8

Clinical Presentation

Samer Katmawi-Sabbagh
Kettering General Hospital NHS Trust
United Kingdom

1. Introduction

Bladder cancer can occur at any age. However, it is known to be a disease of the middle-aged or elderly patient. The incidence is variable in different countries and the risk factors includes male sex, increasing age, smoking, occupational exposure to carcinogens, chronic inflammation, drugs such as phenacitin and cyclophosphamide, and pelvic radiation. In this chapter, we will discuss the different symptoms and signs that the bladder cancer patient could present with, keeping in mind that non of these presenting features are unique for bladder cancer.

2. Haematuria

Haematuria is the presenting symptom in up to 80% of patients with bladder cancer(Cummings et al., 1992). It could be Visible (previously called gross or frank haematuria), or Non Visible (previously called Dipstick or Microscopic haematuria). It is usually intermittent rather than constant, therefore, if a second urine specimen is free of any haematuria after a previous positive sample, investigations are still warranted in a bladder cancer age range patient. It may be initial or terminal if the lesion is at the bladder neck or in the prostatic urethra. The history of smoking or occupational exposure to certain chemicals is relevant. The Renal Association and British Association of Urological Surgeons joint consensus statement uses the abbreviations VH and NVH to refer to visible and non visible haematuria respectively (Kelly et al., 2009). They also define significant haematuria as the one that is visible (VH), Symptomatic non visible (sNVH)ie: associated with lower urinary tract symptoms, and persistent asymptomatic (aNVH)ie: without association with any urinary tract symptoms. Persistence was defined as 2 out of 3 positive urine samples. Microscopic or non visible haematuria (NVH) is defined as more than 3 Red blood cells (RBCs) per high-powered field(HPF) on a spun specimen by the American Urological Association. However, Campbell-Walsh definition is more than 5 RBCs per HPF for spun urine and more than 2 RBCs per HPF for unspun urine. The degree of haematuria does not correlate with the stage or the grade of the bladder cancer but cancer pick up rate is different. Cancer diagnosis is about 20-25% for the VH and 5-10% for the NVH (Khadra et al.,2000; Edwards et al.,2006). Majority of cancers discovered when investigating haematuria are bladder ones and the rarity relate to the upper urinary tract. Haematuria is an alarming presentation especially when asymptomatic. It requires extensive examination and investigations to rule out underlying pathologies and in particular bladder or upper urinary tract cancers. The role of purposely designed one-stop haematuria clinic has been developed

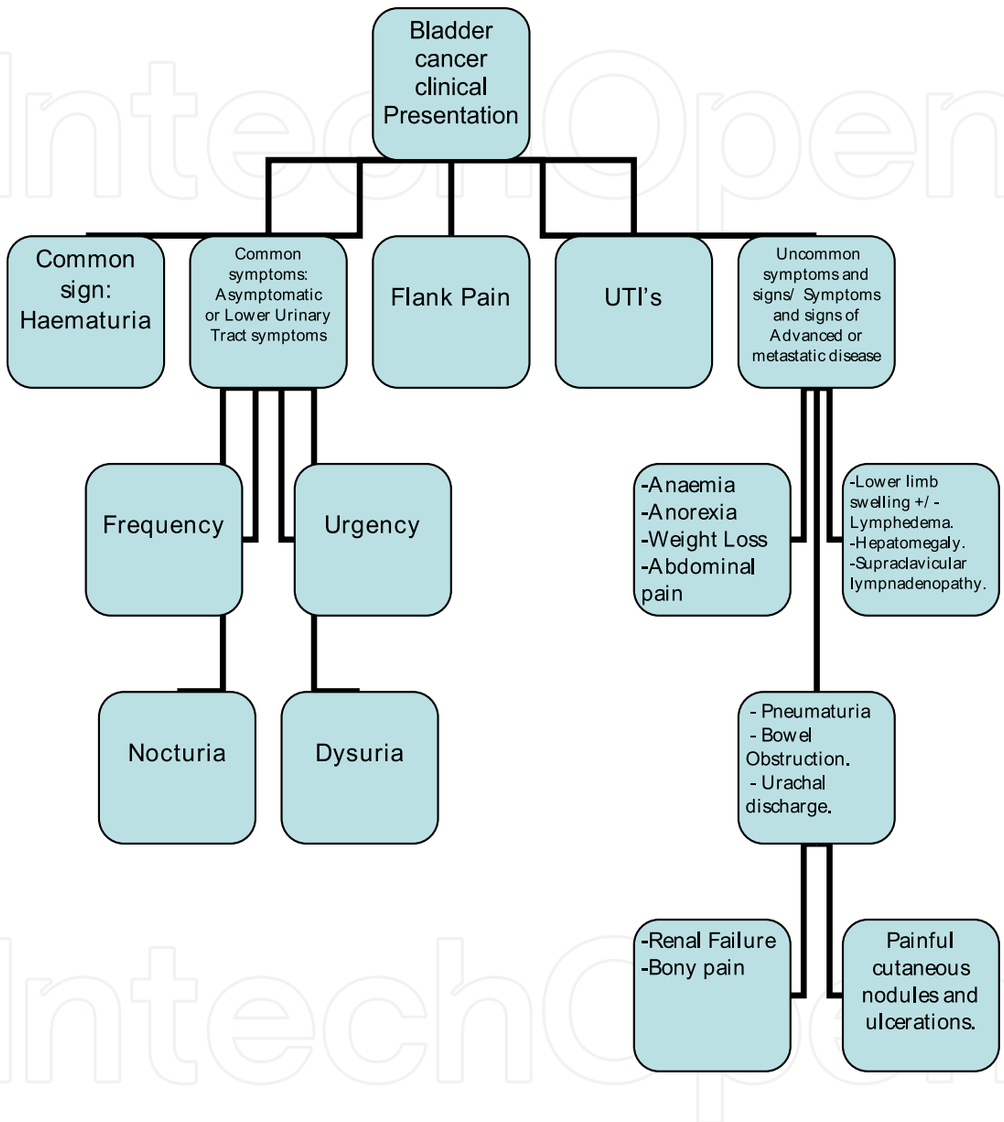


Fig. 1. Diagram showing the common and uncommon presenting symptoms and signs of bladder cancer.

and some evidence is existent that it could well reduce the time to cancer diagnosis and treatment (Katmawi-Sabbagh et al., 2010). Patients will require full history and examination including detailed information abouthaematuria, its duration and any associated symptoms. Smoking, occupation and exposure to chemicals and drugs should be documented. Abdominal, genital, and rectal examinations will be required in men. Vaginal examination is also important as vaginal bleeding is sometimes mistaken as haematuria in women. Details

of required investigations will be discussed at different chapter of this book. Common causes of haematuria are listed below in Table 1:

	Infective	Neoplasic	Others
Kidney	-Pylonephritis -Tuberculosis(TB)	-Renal cell carcinoma -Transitional cell carcinoma (TCC). - Squamous cell carcinoma (SCC).	-Trauma -Stones. -Nephrological: IgA nephropathy, diabetes, Alport's syndrome, interstitial nephritis, papillary necrosis.
Ureter	-Ureteritis -Tuberculosis	-TCC -Adenocarcinoma. -SCC	-Trauma. -Stones.
Bladder	-Bacterial cystitis. -TB cystitis. -Schistosomiasis	-TCC -Adenocarcinoma -SCC	-Trauma -Stones -Foreign bodies.
Prostate	-Bacterial prostatitis -Granulomatous prostatitis.	-Prostate cancer. -Benign prostatic hypertrophy.	-Trauma - Iatrogenic: Post biopsy.
Urethra and penis	-Urethritis.	-SCC. -TCC.	-Trauma. -Stricture. -Iatrogenic: catheterization.

Table 1. Common causes of Haematuria based on the anatomical location and the causative factors.

3. Lower urinary tract symptoms

Frequency, nocturia, urgency, and urge incontinence are symptoms of vesical irritability. These could be seen in association with haematuria in bladder cancer patients (with or without the presence of dysuria or suprapubic pain). These symptoms were previously named as irritative symptoms and they have association with diffuse carcinoma in situ (CIS) as well as invasive cancer (Farrow et al., 1977).

4. Flank pain

Flank pain can be a symptom of advanced bladder cancer representing ureteric obstruction due to invasion of bladder muscular wall or the ureter. Tumours cause hydronephrosis as they become invasive (Figure 2). This is usually seen with high grade TCC rather than low grade (Table 2).

Alternatively hydronephrosis with or without pain could happen when there is involvement of the ureteric orifice (Leibovitch et al., 1993).

1973 World Health Organisation (WHO) grading
Grade 1: Well differentiated Grade 2: Moderately differentiated Grade 3: Poorly differentiated
2004 WHO grading – Flat lesions:
Hyperplasia (flat lesion without atypia or papillary) Reactive Atypia (flat lesion with atypia) Atypia of unknown significance Urothelial dysplasia Urothelial Carcinoma in situ (CIS)
2004 WHO grading – Papillary lesions:
Urothelial Papilloma (wich is a completely benign lesion) Papillary urothelial neoplasm of low malignant potential Low-grade papillary urothelial carcinoma High-grade papillary urothelial carcinoma

Table 2. WHO grading in 1973 and in 2004 (Sauter el al.,2004)

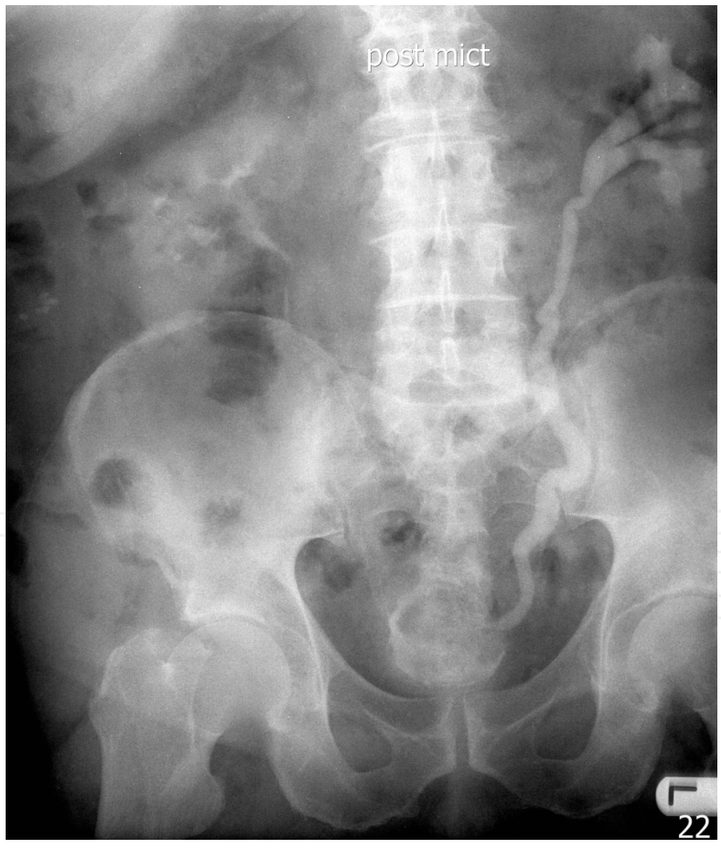


Fig. 2. An Intravenous urography (I.V.U) of a 76 year old man presented with haematuria and left sided loin pain. It shows left sided hydroureteronephrosis and large filling defect in the bladder. Cystoscopy confirmed a bladder tumour and histology revealed invasive G3 pT2 transitional cell carcinoma of the bladder.

Pyelonephritis may result if obstruction is complicated with infection. Flank pain and hydronephrosis could also be seen in cases of retroperitoneal metastasis. Flank pain caused by a bladder tumour is rarely encountered as the obstruction arises gradually. It should be distinguished from the one caused by a urinary stone which could also be associated with a degree of haematuria, but the colicky pain caused by a stone is normally of sudden onset and of higher intensity than that caused by a gradually occurring obstruction. Another differential diagnosis is the flank pain caused by a clot colic related to a bleeding from upper urinary tract transitional cell carcinoma or renal cell carcinoma.

5. Recurrent urinary tract infections (UTI's)

Recurrent urinary tract infections (UTI's) can be the first presentation of patients with necrotic infected bladder tumours. Therefore, it is always recommended to investigate recurrent UTI's with cystoscopic examination to rule out associated bladder tumour. It is also believed that bladder stones, long term catheters, and ova of Schistosoma haematobium (bilharziasis) are all implicated in the development of squamous cell carcinoma of the bladder via the mechanism of chronic inflammation of bladder mucosa.

6. Rare presentation symptoms and signs / symptoms and signs of advanced or complicated disease

The natural history of bladder cancer can be classified as follows:

- No further recurrence following initial presentation, diagnosis and treatment.
- Local recurrence, which can occur on a single occasion or on multiple occasions. The recurrent tumours are usually of the same stage and grade as the primary tumour. Clinically patient may be asymptomatic or represent with haematuria or any other local symptoms.
- Local Progresssion, which represent an increase in the local staging with time, the appearance of distant metastases and subsequent death. It is rare to encounter the symptoms and signs of advanced disease in the first presentation but patients with local recurrence and progression do represent with some of these symptoms and signs that are discussed below.

6.1 Anaemia, Anorexia, weight loss and abdominal mass:

Patients with large volume disease, muscle invasive tumours, or metastatic disease do sometimes present with these symptoms. The mass is properly assessed during bimanual examination under general anaesthesia and if it is immobile, this suggests that it is fixed to adjacent structures. Palpable masses that remain after local resection are likely to be extensive (non organ confined or T3 disease). The Tumour, Node, Metastasis(TNM) classification approved by the Union Internationale Contre le Cancer, which was updated in 2009 is shown in the table 3 (Sobin et al 2009):

T Primary tumour.
TX primary tumour cannot be assessed.
T0 No evidence of primary tumour.
Ta Noninvasive papillary carcinoma.
Tis carcinoma in situ:`Flat tumour`
T1 Tumour invades subepithelial connective tissue.
T2 Tumour invades muscle

T2a Tumour invades superficial muscle (inner half) T2b Tumour invades Deep muscle (outer half) T3 Tumour invades perivesical tissue: T3a Microscopically T3b Macroscopically (extravesical mass) T4 Tumour invades any of the following: Prostate, Uterus, Vagina, Pelvic Wall, abdominal wall. T4a Tumour invades prostate, uterus, or vagina. T4b Tumour invades pelvic wall or abdominal wall.
N Lymph Nodes Nx Regional lymph nodes cannot be assessed. N0 No regional lymph node metastasis N1 Metastasis in a single lymph node in the true pelvis (hypogastric, Obturator, external iliac, or presacral). N2 Metastasis in multiple lymph nodes in the true pelvis (hypogastric, Obturator, external iliac , or presacral). N3 Metastasis in a common iliac lymph node(s).
M Distant metastasis Mx Distant metastasis cannot be assessed. M0 No distant metastasis. M1 Distant metastasis.

Table 3. 2009 TNM classification of urinary bladder cancer

6.2 Lower limb swelling and lymphedema:
This is normally caused by occlusive pelvic lymphadenopathy or venous obstruction in the context of advanced disease.

6.3 Hepatomegaly and supraclavicular lymphadenopathy:
both are signs of metastatic disease.

6.4 Pneumaturia:
uncommon presentation of bladder cancer after enterovesical fistula formation. These type of fistulas are commoner with benign causes such as diverticular and crohn's disease. (Dawam et al.,2004). Nevertheless, pneumaturia warrants further investigations with urine cytology and cystoscopy with bladder biopsy if any neoplastic lesions could be seen.

6.5 Small bowel obstruction:
uncommon and unusual presentation caused by large and advanced disease (Aigen et al.,1983).

6.6 Renal failure:
caused be blocked ureters due to extensive muscle invasive disease or unilateral blockage in case of malfunctioning or absent contralateral kidney. This could also be related to retroperitoneal metastasis.

6.7 Painful cutaneous nodules and ulcerations:
very unusual and rare site of metastasis (Fujita et al., 1994;Block et al.,2006).

6.8 Urachal discharge (mucus or bloody):
a very rare presentation of adenocarcinoma, which is a rare histological subtype of bladder cancer. The tumour could be in the urachus itself or at the dome of the urinary bladder. It could also present with mucosuria.

6.9 Bony pain: a rare symptom that could be seen in cases of bony metastasis (Figure 3).

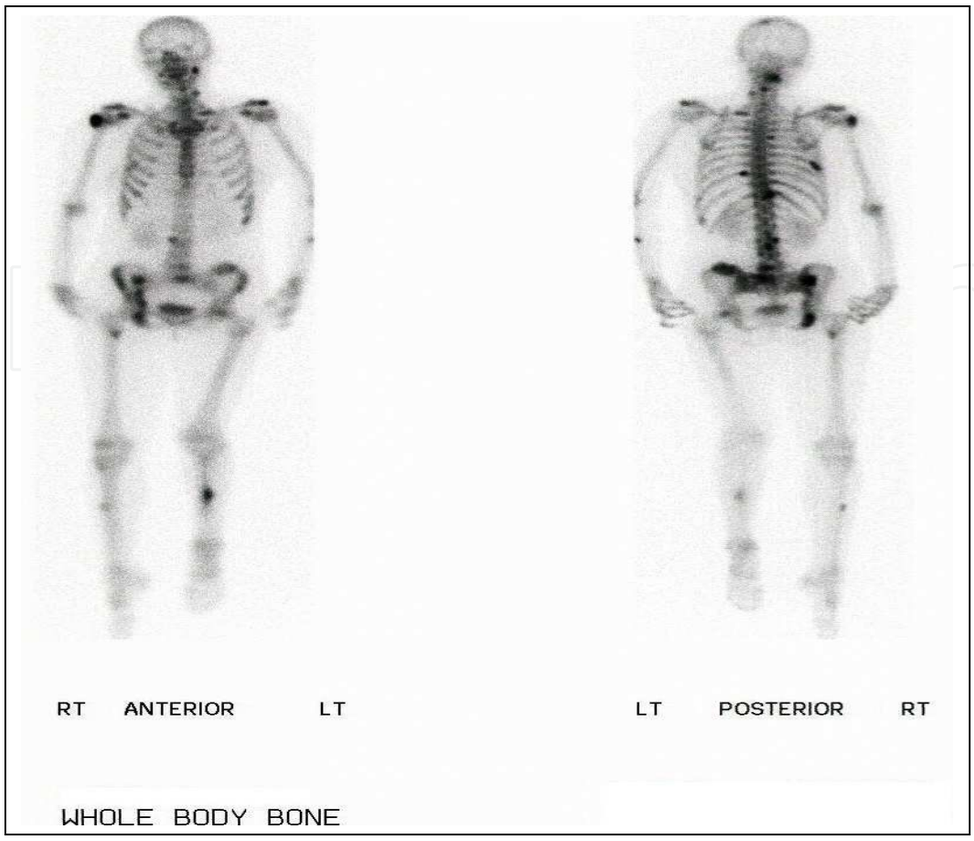


Fig. 3. An isotope bone scan of 38 year-old smoker female patient known to have G3pT2a bladder transitional cell carcinoma. She presented 2 years after radical radiation therapy with left sided hip pain. The bone scan shows wide spread metastasis (Spine, Pelvis, left forearm, left tibia, right femur and tibia).

7. Clinical conditions that could predispose to delayed presentation

7.1 Spina bifida patients

Patients with spinal bifida and bladder cancer present at a young age with variable tumour histology and advanced stage and they also have poor survival. These patients have neuropathic bladder dysfunction in addition to the fact that bladder augmentation is a significant risk factor for developing bladder cancer. Presenting symptoms are often atypical.

Although there has been suggestion of a role for annual serial bladder biopsies (Game et al., 1999) but it is not clear yet if screening would be beneficial for earlier detection and improved outcome. However, bladder cancer should be a consideration in this patient population, even in young adults (Austin et al. 2007).

7.2 Blind and colour blind patients

In a study of 200 bladder cancer patients, we found that those who had colour blindness (21 patients) did present with higher grade and stage disease compared to non colour blind population. The hypothesis is that these patients do not promptly notice the red colour of their urine at earlier stage, However, this is not proven. There is not sufficient evidence for

screening of colour blind patients for bladder cancer. However, it is advisable to keep these findings in mind when assessing colour blind patients as they may help in case finding and early diagnosis of bladder cancer in this group of patients (Katmawi-Sabbagh et al., 2009).

8. References

Aigen AB, Schapira HE, Metastatic carcinoma of prostate and bladder. Causing intestinal obstruction. Urology 1983;21: 464-466.

Austin JC, Elliott S, Cooper CS. Patients with Spina bifida and bladder cancer: Atypical presentation, advanced stage and poor survival. J Urol 2007; 178(3): 798-801

Block CA, Dahmoush L, Konety BR. Cutaneous metastases from transitional cell carcinoma of the bladder. Urology 2006.67:846.

Cummings KB, Barone JG, Ward WS. Diagnosis and staging of bladder cancer. Urologic Clinic of N Am 1992;3: 455-465.

Dawam D, Patel S, Kouriefs C, Masood S, Khan O, Sheriff MK. A "Urological" enterovesical fistula. J Urol 2004;172:943-944.

Edwards TJ,Dickson AJ,Natale S,Gosling J,Mcgrath J. A prospective analysis of the diagnostic yield resulting from attendance of 4020 patients at a protocol-driven haematuria clinic.BJU 2006;97:301-305.

Farrow GM, Utz DC, Rife CC, Greene LF. Clinical observations in 69 cases of in situ carcinoma of the urinary bladder. Cancer Res 1977; 37: 2794.

Fujita K, Sakamoto Y, Fujime M, Kitagawa R. Two cases of inflammatory skin metastasis from transitional cell carcinoma of the urinary bladder. Urol Int 1994;53:114-116.

Game X, Villers A, Malavaud B, Sarramon J. Bladder cancer arising in a Spina bifida patient. Urology 1999;54:923.

Katmawi-Sabbagh S, Haq A, Jane S, Subhas G, Turnham H. Impact of colour blindness on recognition of Haematuria in bladder cancer. Urol Int 2009; 83(3): 289-290

Katmawi-Sabbagh S, Hussain T, Al-Sudani M, England R, Khan Z. The role of the one-stop haematuria clinic in reducing time to diagnsis and treatment of Urological cancers. Italian Journal of Urology and Nephrology 2010;62(3):331-332.

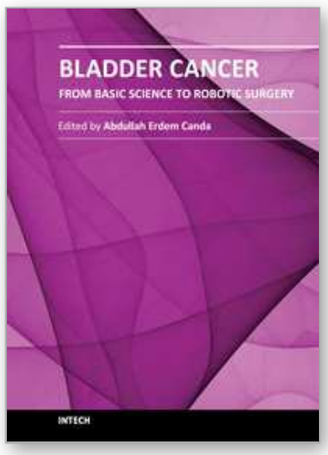
Kelly JD,Fawcett D, Goldberg L. Assessment and investigation of non- visible haematuria in the primary care setting. BMJ 2009; 338:a3021

Khadra MH, Pickard RS, Charlton M. A prospective analysis of 1930 patients with hematuria to evaluate current diagnostic practice. J Urol 2000;163:524-527

Leibovitch I, Ben-Chaim J, Ramon J, Madjar I, Engelberg IS, Goldwasser B. The significance of ureteral obstruction in invasive transitional cell Carcinoma of the urinary bladder. J Surg Oncol 1993; 52: 31-35.

Sauter G, Algaba F, Amin M. Tumours of the urinary system: Non - Invasive urothelial neoplasias. In: Eble JN, Sauter G, Epstein JI, Sesterhenn I. WHO classification of tumours of the urinary system And male genital organs. Lyon, France: IARCC Press; 2004.

Sobin LH, Gospodarowicz MK, wittekind C. TNM classification of Malignant tumours (UICC International Union Against Cancer). Ed 7. New York, NY:Wiley-Blackwell;2009. p.262-265.



Bladder Cancer - From Basic Science to Robotic Surgery
Edited by Dr. Abdullah Canda

ISBN 978-953-307-839-7
Hard cover, 460 pages
Publisher InTech
Published online 01, February, 2012
Published in print edition February, 2012

This book is an invaluable source of knowledge on bladder cancer biology, epidemiology, biomarkers, prognostic factors, and clinical presentation and diagnosis. It is also rich with plenty of up-to-date information, in a well-organized and easy to use format, focusing on the treatment of bladder cancer including surgery, chemotherapy, radiation therapy, immunotherapy, and vaccine therapy. These chapters, written by the experts in their fields, include many interesting, demonstrative and colorful pictures, figures, illustrations and tables. Due to its practicality, this book is recommended reading to anyone interested in bladder cancer.

How to reference
In order to correctly reference this scholarly work, feel free to copy and paste the following:

Samer Katmawi-Sabbagh (2012). Clinical Presentation, Bladder Cancer - From Basic Science to Robotic Surgery, Dr. Abdullah Canda (Ed.), ISBN: 978-953-307-839-7, InTech, Available from: http://www.intechopen.com/books/bladder-cancer-from-basic-science-to-robotic-surgery/clinical-presentation-2

INTECH
open science | open minds

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

IntechOpen