff
- Comprehensive Chemistry panel

Hepatic Function

X-Rays:

Chest X-Ray

CAT Scan of chest and abdomen

MRI of Pelvic and Bladder (except for patients with pacemakers)

EKG

Other Items to Complete:

Physical examination by a physician as medical clearance for surgery

Consultation with the Anesthesia Department at Johns Hopkins Hospital

Appointment with Joanne Walker Enterstomal Nurse Specialist

Receive a copy of the Bowel Prep Instructions to be followed prior to surgery

Pathology glass slides

To send consult slides mail to this address:

Forward slides by courier
or express mail to:

Johns Hopkins Medical Laboratories
1620 McElderry St.
Reed Hall Room 315
Baltimore, MD 21205
Fax: (410) 614-7712
Phone: (410) 955-2405 / 8am - 5pm

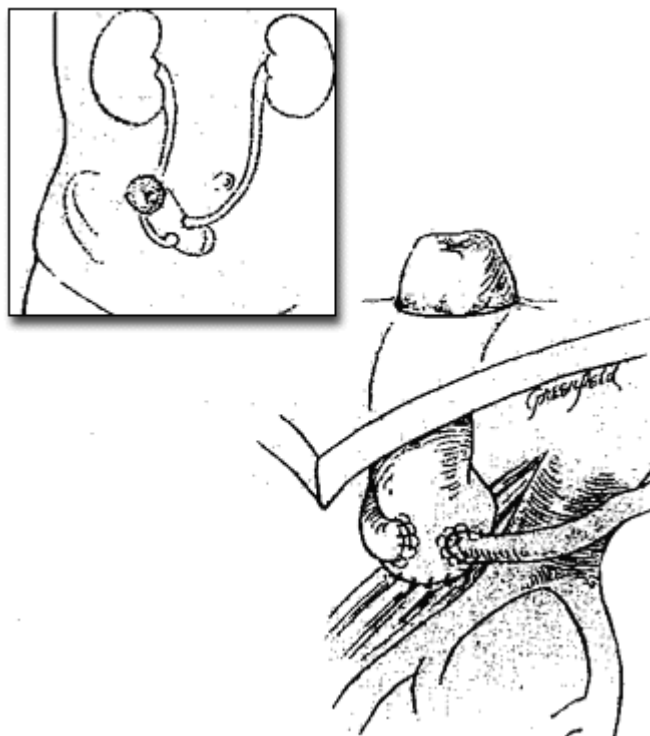
Organs that are removed during a Cystectomy

MEN	WOMEN
Bladder Prostate Seminal vesicles Pelvic lymph nodes	Bladder Uterus Fallopian tubes Ovaries Anterior (front) part of the vagina Cervix Pelvic lymph nodes

TYPES OF BLADDER RECONSTRUCTION:

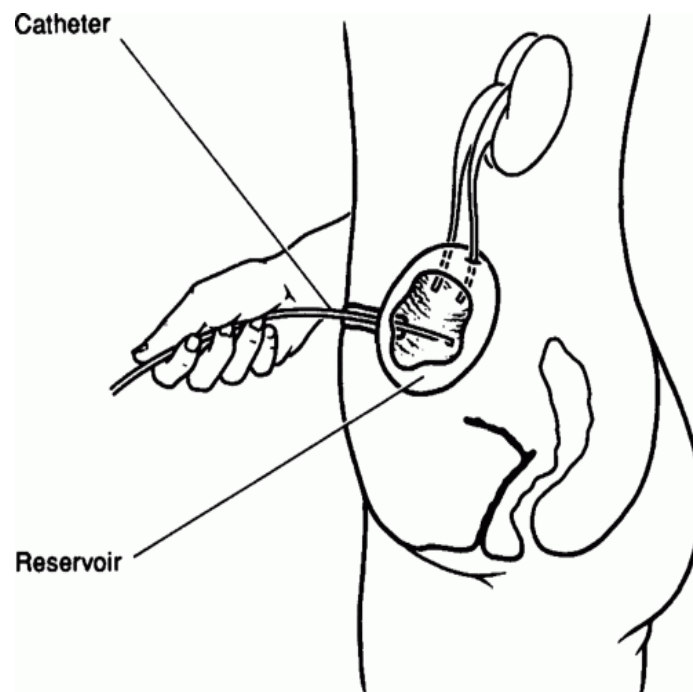
All three types of bladder reconstruction are similar in that the reconstructed bladder is made of intestine. Any time the bladder is removed there is an increase chance of urinary tract infection.

Ileal-Conduit



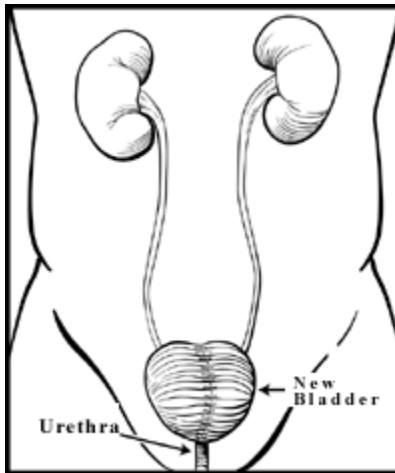
- ◆ Simplest form of reconstruction
- ◆ Routinely performed since the 1950's
- ◆ Small portion of the intestine (ileum) is disconnected from intestinal tract. One end is closed with sutures, the other end is attached to the skin on the right side of the abdomen.
A stoma is the open end of the conduit attached to the skin. An external appliance (ostomy bag) covers the stoma to collect urine. The ureters are implanted into the side of the ileal conduit.

Catheterizable Continent Diversion



- ◆ Reservoir of bowel with stoma that is catheterizable for emptying bladder
- ◆ Drain urine out of the reservoir with a catheter
- ◆ Need to have a watch with an alarm to empty the bladder every 4-6 hours
- ◆ May require surgery for repair of stoma due to the “wear and tear” from multiple catheterizations (20% of time).
- ◆ Contraindications
 - Bowel Disease (diverticulitis, ulcerative colitis)

Neo-Bladder (New Bladder)



- ◆ Internal reservoir connected to urethra
- ◆ Need to relearn how to void by having appointments with a therapist that is trained in pelvic floor exercises
- ◆ Need to have a watch to remind you to empty bladder every 4-6 hours

- ◆ Side effects
 - incontinence chronic (15%)
 - urinary tract infection (10%)
 - failure to empty bladder (5% in male & 40% females) may require intermittent catheterization
 - scar tissue formation at connection of urethra and new bladder (3-5%)

Abdominal Staples

After surgery you will have metal staples to close the incision. If these are not removed before you leave the hospital, please have your local primary care doctor removed them 7 – 10 days after surgery.

You do not need to come back to Johns Hopkins for staple removal. If you would like to have them removed here, **please contact Charlene at 410-502-3693.**

If your incision becomes swollen, reddened or has drainage, please contact your surgeon.

Physical Therapy and your Neobladder

During the first post-operative visit with Dr. Schoenberg your foley catheter will be removed and you will be taught how to catheterize yourself. Three weeks later you will start physical therapy with a therapist that has been trained in pelvic floor exercise for urinary incontinence.

Many patients are confused as to what the role of physical therapy could be for bladder surgery. There are actually muscles that travel from the pubic bone in the front, all of the way back to the tail bone in the back that are collectively called pelvic floor muscles. These muscles play an important role in bowel and bladder control. The job of the physical therapist is to help the patient use these muscles correctly so that they can have full bladder control and ease with emptying the neobladder.

There are physical therapists that specialize in pelvic floor muscle function. We have one at Johns Hopkins and one at our sister hospital Bayview. There is a website that helps in finding a therapist closer to your home.

The evaluation of these muscles on the first visits may involve either a vaginal or rectal muscle assessment. The therapist will then be able to direct the patient in a specific pelvic floor muscle exercise program. These muscles are tricky and many people do not perform the exercises correctly if they do not have professional help. The therapist will use several tools to help evaluate the muscles and provide the proper exercises for you.

Bowel preparation for Cystectomy patients

1. Clear liquids starting 24 hours prior to surgery.
2. Saline fleet enema the evening before surgery (approx. 7pm.)
3. Nothing to eat or drink after midnight the night before surgery
4. If you have any questions about the bowel prep, **please call Charlene at 410-502-3693.**

Clear liquid diet

THESE ITEMS ARE ALLOWED:

Water

Clear Broths

- Chicken broth
- Beef broth

Juices

- Apple juice or cider
- Prune juice
- Grape juice
- Grapefruit juice
- Cranberry juice
- Tang
- Hawaiian punch
- Lemonade
- Kool Aid

Sodas

Tea

Coffee

Clear jello (without fruit)

Popsicle (without fruit/without cream)

Italian Ices

Salt, pepper, and sugar may be used

THESE ITEMS ARE ALLOWED:

THESE ITEMS ARE NOT ALLOWED:

Milk

Cream

Milkshakes

Orange juice

Tomato juice

Cream Soups

Any soups other than clear broth

Oatmeal

Cream of Wheat

Bowel prep

This is a saline enema that you will need to use prior to surgery. It is sold in most grocery or drugstores. For your procedure you only need to purchase one.



Follow up care for cystectomy patients

Schedules may vary if you are being followed for a research study

What is the schedule for follow up care after being discharged from the hospital?

3 Weeks after surgery

- Outpatient visit with the urologist
- Conduit- exam by Enterostomal Nurse
- Neobladder – foley catheter removed
 - learn self catheterization
 - voiding trial

6 Weeks after surgery

- Renal ultrasound
- Visit with the urologist

3 Months post op

- Outpatient visit with the urologist
- Heme 8, chem. 12, folate and B12
- Renal ultrasound

9 Months post op

- If T1, CIS or Ta
 - CT of chest, abdomen and pelvis
 - Heme 8, chem. 12, folate and B12
- Every year for the next five years

If T2 or greater→

-CT of chest, abdomen and pelvis

-Heme 8, chem. 12, folate and B12

-Every 6 months for the next 5 years – alternate with renal ultrasound

RELATED PUBLICATIONS

Assessment of perioperative psychological distress in patients undergoing radical cystectomy for bladder cancer.

Palapattu GS, Haisfield-Wolfe ME, Walker JM, BrintzenhofeSzoc K, Trock B, Zabora J, Schoenberg M. [J Urol.](#) 2004 Nov;172(5 Pt 1):1814-7.

Source

The James Buchanan Brady Urological Institute, Johns Hopkins Bladder Cancer Research Program, Baltimore, Maryland 21287-2101, USA.

Abstract

PURPOSE:

Despite a recent growth in our understanding of the impact of psychosocial factors on the outcome of patients with cancer there is still relatively little known about the effect of these issues on patients with genitourinary malignancies. We determined the prevalence of psychological distress in patients with bladder cancer prior to and following radical cystectomy.

MATERIALS AND METHODS:

A total of 74 consecutive patients with clinically organ confined bladder cancer were prospectively surveyed preoperatively using the Basic Symptom Inventory-18, a validated

instrument that measures the psychological domains of general distress, anxiety, depression and somatization. Of the initial 74 patients 62 were available for postoperative assessment 1 month following cystectomy. Preoperative and postoperative distress scores were evaluated with respect to age, sex, marital status, type of surgical reconstruction and tumor stage.

RESULTS:

The preoperative prevalence of psychological distress in patients diagnosed with bladder cancer was 45% and it remained somewhat increased at 34% approximately 4 weeks after cystectomy. Demographic factors such as gender, age, and marital status were not significantly associated with the overall prevalence of distress. In the entire study group there was a statistically significant decrease in general distress ($p = 0.028$), depression ($p = 0.034$) and anxiety ($p = 0.0004$) from the preoperative to the postoperative assessments. Pathological stage was significantly associated with post-cystectomy anxiety ($p = 0.040$) and general distress ($p = 0.042$).

CONCLUSIONS:

Our findings indicate that a large proportion of patients with bladder cancer undergoing radical cystectomy experience psychological distress during the perioperative period. The identification of psychological distress in this population has the potential to influence health related quality of life as well as recovery in all individuals with bladder cancer.

Local recurrence and survival following nerve sparing radical cystoprostatectomy for bladder cancer: 10-year follow up.

Schoenberg MP, Walsh PC, Breazeale DR, Marshall FF, Mostwin JL, Brendler CB. J Urol. 1996 Feb;155(2):504-5.

Source

James Buchanan Brady Urological Institute, Johns Hopkins Medical Institutions, Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland, USA.

Abstract

PURPOSE:

The efficacy of nerve sparing radical cystoprostatectomy for the treatment of bladder cancer has been evaluated. We reviewed our 10-year experience with this technique to ascertain survival and local recurrence rates.

MATERIALS AND METHODS:

The charts of 101 patients treated with nerve sparing cystoprostatectomy between March 1982 and November 1989 were reviewed and updated.

RESULTS:

The disease-specific 10-year survival rate for all stages of bladder cancer treated was 69% and the 10-year survival rate free of local recurrence was 94%. Recovery of sexual function following nerve sparing cystectomy correlated with patient age: 62% in men 40 to 49 years old, 47% in men 50 to 59 years old, 43% in men 60 to 69 years old and 20% in men 70 to 79 years old.

CONCLUSIONS:

Nerve sparing radical cystoprostatectomy does not compromise cancer control and provides improved postoperative quality of life.

Stage pT0 at radical cystectomy confers improved survival: an international study of 4,430 patients.

Tilki D, Svatek RS, Novara G, Seitz M, Godoy G, Karakiewicz PI, Kassouf W, Fradet Y, Fritsche HM, Sonpavde G, Izawa JJ, Ficarra V, Lerner SP, Schoenberg M, Stief CG, Dinney CP, Skinner E, Lotan Y, Saqalowsky AI, Reich O, Shariat SF.

Source

Department of Urology, Ludwig-Maximilians-University Munich, Klinikum Grosshadern, Munich, Germany.

Erratum in

- J Urol. 2010 Nov;184(5):2218.

Abstract

PURPOSE:

We describe the cancer related outcome in patients with pT0 bladder urothelial carcinoma at radical cystectomy who did not receive preoperative chemotherapy in a large multicenter series. We also compared outcomes in patients with pT0 bladder urothelial carcinoma to those in patients with other stages and assessed the effect of clinical stage on outcome.

MATERIALS AND METHODS:

We reviewed the records of 4,430 patients treated with radical cystectomy for bladder urothelial carcinoma without neoadjuvant chemotherapy at 12 centers in the United States, Canada and Europe.

RESULTS:

Of the patients 228 (5.1%) had pT0 disease at radical cystectomy. Clinical stage was cTa or cTis in 13.6% and cT1 in 29.8% of these patients, and disease was muscle invasive (cT2-4a) in 56.2%. Metastasis developed to regional lymph nodes in 17 cases (7.5%). At a median 48.2-month followup 15 patients (6.6%) had died of bladder cancer. Five-year recurrence-free and cancer specific survival estimates were 89.7% (95% CI 85.3-93.1) and 93.1% (95% CI 88.9-95.6), respectively. Disease-free and cancer specific survival in pT0 cases was similar to that in pTa/pTis cases but significantly better than in pT1 or pT2 cases. On multivariate analysis increased disease recurrence and cancer specific mortality risks were significantly associated with lymph node metastasis (each $p < 0.001$) and female gender ($p < 0.001$ and 0.013, respectively).

CONCLUSIONS:

Although stage pT0 at radical cystectomy confers a benefit in survival, some patients experience disease recurrence and eventual death. Identifying these patients may help tailor postoperative decision making in patients with pT0.

2010 American Urological Association Education and Research, Inc. Published by Elsevier Inc. All rights reserved.

The effectiveness of off-protocol adjuvant chemotherapy for patients with urothelial carcinoma of the urinary bladder.

Svatek RS, Shariat SF, Lasky RE, Skinner EC, Novara G, Lerner SP, Fradet Y, Bastian PJ, Kassouf W, Karakiewicz PI, Fritsche HM, Müller SC, Izawa JJ, Ficarra V, Saqalowsky AI, Schoenberg MP, Siefker-Radtke AO, Millikan RE, Dinney CP. [Clin Cancer Res](#). 2010 Sep 1;16(17):4461-7. Epub 2010 Jul 22.

Source

University of Texas MD Anderson Cancer Center, Houston, TX, USA.

Abstract

PURPOSE:

The role of adjuvant chemotherapy for patients with high-risk urothelial carcinoma of the bladder (UCB) is not well defined. Here we address the value of adjuvant chemotherapy in patients undergoing radical cystectomy for UCB in an off-protocol routine clinical setting.

EXPERIMENTAL DESIGN:

We collected and analyzed data from 11 centers contributing retrospective cohorts of patients with UCB treated with radical cystectomy without neoadjuvant chemotherapy. Patients were

grouped into quintiles based on their risk of disease progression using estimates from a fitted multivariable Cox proportional hazards model. The association of adjuvant chemotherapy with survival was explored across separate quintiles.

RESULTS:

The cohort consisted of 3,947 patients, 932 (23.6%) of whom received adjuvant chemotherapy. Adjuvant chemotherapy was independently associated with improved survival (hazard ratio, 0.83; 95% confidence interval, 0.72-0.97%, $P = 0.017$). However, the effect of adjuvant chemotherapy was significantly modified by the individual's risk of disease progression such that an increasing benefit from adjuvant chemotherapy was seen across higher-risk subgroups ($P < 0.001$). There was a significant improvement in survival between the treated and nontreated patients in the highest-risk quintile (hazard ratio, 0.75; 95% confidence interval, 0.62-0.90; $P = 0.002$). This group was characterized by an estimated 32.8% 5-year probability of cancer-specific survival, with 86.6% of patients having both advanced pathologic stage ($\geq T(3)$) and nodal involvement.

CONCLUSION:

Adjuvant chemotherapy is associated with a significant improvement in survival for patients treated in an off-protocol clinical setting. Selective administration in patients at the highest risk for disease progression, such as those with advanced pathologic stage and nodal involvement, may optimize the therapeutic benefit of adjuvant chemotherapy.

International validation of the prognostic value of lymphovascular invasion in patients treated with radical cystectomy.

Shariat SF, Svatek RS, Tilki D, Skinner E, Karakiewicz PJ, Capitanio U, Bastian PJ, Volkmer BG, Kassouf W, Novara G, Fritsche HM, Izawa JJ, Ficarra V, Lerner SP, Saqalowsky AI, Schoenberg MP, Kamat AM, Dinney CP, Lotan Y, Marberger MJ, Fradet Y. BJU Int. 2010 May;105(10):1402-12. Epub 2010 Feb 2.

Source

University of Texas Southwestern Medical Center, Dallas, Texas, USA. sfshariat@gmail.com

Abstract

OBJECTIVE:

To externally validate the prognostic value of lymphovascular invasion (LVI) in a large international cohort of patients treated with radical cystectomy (RC) for urothelial carcinoma of the bladder (UCB).

PATIENTS AND METHODS:

We collected data from 4257 patients treated with RC and pelvic lymphadenectomy for UCB, without neoadjuvant chemotherapy, at 12 centres. LVI was defined as presence of nests of tumour cells within an endothelium-lined space.

RESULTS:

LVI was detected in 1407 patients (33.1%); the proportion of LVI increased with advancing stage, higher grade, soft-tissue surgical margin involvement, and lymph node metastasis ($P < 0.001$ for all). In standard multivariate models, LVI was associated with both disease recurrence (hazard ratio 1.43, $P < 0.001$) and cancer-specific mortality (1.45, $P < 0.001$). In the entire cohort, adding LVI to a base model that included standard features improved only minimally its predictive accuracy for both recurrence and cancer-specific mortality (by 1.1% and 1.2%, respectively). In 3122 patients with negative lymph nodes, LVI remained independently associated with and improved the predictive accuracy of the standard predictors for recurrence (hazard ratio 1.68, $P < 0.001$; +2.3%) and cancer-specific mortality (1.70, $P < 0.001$; +2.4%). By contrast, in 1071 node-positive patients, LVI only marginally improved the prediction of cancer-specific recurrence (hazard ratio 1.20, $P < 0.001$; +0.2%) and survival (1.23, $P < 0.001$; +0.5%).

CONCLUSIONS:

LVI is strongly associated with clinical outcome in node-negative patients treated with RC. The assessment of LVI might help to identify patients who could benefit from adjuvant therapy after RC. After confirmation in different populations, LVI should be included in the staging of UCB.

Expression status and prognostic significance of mammalian target of rapamycin pathway members in urothelial carcinoma of urinary bladder after cystectomy.

Schultz L, Albadine R, Hicks J, Jadallah S, DeMarzo AM, Chen YB, Neilsen ME, Gonzalqo ML, Sidransky D, Schoenberg M, Netto GJ. [Cancer](#). 2010 Dec 1;116(23):5517-26. doi: 10.1002/cncr.25502. Epub 2010 Oct 11.

Source

Department of Pathology, Johns Hopkins University, Baltimore, Maryland 21231, USA.

Abstract

BACKGROUND:

Bladder urothelial carcinoma has high rates of mortality and morbidity. Identifying novel molecular prognostic factors and targets of therapy is crucial. Mammalian target of rapamycin (mTOR) pathway plays a pivotal role in establishing cell shape, migration, and proliferation.

METHODS:

Tissue microarrays were constructed from 132 cystectomies (1994-2002).

Immunohistochemistry was performed for Pten, c-myc, p27, phosphorylated (phos)Akt,

phosS6, and 4E-BP1. Markers were evaluated for pattern, percentage, and intensity of staining.

RESULTS:

Mean length of follow-up was 62.6 months (range, 1-182 months). Disease progression, overall survival (OS), and disease-specific survival (DSS) rates were 42%, 60%, and 68%, respectively. Pten showed loss of expression in 35% of bladder urothelial carcinoma. All markers showed lower expression in invasive bladder urothelial carcinoma compared with benign urothelium with the exception of 4E-BP1. Pten, p27, phosAkt, phosS6, and 4E-BP1 expression correlated with pathologic stage (pathological stage; $P < .03$). Pten, 4E-BP1, and phosAkt expression correlated with divergent aggressive histology and invasion. phosS6 expression inversely predicted OS ($P = .01$), DSS ($P = .001$), and progression ($P = .05$). c-myc expression inversely predicted progression ($P = .01$). In a multivariate analysis model that included TNM stage grouping, divergent aggressive histology, concomitant carcinoma in situ, phosS6, and c-myc expression, phosS6 was an independent predictor of DSS ($P = .03$; hazard ratio [HR], -0.19), whereas c-myc was an independent predictor of progression ($P = .02$; HR, -0.38). In a second model substituting organ-confined disease and lymph node status for TNM stage grouping, phosS6 and c-myc remained independent predictors of DSS ($P = .03$; HR, -0.21) and progression ($P = .03$; HR, -0.34), respectively.

CONCLUSIONS:

We found an overall down-regulation of mTOR pathway in bladder urothelial carcinoma. phosS6 independently predicted DSS, and c-myc independently predicted progression.

Is prostate-specific antigen surveillance necessary in men with benign prostate pathology following radical cystoprostatectomy for bladder cancer?

Bivalacqua TJ, Loeb S, Pierorazio PM, Schoenberg MP, Partin AW, Guzzo TJ. Urol Int. 2010;85(4):466-9. Epub 2010 Nov 13.

Source

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Abstract

BACKGROUND:

Radical cystoprostatectomy (RCP) remains the gold standard for the treatment of muscle-invasive bladder cancer. There are limited data regarding the clinical impact and detection of PSA following complete prostatectomy or the need to monitor serum PSA in patients with benign prostate pathology at time of RCP. The purpose of our study was to analyze the postoperative PSA characteristics of men without prostate cancer who underwent a RCP for bladder cancer.

METHODS:

The demographic, clinical and pathologic data were reviewed on 138 men who underwent RCP for bladder cancer from 1994 to 2008. Patients with known or incidentally discovered prostate cancer on final pathology were excluded from this study, and postoperative serum PSA values were reviewed in the remaining men.

RESULTS:

The median age of the study population was 64 years (range 40-84). At a mean follow-up of 40.7 months, 137 (99.3%) of patients had an undetectable serum PSA. The one (0.7%) case in which serum PSA was not undetectable underwent an apex-sparing prostatectomy at the time of cystectomy.

CONCLUSIONS:

Serum PSA should remain undetectable for men with benign prostate pathology undergoing complete prostatectomy at the time of RCP. Elevated serum PSA following complete RCP in men with bladder cancer and pathologically confirmed benign prostate findings is rare. If the serum PSA is undetectable 3 months after RCP with benign prostate pathology, there is no

need for continued PSA monitoring. These data support the notion that potential nonprostatic sources of PSA are clinically insignificant following complete removal of the prostate.

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Disease-free survival at 2 or 3 years correlates with 5-year overall survival of patients undergoing radical cystectomy for muscle invasive bladder cancer.

Sonpavde G, Khan MM, Lerner SP, Svatek RS, Novara G, Karakiewicz PI, Skinner E, Tilki D, Kassouf W, Fradet Y, Dinney CP, Fritsche HM, Izawa JJ, Bastian PJ, Ficarra V, Schoenberg M, Sagalowsky AI, Lotan Y, Shariat SF. J Urol. 2011 Feb;185(2):456-61. Epub 2010 Dec 17.

Source

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Abstract

PURPOSE:

The conventional primary end point in trials of perioperative systemic therapy for muscle invasive bladder cancer is 5-year overall survival. We identified an association between disease-free survival at 2 to 3 years and 5-year overall survival.

MATERIALS AND METHODS:

We retrospectively analyzed a multicenter database containing records of 2,724 patients treated with radical cystectomy for muscle invasive bladder cancer with negative margins. Of these patients 844 had received adjuvant chemotherapy. We evaluated the association of disease-free survival at 2 and 3 years with overall survival at 5 years using Cox proportional hazards modeling and the kappa statistic.

RESULTS:

Overall 2-year/3-year disease-free survival was 0.63/0.57 and 5-year overall survival was 0.47. The overall agreement between 2-year disease-free survival and 5-year overall survival was 79%, and between 3-year disease-free survival and 5-year overall survival was 81%. Agreements were similar when analyzed within pathological substages, radical cystectomy decades and adjuvant chemotherapy subgroups. The kappa statistic was 0.57 (95% CI 0.53-0.60) for 2-year disease-free survival/5-year overall survival and 0.61 (95% CI 0.58-0.64) for 3-year disease-free survival/5-year overall survival, indicating moderate agreement. The hazard ratio for disease-free survival as a time dependent variable was 12.7 (95% CI 11.60-13.90), indicating a strong relationship between disease-free and overall survival.

CONCLUSIONS:

Disease-free survival rates at 2 and 3 years correlate with and are potential intermediate surrogates for 5-year overall survival in patients treated with radical cystectomy for muscle invasive bladder cancer regardless of adjuvant chemotherapy. These data warrant external validation and may expedite the development of adjuvant systemic therapy. In addition, they may be applicable to the neoadjuvant setting.

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Metabolomics and bladder cancer

[Hyndman ME](#), [Mullins JK](#), [Bivalacqua TJ](#).

Abstract

Diagnosis of bladder cancer is primarily made based on clinical presentation and then by direct visualization with cystoscopy. Despite the massive investments recently made to identify urinary-based assays that are able to diagnosis urothelial carcinoma, urine cytology and cystoscopy still remain the gold standard. Recently proof of principle studies have shown that noninvasive urine-based metabolomics, using high pressure liquid chromatography (HPLC) and nuclear magnetic resonance (NMR), may be able to accurately diagnosis bladder cancer. This

review discusses the published studies investigating metabolomics and bladder cancer and the future potential of this developing field.

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Pathological upstaging during radical cystectomy is associated with worse recurrence-free survival in patients with bacillus Calmette-Guerin-refractory bladder cancer.

[Guzzo TJ](#), [Magheli A](#), [Bivalacqua TJ](#), [Nielsen ME](#), [Attenello FJ](#), [Schoenberg MP](#), [Gonzalvo ML](#).

Abstract

OBJECTIVES:

To compare the outcomes of patients who were upstaged to pT2 at the time of radical cystectomy (RC) to those who were correctly staged as T2 before RC.

METHODS:

The clinical and pathologic data were reviewed of 496 patients who underwent RC from 1994 to 2008. Patients who underwent RC for high-grade T1 (HGT1) or carcinoma in situ (CIS) (184) were compared with those with known muscle-invasive cancer (312) before RC. Patients were substratified based on preoperative intravesical therapy status. Recurrence-free survival (RFS) for patients who were upstaged to muscle-invasive disease was compared with patients who were correctly staged T2 preoperatively.

RESULTS:

Patients who were upstaged to pT2 disease had significantly worse 3- and 5-year RFS compared with those who were accurately staged (cT2 = pT2) (64% and 61% vs 83% and 74%, respectively; $P = .04$). Upstaging to pT2 in patients with a history of bacillus Calmette-Guerin treatment resulted in worse 3- and 5-year RFS rates compared with those accurately staged (69% and 57% vs 100% and 86%, respectively; $P = .03$).

CONCLUSIONS:

Upstaging to pT2 among patients with HGT1 or CIS is associated with worse RFS compared with patients with known muscle invasion before RC (HGT1/CIS = pT2 vs cT2 = pT2). This finding was most significant among patients with a history of bacillus Calmette-Guerin treatment. Factors such as understaging of disease or treatment delay may contribute to worse outcomes among this subset of patients and should be considered when discussing treatment options.

[Urology](#). 2009 Dec;74(6):1276-80. Epub 2009 Sep 16.

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DIAGNOSIS IN ONCOLOGY

Paraneoplastic Polyarthritides From Non–Small-Cell Lung Cancer Metastatic to the Bladder

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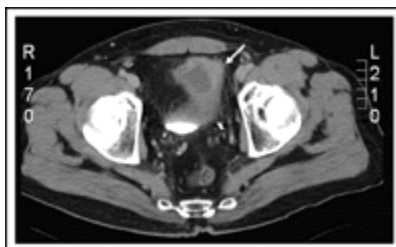
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A 52-year-old white man presented with a 1-month history of glands penis pain and tenderness to palpitation, as well as microscopic hematuria, dysuria, and urgency. In addition, he had a 3-month history of pain and weakness in the shoulders and elbows. Past medical history was unremarkable and social history was positive for 30 pack-years of smoking. Six months prior, the patient presented to his medical oncologist with 4 months of gradually worsening pain involving the ankles, knees, hands, elbows, and shoulders. Around the same time he developed shortness of breath and wheezing. Chest x-ray showed a right upper lobe

mass. This was confirmed with subsequent axial fused fluorodeoxyglucose positron emission tomography computed tomography (FDG-PET/CT) imaging of the chest, abdomen, and pelvis that demonstrated a single focus of increased FDG uptake in the lung. Right upper lobectomy with mediastinal lymphadenectomy was performed; and 1 day after surgery, the patient reported complete resolution of the pain. Histology of the tumor demonstrated poorly differentiated non–small-cell adenocarcinoma of the lung with no evidence of tumor in the hilar or mediastinal lymph nodes (T2N0Mx). Six months after resection of his primary lung non–small-cell adenocarcinoma, the patient was referred to a urologist because of microscopic hematuria and penile pain. There was also pain and weakness in the shoulders and elbows reminiscent of his presentation before lung surgery. There was no flank pain, gross hematuria, fever, or chills, and no evidence of recurrent infections. Radiographic studies were repeated and demonstrated no evidence of progression of his lung cancer with no lymphadenopathy; however, a new bladder mass was found on CT imaging of the abdomen and pelvis ([Fig 1](#); arrow) associated with increased uptake by FDG-PET/CT imaging. Cystoscopy confirmed presence of a mass in the dome of the bladder. Biopsy of the bladder mass showed poorly differentiated carcinoma with no associated intestinal-type metaplasia or cystitis glandularis. Random biopsies were negative for tumor. The patient underwent partial cystectomy. The tumor from the patient's previous lung resection specimen was concurrently reviewed and was found to be morphologically similar to the bladder mass ([Figs 2A and 2B](#)). Immunohistochemical stains showed that the neoplasm was positive for cytokeratin-7 ([Fig 2C](#)) and TTF-1 ([Fig 2D](#)), and negative for cytokeratin 20 ([Fig 2E](#)) and thrombomodulin ([Fig 2F](#)), consistent with immunostaining patterns of non–small-cell adenocarcinoma of the lung suggesting that this tumor was nonurothelial in nature. Overall, the immunohistochemical profile as well as the tumor morphology was most consistent with a metastasis from the patient's primary lung carcinoma. One day after surgery, patient again reported complete resolution of both musculoskeletal and penile pain.



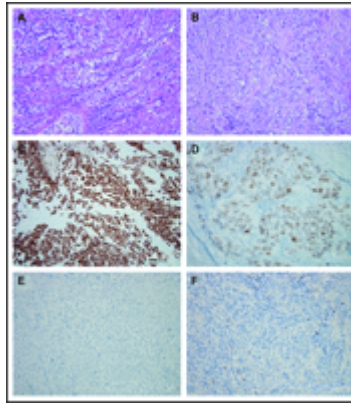
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Fig 1.



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Fig 2.

Secondary neoplasms of the genitourinary tract are rare.^{1,2} The kidney is the most likely genitourinary site for secondary tumor, followed by the bladder.² It is estimated that approximately 3% to 33% of bladder tumors are secondary in nature, with larger numbers coming from autopsy studies and smaller numbers coming from studies of surgical specimens.^{1,2} While most secondary neoplasm's represent direct invasion of tumors from adjacent sites (eg, cervix, prostate, colon and rectum), the most common primary sites of secondary metastases to the bladder include gastric carcinoma,³⁻⁵ breast carcinoma,⁶ malignant melanoma,⁷ and lung carcinoma.^{1,2} Other primary sites metastatic to the bladder reported in the literature include the cecum,^{8,9} pancreas,¹⁰ and thyroid.¹¹ Interestingly, the incidence of secondary tumors of the bladder is estimated to be approximately the same as that of nontransitional cell primary tumors, including adenocarcinomas, squamous cell carcinomas, small cell carcinoma, and other rarer entities.¹ Primary adenocarcinomas of the bladder are somewhat less common than secondary ones.^{1,2} Thus, the distinction between primary and secondary adenocarcinomas is a common diagnostic problem. In general, histomorphology remains the best diagnostic test to assess the origin and prognosis of a bladder tumor. Histological evidence of concomitant intestinal-type metaplasia or cystitis glandularis is suggestive of primary adenocarcinoma. Immunohistochemistry can also be helpful when the primary lesion is known. Herein we report a case of secondary adenocarcinoma to the bladder presenting with an array of signs and symptoms which included a paraneoplastic syndrome consistent with initial presentation of the patient's known

history of lung cancer. To our knowledge, this is the first report of a secondary bladder cancer presenting as a paraneoplastic syndrome. Paraneoplastic syndromes are a constellation of signs and symptoms that are unrelated to the local effect of the primary tumor or its metastases. Unusual presentation, lack of response to treatment, and parallel course with an underlying neoplasm are consistent with the diagnosis of a paraneoplastic syndrome. Diagnosis of a paraneoplastic syndrome is largely determined by clinical symptoms. A variety of musculoskeletal syndromes, including the inflammatory myopathies and polyarthritis, are known to be associated with malignancy.¹²⁻¹⁵ Certain tumor types, including cancer of the lung, are more commonly associated with paraneoplastic myopathies.^{12,13} Most recently, a study of dermatomyositis and polymyositis patients identified cancer in a respective 30% and 15% of patients.¹³ Of note, cancer developed most commonly within 1 year after the onset of myositis and the most common cancer histology reported was adenocarcinoma.¹³ Recent research in the field supports a model for paraneoplastic myositis pathogenesis whereby myositis-specific autoantigens, which have been found to be specifically increased in several cancer types including lung, lead to both specific T and B cells against those antigens. Subsequent muscle damage leading to elevated levels of MSAs is then thought to reactivate immune responses previously generated in the initial antitumor response. Motorsensory neuropathy, arthritis, and arthralgias to the knees as well as peri-arthritis to the shoulder are early signs of polyarthritis syndrome associated with paraneoplastic syndrome.^{14,15} Musculoskeletal symptoms may precede neoplastic manifestations by many months and may improve with appropriate treatment. As with the case described herein, marked improvement of signs and symptoms of paraneoplastic polyarthritis/myositis has been described after removal of the tumor, suggesting that it is the tumor burden that mitigates suprathreshold autoantigen burden. We describe a case of secondary adenocarcinoma to the bladder metastatic from the lung presenting with a symptoms consistent with paraneoplastic polyarthritis. Clinical history is the most important factor in correctly diagnosing secondary neoplasms of the bladder. While hematuria and/or pelvic pain are the most frequent symptoms of secondary bladder involvement, other more subtle symptoms which provide clues to the origin of the primary may be present as is described herein. Furthermore, once an association between a malignancy and a paraneoplastic syndrome has been identified, reappearance of those symptoms can be used to help monitor the patient for early signs of cancer recurrence.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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T.J.B. and H.A. contributed equally to this manuscript.

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