

Educational Case: Bladder Carcinoma In Situ

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The following fictional case is intended as a learning tool within the Pathology Competencies for Medical Education (PCME), a set of national standards for teaching pathology. These are divided into three basic competencies: Disease Mechanisms and Processes, Organ System Pathology, and Diagnostic Medicine and Therapeutic Pathology. For additional information, and a full list of learning objectives for all three competencies, see <http://journals.sagepub.com/doi/10.1177/2374289517715040>.

Keywords

pathology competencies, organ system pathology, bladder neoplasia, bladder washings, carcinoma in situ (CIS) of the urinary bladder, FISH, screening urine cytology, voided urine cytology

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Primary Objective

Objective UTB1.3: Diagnosis and Surveillance of Urothelial Carcinoma. Describe the typical clinical presentation of urothelial carcinoma and the advantages and limitations of urine cytology in diagnosis and surveillance of urothelial carcinoma.

Competency 2: Organ System Pathology; Topic UTB: Bladder; Learning Goal 1: Bladder Neoplasia.

Patient Presentation

A 57-year-old man presents with a complaint of cramping pain on urination (dysuria) and red coloration of his urine (gross hematuria).

On physical examination, the patient has vague abdominopelvic discomfort on compression with no palpable mass. The physical examination was otherwise unremarkable, and the patient is afebrile.

Diagnostic Findings

Initial laboratory tests revealed a urinalysis with numerous red blood cells and rare white blood cells, a negative urine culture, normal complete blood cell count, and a normal serum creatinine level.

Questions/Discussion Points

What pertinent questions would you ask the patient?

- How long have these symptoms been present?
- Have they been decreasing or increasing in severity?
- Are there difficulties passing urine or associated burning?
- Have you passed any stones, clots, or tissues?
- Have you ever had these symptoms before?
- Are you a smoker?
- What kind of work do you do and have you had different jobs in the past?
- Do you take any medications?
- Have you ever been diagnosed with a malignancy?
- Is there a family history of cancer and, if so, what kind?

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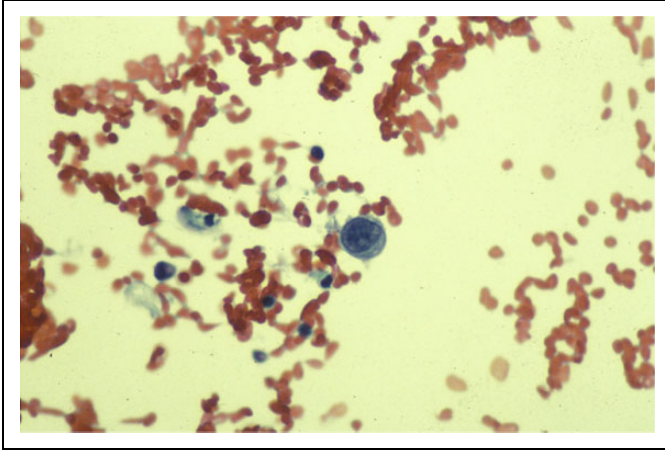


Figure 1. Urine cytology.

What additional laboratory test(s) would you consider at this point?

Urine cytology (see Figure 1).

Describe the findings on voided urine cytology (see Figure 1). What is your diagnosis?

There is a single cell with markedly enlarged hyperchromatic nuclei with irregular borders and high N/C ratio in a background of blood. Voided urine normally is hypocellular with few single benign urothelial cells and inflammatory cells. The presence of cohesive groups of cytologically bland urothelial cells in a voided urine is considered an abnormal finding that may be associated with stones, UTI, recent instrumentation, or low-grade papillary neoplasm.² In contrast, the presence of cohesive groups of cytologically bland urothelial cells in a bladder washing is a common finding due to instrumentation and mechanical dislodging of cells from the washing pressure. While this may raise concern for a low-grade papillary lesion on cytology, clinically it is not an issue as a papillary lesion would be seen and biopsied on cystoscopy. Bladder washings are useful for detecting flat CIS when there is not a papillary lesion seen on cystoscopy. Flat CIS as seen on urine cytology (voided or washings) has high-grade cytologic features as seen in this exercise.

The diagnosis is: positive for malignant cells, high-grade urothelial carcinoma.

What would be your next step?

The patient is referred to an urologist who performs cystoscopy. On cystoscopy, no discrete lesions or masses are seen. There are several erythematous (reddened) patchy areas which are biopsied and a bladder washing is obtained. Describe the cytologic findings in the bladder washing (see Figure 2).

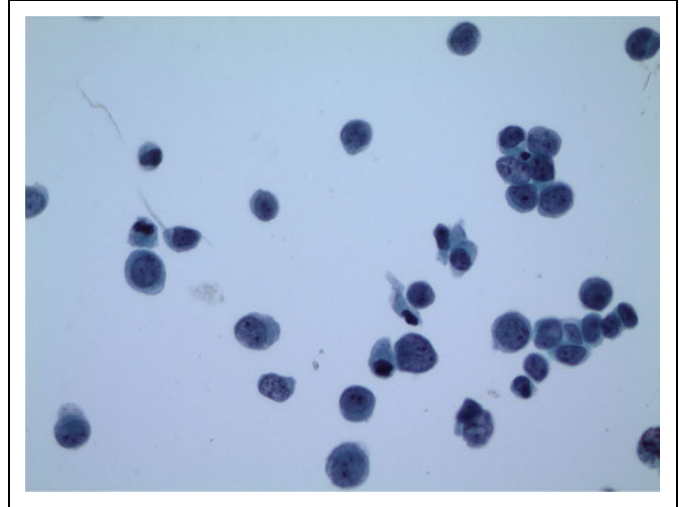


Figure 2. Bladder washing cytology.

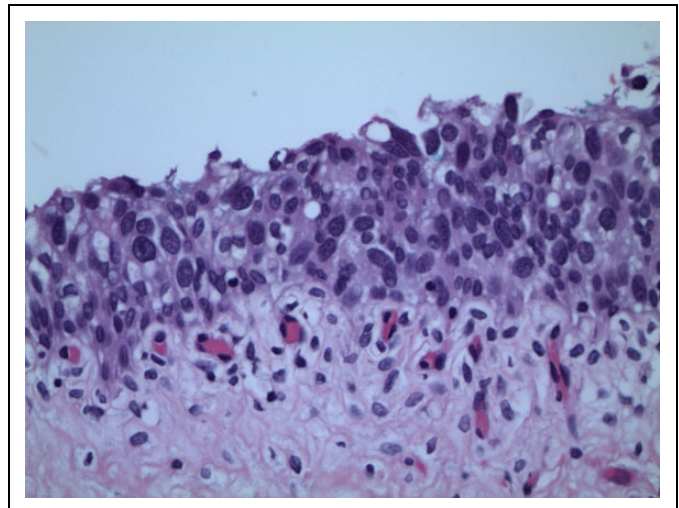


Figure 3. Bladder biopsy from an erythematous patch seen on cystoscopy.

How would you explain these findings in the absence of an identifiable mass on cystoscopy?

In the absence of a discrete lesion/mass in the bladder, the possibility the malignant cells could be arising in the renal pelvis or ureters should be considered.

Describe the histologic findings in the bladder biopsy taken from one of the erythematous patches seen on cystoscopy (see Figure 3). What is your diagnosis?

Carcinoma in situ (CIS) of the urinary bladder. The bladder washing has numerous single discohesive cells similar to that seen in the voided urine sample. In the bladder biopsy the urothelium is replaced by disorganized cells with enlarged hyperchromatic nuclei with increased N/C ratio and occasional

mitoses. Note the basement membrane is intact with no evidence of invasion of the underlying stroma.

In addition to aiding in the primary diagnosis of urinary malignancies, what other use is there for urine cytology?

Once a patient has been diagnosed and treated for an urothelial malignancy, the patient is at risk of recurrence or development of additional urothelial malignancies. In addition to periodic cystoscopy, urine cytologies are a useful screening test to detect a recurrent or new malignancy. As an adjuvant study, fluorescence in situ hybridization can be performed on the urine specimen looking for chromosomal abnormalities (aneuploidy of chromosomes 3, 7, and 17 and 9p deletions).¹

Teaching Points

- Bladder CIS can present with irritative bladder symptoms (dysuria, nocturia, urinary frequency) or hematuria. Other clinical possibilities for patients with these symptoms include urinary tract infection (UTI), interstitial cystitis, prostatitis (in men), and renal stones. Particularly, in older patients, the possibility of an urothelial malignancy should be considered.
 - High-grade urothelial carcinoma can be identified in voided urine; however, it does not distinguish between flat in situ carcinoma versus a papillary urothelial neoplasm.
 - Voided urine normally is hypocellular with few single benign urothelial cells and inflammatory cells. The presence of cohesive groups of cytologically bland urothelial cells in a voided urine may be associated with stones, UTI, recent instrumentation, or low-grade papillary neoplasm.²
- The presence of cohesive groups of cytologically bland urothelial cells in a bladder washing is a common finding due to instrumentation and mechanical dislodging of cells.
 - Bladder washings are useful for detecting flat CIS when there is not a papillary lesion seen on cystoscopy. Flat CIS as seen on urine cytology (voided or washings) has high-grade cytologic features as seen in this exercise.
 - Urine cytology is an important means of follow-up surveillance in patients who have had urothelial malignancy.

Declaration of Conflicting Interests

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Other Suggested Resources

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