Prostatic Disorders

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22

Management of Metastatic Carcinoma of the Prostate—Treatment Options and Controversies

Marc B. Garnick

INCIDENCE

Prostate cancer is the second most common carcinoma in males in the United States and the third leading cause of male death from neoplasia.[1] In the United States in 1987, 83,000 cases were diagnosed in whites (44.7 per 100,000 population) and 13,000 (79 per 100,000) in blacks. More than 26,000 men died of prostate carcinoma in the United States in 1987. The cause of the disease is unknown. Moreover, this disease occurs more frequently in first-generation Japanese in this country than in native Japanese.

American blacks have the highest prostate cancer rate in the world. Although no explanations for such racial differences are universally accepted, recent data suggest that college-aged black males have a 15% higher testosterone level and a 13% higher dihydrotestosterone level than white college students.[2] These higher levels have been postulated as a possible explanation for this increased rate of cancer.

PATHOLOGIC FEATURES AND STAGING

Prostatic neoplasms are nearly always adenocarcinomas. The prognosis can be correlated with grade of the cancer. Using the system devised by Gleason (Fig. 22–1), in which five separate histologic patterns are identified, one may correlate the incidence of metastases, bone pain, hydronephrosis, elevation of acid phosphatase levels, and ultimately, cancer deaths both with histologic features and with differentiation (Fig. 22–2). Although no universal grading schema exists, clinical pathologic correlations of the primary lesion are usually based on three grades of adenocarcinoma: well-differentiated (Gleason patterns 1 and 2); moderately differentiated (Gleason pattern 3); and poorly differentiated (Gleason patterns 4 and 5). Based on more than 3000 cases from the Veterans Administration studies, patients with well-differentiated tumors had a good prognosis, whereas those with poorly differentiated tumors had more advanced disease and neoplasms that were more biologically virulent than either well or moderately differentiated tumors.[3]

Stage D1 indicates metastases to the pelvic lymph nodes below the aortic

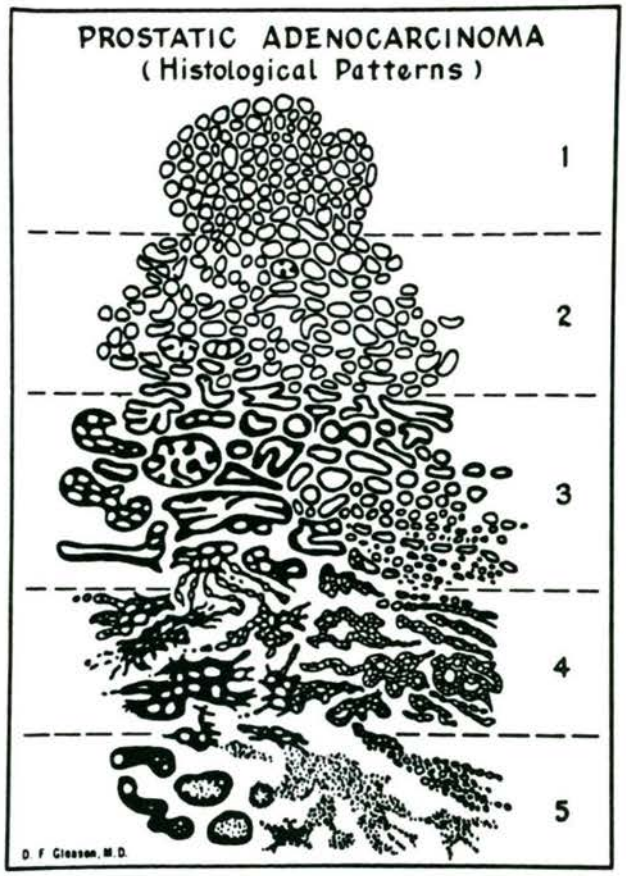

Fig. 22–1. The Gleason Grading System. Patterns 1 and 2 correspond to a well-differentiated lesion. Pattern 3 corresponds to a moderately well-differentiated lesion, and patterns 4 and 5 correspond to poorly differentiated, or anaplastic, lesions. The primary and secondary scores are obtained from the sum of the two predominant types at the time of pathologic evaluation. (From Gleason, D.F.: Histologic grading and clinical staging of prostatic carcinoma. *In* Urologic Pathology: The Prostate. Edited by M. Tannenbaum, Philadelphia, Lea & Febiger, 1977.)

bifurcation, and stage D2 represents bone metastases, lymph node metastases above the aortic bifurcation, or other soft tissue metastases. Most physicians treating patients with prostate cancer today believe that an elevation in the serum acid phosphatase level indicates systemic metastatic disease, whether macroscopic or microscopic, and a higher risk of demonstrable metastasis within 2 to 3 years. Such patients have stage D0 disease.

OPTIONS IN MANAGEMENT

For 40 years, hormonal therapy for prostate cancer has been the mainstay of treatment in patients with advanced disease, although the optimal use of androgen ablative therapy remains controversial. The original observations by Huggins, Hodges, and Stevens showed not only that prostate cancer was under

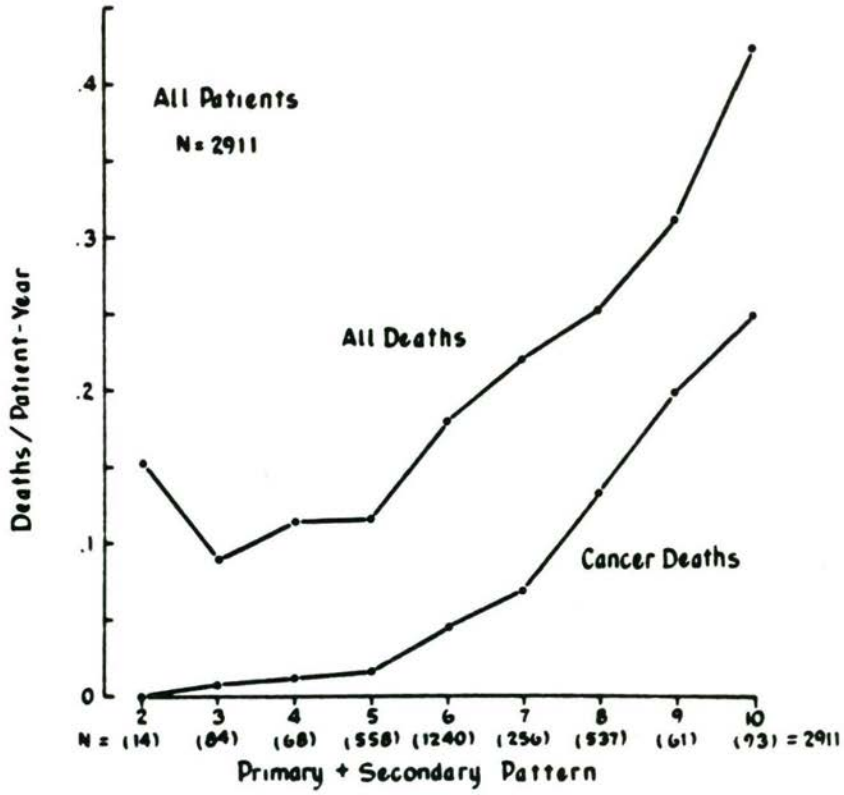

Fig. 22–2. As demonstrated by the VA studies, the influence of the primary and secondary patterns, according to the Gleason Grading System, predicted for a higher likelihood of cancer deaths as the lesions approached more poorly differentiated states. (Same source as Fig. 22–1.)

the trophic influence of male hormones, but also that the disease regressed with androgen ablation and progressed with exogenous androgen administration.[4,5] This finding provided the rationale for altering the patient's hormonal milieu in the treatment of this disease. Until the cardinal studies of the Veterans Administration Cooperative Urologic Research Group (VACURG), many physicians believed that all patients with prostate cancer were to be treated with hormonal therapy and that such treatment could improve survival rates and could possibly even cure the disease. As discussed in the following paragraphs, the VACURG studies cast doubt on hormonal therapy as a means of prolonging survival.

VACURG Studies

The studies made under the direction of the VACURG have been essential in defining the value of various hormonal methods in the treatment of prostate cancer.[6,8] In study 1, patients with stage C and D disease (VACURG classification III and IV, respectively) were randomized to 1 of 4 treatments: placebo; orchiectomy plus placebo; diethylstilbestrol (DES) (5 mg daily); or orchiectomy

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