diagnosis. Inclusion of muscle in the pathologic specimen is necessary to exclude muscle invasion. Additional evaluation includes CT scanning of the abdomen and pelvis (or CT urogram). For patients with muscle-invasive disease, CT imaging of the chest is indicated; and in patients with bone pain, bone scintigraphy. Most new cases of UCB are staged as Ta (involvement of epithelial lining), T1 (invasion of lamina propria), or carcinoma in situ (CIS); these are typically grouped and considered as non–muscle-invasive bladder cancer (NMIBC).

Patients with low-grade, low-stage bladder cancer remain at high risk for non–muscle-invasive recurrence, whereas patients with higher-grade, higher-stage disease are at increased risk for both recurrence and progression to muscle-invasive disease. Secondary involvement of the bladder with other cancers (e.g., lymphoma, sarcoma) is uncommon.

Treatment

Organ-Confined Disease

Low-grade, low-stage, non–muscle-invasive UCBs are typically managed with TURBT and intravesically administered cytotoxic agents. Multifocal, low-grade recurrent disease or high-risk NMIBC (high-grade T1 or CIS) is managed with intravesically administered bacillus Calmette-Guérin (BCG) or cystectomy.

Muscle-invasive bladder cancer is optimally managed with radical cystectomy and bilateral pelvic lymphadenectomy. For patients who are deemed poor surgical candidates or who refuse cystectomy, external beam radiotherapy and TURBT are alternative management options.

Cisplatin-based multiagent chemotherapy administered before cystectomy (i.e., neoadjuvant chemotherapy) has been shown by level I evidence to improve survival. Although it has not been prospectively evaluated in the neoadjuvant setting, the regimen of gemcitabine plus cisplatin (GC) is widely substituted for the older combination of methotrexate, vinblastine, doxorubicin, and cisplatin (M-VAC).

Metastatic Disease

Level I evidence from a series of phase III trials provides evidence that cisplatin-based chemotherapy (i.e., M-VAC or GC) in patients with de novo metastatic disease leads to median survival times in the range of 14 to 15 months, with 5% to 15% of patients likely to be cured. The latter group is made up primarily of patients with nodal metastatic disease.

Between 30% and 50% of patients with advanced UCB are ineligible for cisplatin because of concomitant renal insufficiency, typically as a consequence of age-related renal comorbidity or disease-related extrinsic obstruction. Although there have been no completed randomized phase III trials comparing cisplatin-based chemotherapy with carboplatin-based therapy in patients with advanced UCB, multiple randomized phase II trials have reported superior activity with cisplatin-based regimens.

The management of disease progression after front-line therapy (either perioperative or in the metastatic setting) is primarily palliative. Currently, there is no level I evidence that systemic therapy yields meaningful improvement in progression-free or overall survival. A large number of chemotherapeutic agents have been studied in the "salvage" setting, and there is no evidence that multiagent therapy is more effective than single-agent therapy in palliating disease-related symptoms.

Prognosis

Patients with low-grade, low-stage NMIBC typically do not progress to muscle-invasive disease. Their disease does not alter life expectancy but is associated with morbidity and use of health care resources and requires long-term follow-up. Patients with muscle-invasive disease who undergo cystectomy are at risk for systemic failure based on the T stage and extent of nodal involvement. Patients with organ-confined disease without nodal involvement have cure rates greater than 50%. Patients with metastatic disease have median survival times in the range of 14 to 16 months with systemic therapy, and only a small subset (5% to 15%) are long-term survivors.

PROSTATE CANCER

Definition and Epidemiology

Prostate cancer is the most common malignancy among men in the United States; more than 239,000 cases were expected to be diagnosed in 2013. Biologically, prostate cancer is a heterogeneous disease with a diverse but often long natural history. Although the lifetime risk of developing prostate cancer is approximately 1 in 6, most men do not die of the disease. The promiscuous use of prostate-specific-antigen (PSA) measurement as a screening tool has affected the incidence of prostate cancer. Despite a recent transient decline, incidence rates remain high compared with the pre-PSA era.

Multiple risk factors, including age, race, dietary factors, and genetic factors, have been linked to prostate cancer. The median age at diagnosis is 65 years, and younger men (<40 years) rarely develop prostate cancer. African American men have a greater risk of developing prostate cancer compared with white or Hispanic men. Genetic mutations such as *BRCA1/2*, Lynch syndrome, and, more recently, abnormalities in homeobox B13 (*HOXB13*) have been linked to prostate cancer. A man with first-degree relatives affected by prostate cancer has a five-fold to ten-fold increased risk of prostate cancer. Whereas high animal fat intake has been linked to prostate cancer, no association between a diet rich in antioxidants, lycopene, fruit, or vegetables and prostate cancer has been identified.

Recently, a large chemoprevention trial (SELECT) demonstrated that intake of selenium and vitamin E does not reduce the risk of prostate cancer. Two studies evaluating the 5α-reductase inhibitors, finasteride and dutasteride, demonstrated a 23% to 25% reduction in relative risk of prostate cancer. Despite these benefits, the use of these agents remains low, primarily because of side effects such as erectile dysfunction, lack of libido, and gynecomastia.

Pathology

Prostate cancer is typically diagnosed by transrectal ultrasound and biopsy, often performed after an abnormal PSA level or digital rectal examination result. In patients undergoing radical prostatectomy, the entire prostate, including seminal vesicles and lymph nodes (if present), is analyzed. Prognosis and treatment depend on tumor volume, the presence of perineural invasion,