

infiltrate the underlying lamina propria and superficial detrusor muscle, mimicking a malignant process.

KEY CONCEPTS

Inflammatory disorders and metaplasias of the bladder

- The bladder can be involved by a number of inflammatory lesions, many of which manifest with frequency and dysuria.
- Acute or chronic bacterial cystitis is extremely common, particularly in women, and results from retrograde spread of colonic bacteria in most cases.
- Other forms of cystitis have iatrogenic causes, such as radiation cystitis and hemorrhagic cystitis due to antitumor chemotherapeutics.
- Some inflammatory or metaplastic bladder lesions are significant in that they may clinically mimic bladder cancer, including malakoplakia, polypoid cystitis, cystitis cystica et glandularis and nephrogenic adenoma.

Neoplasms

Bladder cancer accounts for approximately 7% of cancers and 3% of cancer mortality in the United States. About 95% of bladder tumors are of epithelial origin, the remainder being mesenchymal tumors (Table 21-2). Most epithelial tumors are urothelial (transitional cell) type and are thus interchangeably called *urothelial or transitional tumors*, but squamous and glandular carcinomas also occur. Here we focus on urothelial tumors and touch briefly on the others.

Urothelial Tumors

Urothelial tumors represent about 90% of all bladder tumors and run the gamut from small benign lesions that do not recur to aggressive cancers that are often fatal. Many of these tumors are multifocal at presentation. Though most common in the bladder, all of the urothelial lesions described here may be seen at any site where there is urothelium, from the renal pelvis to the distal urethra.

There are two distinct precursor lesions to invasive urothelial carcinoma: **noninvasive papillary tumors and flat noninvasive urothelial carcinoma**. The most common precursor lesions are the noninvasive papillary tumors, which originate from papillary urothelial hyperplasia. These tumors have a range of atypical changes, and are graded according to their biologic behavior. The other precursor lesion to invasive carcinoma, flat noninvasive urothelial carcinoma is referred to as carcinoma in situ, or CIS.

Table 21-2 Tumors of the Urinary Bladder

Urothelial (transitional) tumors
Exophytic papilloma
Inverted papilloma
Papillary urothelial neoplasms of low malignant potential
Low-grade and high-grade papillary urothelial cancers
Carcinoma in situ (CIS, or flat noninvasive urothelial carcinoma)
Mixed carcinoma
Adenocarcinoma
Small-cell carcinoma
Sarcomas

Table 21-3 Grading of Urothelial (Transitional Cell) Tumors

WHO/ISUP Grades
Urothelial papilloma
Urothelial neoplasm of low malignant potential
Papillary urothelial carcinoma, low grade
Papillary urothelial carcinoma, high grade
WHO Grades
Urothelial papilloma
Urothelial neoplasm of low malignant potential
Papillary urothelial carcinoma, grade 1
Papillary urothelial carcinoma, grade 2
Papillary urothelial carcinoma, grade 3

ISUP, International Society of Urological Pathology; WHO, World Health Organization.

As discussed in Chapter 7, CIS is a term used to describe epithelial lesions that have the cytologic features of malignancy but are confined to the epithelium, showing no evidence of basement membrane invasion. Such lesions are considered to be high grade. In about one half of individuals with invasive bladder cancer, the tumor has already invaded the bladder wall at the time of presentation, and precursor lesions are not detected. It is presumed in such cases that the precursor lesion was destroyed by the high-grade invasive component, which typically appears as a large, frequently ulcerated mass. Although invasion into the lamina propria worsens the prognosis, the major decrease in survival is associated with invasion of the muscularis propria (detrusor muscle). Once muscularis propria invasion occurs, there is a 30% 5-year mortality rate.

Table 21-3 lists two of the most common grading systems of these tumors. The World Health Organization (WHO) 1973 classification grades tumors into a rare totally benign papilloma and three grades of transitional cell carcinoma (grades I, II, and III). A more recent classification, based on a consensus reached at a conference by the International Society of Urological Pathology (ISUP) in 1998 and adopted by the WHO in 2004, recognizes a rare benign papilloma, a group of papillary urothelial neoplasms of low malignant potential, and two grades of carcinoma (low and high grade).

Epidemiology and Pathogenesis. The incidence of carcinoma of the bladder is higher in men than in women, in developed than in developing nations, and in urban than in rural dwellers. The male-to-female ratio for urothelial tumors is approximately 3:1. About 80% of patients are between 50 and 80 years of age. Bladder cancer, with rare exceptions, is not familial.

Several factors have been implicated in the causation of urothelial carcinoma. Some of the more important contributors include the following:

- **Cigarette smoking is clearly the most important influence, increasing the risk threefold to sevenfold, depending on the duration and type of tobacco use.** Between 50% and 80% of all bladder cancers among men are associated with the use of cigarettes. Cigars, pipes, and smokeless tobacco are associated with a smaller risk.
- **Industrial exposure to aryl amines, particularly 2-naphthylamine and related compounds, as pointed out in our earlier discussion of chemical carcinogenesis**