extraprostatic extension, Gleason score, margin status, and involvement of seminal vesicles. Adenocarcinoma accounts for more than 95% of all prostate cancers. The remaining histologic subtypes include small cell carcinoma and sarcoma. Neuroendocrine differentiation and papillary features carry a poor prognosis.

The Gleason scoring system is pivotal in the management of prostate cancer, but its interpretation requires expertise in pathology. The score is based on growth pattern and degree of differentiation and ranges from 1 to 5 (5 being the least differentiated). The composite Gleason score is derived by adding together the numerical values for the two most prevalent differentiation patterns. For instance, if a specimen comprises primarily a grade 3 pattern and secondarily a grade 4 pattern, the score is reported as 7 (3 + 4). Scores of 8 to 10 represent poorly differentiated cancers, which are associated with poorer outcomes.

Diagnosis and Differential Diagnosis

With the exception of men with metastatic disease at presentation, most patients are diagnosed with the use of extended core biopsies (12 cores). A negative prostate biopsy result does not rule out prostate cancer. For men with metastatic disease, lymph node or bone biopsies can be performed. If the disease is confined to the prostate, imaging studies (bone scans and CT scans of the abdomen and pelvis) are obtained only in high-risk patients (i.e., high Gleason score, high PSA level). After diagnosis, risk stratification based on PSA level, Gleason score, and clinical stage becomes crucial to define management. Other important features determining treatment include age, comorbidities, patient preferences, and life expectancy.

Clinical Presentation

Because prostate cancer can be detected in small subsets even with very low PSA levels (i.e., <1 ng/mL) there is no "normal" PSA value. PSA values can be affected by rectal examination, ejaculation, infection, and urinary obstruction. PSA screening has been used extensively in the United States, but there is no evidence for a consequent reduction in mortality from prostate cancer.

Most men with early disease have no symptoms; however, urinary frequency, urgency, nocturia, and hesitancy do occur. The presence of hematuria or hematospermia should prompt consideration of prostate cancer. An abnormal rectal examination result (asymmetric mass/nodule) is also suggestive of cancer.

Treatment

Available treatment options for localized prostate cancer include radical prostatectomy, radiation therapy (either external beam radiation or brachytherapy), and active surveillance. For men with very-low-risk prostate cancer, active surveillance is appropriate. The selection between radical prostatectomy and radiation therapy is based on risk stratification and patient preferences. Surgery carries risks of urinary incontinence and erectile dysfunction. Radiation therapy has fewer local complications but can cause myelosuppression fatigue and a 3% to 5% lifetime risk of a secondary malignancy. Primary radiation therapy for intermediate- and high-risk patients is often given in combination with androgen deprivation therapy.

Once patients develop advanced disease, androgen deprivation therapy is widely used, although the appropriate timing remains unknown. For men with metastatic disease, continuous therapy with leutenizing hormone releasing hormone (LHRH) agonist with or without anti-androgen is the most common form of treatment, but intermittent androgen deprivation therapy is an effective alternative for patients whose only sign is a rising PSA level. In the setting of de novo metastatic disease, achievement of an undetectable PSA level at 6 months with androgen deprivation therapy predicts good outcome. Androgen deprivation therapy also has major side effects, including night sweats, hot flashes, erectile dysfunction, weight gain, loss of muscle mass, fatigue, bone loss, and metabolic syndrome.

Bone health is a significant problem in men with prostate cancer. Osteoporosis and skeletal-related events from metastases are both common. Two agents are available to prevent these complications: zoledronic acid, a bisphosphonate, and denosumab, a RANK-ligand inhibitor.

All patients with metastatic prostate cancer eventually develop castrate-resistant prostate cancer (CRPC), defined by serologic, clinical, or objective progression in the setting of a castrated testosterone level. Although the mechanism of CRPC is not well understood, several treatment options are now available. Sipuleucel-T, an autologous cell product capable of prolonging survival, and abiraterone acetate, a novel CYP17A1 (C17,20-lyase) inhibitor, are often used in the prechemotherapy setting. Two additional agents, cabazitaxel (a novel chemotherapy agent) and the androgen receptor inhibitor enzalutamide, have become a standard of care after docetaxel-based chemotherapy.

Prognosis

Many patients with favorable-risk, organ-confined disease are cured with surgery or radiotherapy. Most patients who have evidence of PSA recurrence after therapy will eventually manifest metastatic disease, but the natural history is variable. Patients with metastatic disease at presentation typically live for 3 to 5 additional years.

TESTICULAR CANCER

Definition and Epidemiology

The incidence of testis cancer varies widely among racial groups and geographic regions. In the United States, it is the most common cancer diagnosed in men aged 20 to 40 years of age, but it is rarely diagnosed before age 15 or after age 55. It is five times more common in whites than in blacks. The incidence has increased by more than 50% since 1975. Currently, a U.S. male faces a 0.37% lifetime risk of testis cancer and a 0.02% risk of dying from it. Risk factors include cryptorchidism and a personal or family history of testis cancer. Orchiopexy for cryptorchism before puberty reduces the risk of testis cancer.

Pathology

Approximately 95% of testis cancers are germ cell tumors; the others are mostly lymphomas, sex-cord stromal tumors, and adenocarcinomas of the rete testis. Germ cell tumors are divided into two broad categories: seminomas and nonseminomas (i.e., nonseminomatous germ cell tumors, or NSGCTs). Seminomas