Diagnosis of Bladder Carcinoma
A Clinician's Perspective

Lauren C. Harshman, MD[a,*,1], Mark A. Preston, MD, MPH[b,1], Joaquim Bellmunt, MD, PhD[a], Clair Beard, MD[c]

KEYWORDS

• Bladder cancer • Nonmetastatic muscle-invasive bladder cancer
• Non–muscle-invasive bladder cancer • Histologic variants

ABSTRACT

In 2014, more than 74,000 new cases and 15,000 deaths from bladder cancer were estimated to occur. The most reliable prognostic factors for survival are pathologic stage and histologic grade. Accordingly, a good understanding of the pathologic features of these cancers is essential to guide optimal clinical treatment, which requires a multidisciplinary team of pathologists, urologists, radiation oncologists, and medical oncologists. This review highlights several clinical scenarios in which detailed pathologic evaluation and accurate reporting impact clinical management.

OVERVIEW

Optimizing the treatment of bladder cancer requires accurate staging and precise pathologic evaluation. Bladder cancer encompasses a spectrum of disease states from superficial, non-invasive tumors to advanced localized muscle invasive cancer to metastatic spread. Identifying the extent of disease and characterizing the histology is critical to tailoring the treatment for the patient with the overall objectives of minimizing the degree of therapy administered and maintaining quality of life. Close multidisciplinary collaborations between clinicians and pathologists is essential to enhanced clinical outcomes for our patients.

NON–MUSCLE-INVASIVE BLADDER CANCER

Approximately 75% of patients with bladder cancer present with disease confined to the mucosa (noninvasive papillary urothelial carcinoma, stage Ta or urothelial carcinoma in situ [CIS], stage Tis) or submucosa (superficially invasive urothelial carcinoma, stage T1) (**Fig. 1**).[1] Although these cancers have been called "superficial" in the past, the more accurate terminology is non–muscle-invasive bladder cancer (NMIBC), as the highest form of NMIBC is T1 disease, which is invasive into the lamina propria (see **Fig. 1**) and has the potential for aggressive distant spread. Because of its high prevalence and the more than 500,000 people in the United States living with NMIBC, it is one of the most expensive cancers to manage on a per-patient basis.[2] Clinical and pathologic factors that contribute to the risks of recurrence and progression include number of tumors, tumor size, prior recurrence, T-stage (see **Fig. 1**), concurrent CIS, and tumor grade (see also Solomon and Hansel, Morphology and Molecular Characteristics of Bladder Cancer, Surgical Pathology Clinics, 2015, Volume 8, Issue 4). Depending on the presence of these risk factors, 5-year rates of recurrence and progression can range from 31% to 78% and 0.8% to 45%, respectively.[3] The high risk of recurrence with NMIBC requires frequent and long-term monitoring with close cystoscopic surveillance as well as consideration of intravesical

[a] Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute, Harvard Medical School, 1230 DANA, 450 Brookline Ave, Boston, MA 02215, USA; [b] Division of Urology, Brigham and Women's Hospital, Harvard Medical School, 45, Francis street, Boston, MA 02115, USA; [c] Department of Radiation Oncology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA
[1]Contributed equally.
* Corresponding author.
E-mail address: LaurenC_Harshman@DFCI.HARVARD.EDU

Surgical Pathology 8 (2015) 677–685
http://dx.doi.org/10.1016/j.path.2015.07.004
1875-9181/15/$ – see front matter

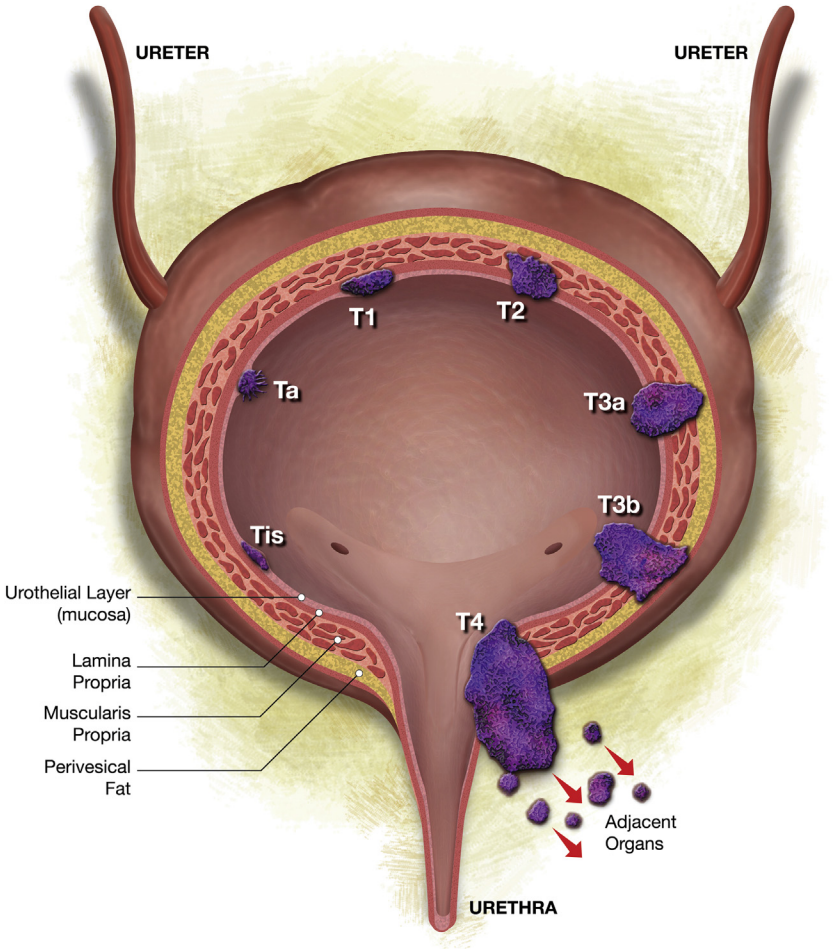

Fig. 1. Bladder cancer staging (TNM).

instillations of bacillus Calmette-Guerin (BCG) or chemotherapeutics aimed at preventing or delaying recurrence and progression.

Patients with NMIBC commonly present with gross or microscopic hematuria or lower urinary tract symptoms, such as urinary frequency or dysuria. Evaluation includes a thorough history and physical, urinalysis, urine cytology, cystoscopy, and upper tract imaging with computed tomography scan. To evaluate the urethra and bladder, the urologist will perform a cystoscopy. If tumor or erythema is visualized, the site, size, number of lesions, and appearance, whether papillary or solid, should be noted. If a suspicious area is seen, the patient should be taken to the operating room for biopsy and fulguration. If actual tumor is found, a transurethral resection of a bladder tumor (TURBT) should be performed. The goal of endoscopic treatment is full assessment of the bladder mucosa and urethra so as to make the correct diagnosis with regard to subtype, grade, and extent (stage) (see also Solomon and Hansel, Morphology and Molecular Characteristics of Bladder Cancer, Surgical Pathology Clinics, 2015, Volume 8, Issue 4), and to remove all visible lesions. If done correctly, the procedure may be curative in addition to diagnostic. It is critical to evaluate whether there is deep detrusor muscle (muscularis propria) invasion present and, thus, additional biopsies taken from the tumor base should be performed.

Important components of the pathology summary include the histologic subtype (eg, urothelial carcinoma, small cell, squamous cell, adenocarcinoma), location of the evaluated sample, grade of each lesion, depth of tumor invasion (stage), presence of CIS, presence of detrusor muscle in the specimen, presence of lymphovascular invasion (LVI), and presence of aberrant variants (eg, micropapillary, plasmacytoid) (see also Solomon and Hansel, Morphology and Molecular Characteristics of Bladder Cancer, Surgical Pathology Clinics,