CHAPTER 1

RECENT DEVELOPMENTS IN THE TREATMENT OF BLADDER CANCER

Raymond S. Lance and H. Barton Grossman

M.D. Anderson Cancer Center
Department of Urology
The University of Texas

INTRODUCTION

Transitional cell carcinoma of the bladder (TCC) is a significant cause of suffering and death. It is estimated that 53,200 persons will be diagnosed with TCC and 12,200 will die of this disease in the United States in 2000. Though the majority of people diagnosed with TCC have superficial disease, most who die of bladder cancer present with invasive disease. Although patients with superficial TCC experience recurrence rates as high as 82%, the rate of progression to muscle-invasive disease or metastasis is only 10 to 15%.

The waning years of the second millennium have produced many advances in the diagnosis and treatment of bladder cancer. This chapter highlights some of these developments.

BIOMARKERS

There is considerable evidence indicating that there are 2 separate pathways in the development of bladder cancer, one leading to frequently recurring, superficial tumors with low metastatic potential, and the other to carcinoma in situ with a high propensity for invasion and metastasis. While alterations in chromosome 9 are the most common genomic aberrations in bladder cancer, alterations in p53 are more frequently observed in Tis, T1,
and muscle-invasive TCC. This body of evidence and the fact that low-grade Ta lesions rarely progress support the theory that invasive TCC occurs through a separate carcinogenic pathway. These studies suggest that carcinoma in situ and T1 lesions share common chromosomal alterations with invasive lesions and a higher probability of progression and metastasis. The definition of the resultant protein changes may provide novel prognostic biomarkers.

Since only 10 to 15% of patients with papillary TCC experience progression to invasive disease, transurethral resection with endoscopic surveillance remains the preferred initial staging and treatment modality. A number of risk factors have been identified that predict recurrence and that can be used to guide subsequent therapy. These include tumor grade, associated Tis, multifocal tumors, tumor size, and recurrence within the first 3 months of resection of a primary bladder tumor. Although these clinical variables effectively define high- and low-risk groups, they are imprecise in defining individual risk. Similarly, risk factors for progression have been identified, including expression of the p53 and retinoblastoma proteins, vascular invasion, and depth of lamina propria invasion.

A number of biomarkers for detection are available for clinical use, and others are being developed. These assays differ in sensitivity, specificity, rapidity of result, and the ability to quantify the analyte. A select number are reviewed here.

**Cytology**

Urine cytology remains the comparative standard for new biomarkers. It samples cells shed from the entire urinary tract and is widely available. Although urine cytology is highly operator-dependent and has poor sensitivity in detecting low-grade tumors, it has high specificity. Studies have reported sensitivity as low as 20 to 30% with a specificity of 95%. In experienced hands, sensitivity is a function of grade, ranging from 26% with low-grade TCC to 79% with high-grade tumors. Bladder barbotage increases sensitivity by increasing the number of cells in a specimen, and it appears that a single barbotage is equivalent to 3 voided cytology specimens. Flow cytometry and image analysis have also been used to increase the sensitivity of conventional cytology and are increasingly being used by commercial laboratories.