TESTICULAR CANCER

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It is estimated that 8,090 new cases of testicular cancer will be diagnosed in men, and 380 men will die of this disease in the United States in 2008.1 Testicular cancer is the most common malignancy in men aged 15 to 35 years. It accounts for approximately 1% of all cancers in men. Worldwide, testicular cancer has more than doubled in the last 40 years. Incidence varies considerably in different geographical areas, being highest in Scandinavia and Switzerland; intermediate in the United States, Australia, and the United Kingdom; and lowest in Asia and Africa. It also varies according to ethnic groups, with a much higher rate among whites than blacks in the American population.2 An annual increase of 3% is reported for Caucasian populations.3 Despite the increase in observed incidence, there has been a dramatic decrease in mortality as a result of effective treatments.

Germ cell tumors (GCT) of the testis constitute 94% of testicular tumors and include five basic cell types: seminoma, embryonal carcinoma, yolk sac tumor, teratoma, and choriocarcinoma. Sixty percent of GCT are seminomas; the remainder are nonseminomatous germ cell tumors. Almost half of all germ cell tumors contain more than one of the five cell types.

Three subtypes of pure seminomas have been described: classic, anaplastic, and spermatocytic. Classic seminoma accounts for 80% to 85% of all seminomas and occurs most commonly in men aged 30 to 50 years. Anaplastic seminoma accounts for 5% to 10% of all seminomas and has an age distribution similar to that of the typical subtype. A number of features suggest that anaplastic seminoma is a more aggressive and potentially more lethal variant of typical seminoma. These characteristics include greater mitotic activity, higher rate of local invasion, increased rate of metastatic spread, and higher rate of tumor marker (human chorionic gonadotropin beta, or beta hCG) production. Spermatocytic seminoma accounts for 2% to 12% of all seminomas, and nearly half occur in men older than 50 years. The cells closely resemble different phases of maturing spermatogonia. The metastatic potential of this tumor is extremely low, and the prognosis is favorable.4

Risk Factors

Unlike most other cancers, testicular cancer is generally found in young men.5 In white men, testicular cancer is the most common cancer from age 20 years to age 34 years, the second most common from age 35 years to age 39 years, and the third most common from age 15 years to age 19 years. This type of cancer is 4.5 times more common among white men than black men,6 with intermediate incidence rates for Hispanics, American Indians, and Asians. High-risk groups exist. Males with cryptorchidism have 3 to 17 times the average risk. Approximately 7% to 10% of patients with testicular tumors have a history of cryptorchidism.4, 7 Orchiopexy may not prevent cancer in these children but allows clinical surveillance of patients with a previously impalpable gonad. There is also an increased risk in males with gonadal dysgenesis and Klinefelter syndrome.8 Men with a family history of testicular cancer may be at a higher risk of this disease.9 A history of testicular cancer is associated with a higher risk of a contralateral tumor.4, 7

Although not consistently found to confer a higher risk, infertility, testicular atrophy, twinship, or abnormal semen parameters have been associated with a higher risk of testicular cancer, but the

evidence is weak.7, 10

An additional risk factor for the development of testicular cancer is the presence of carcinoma in situ (CIS), also called intratubular germ cell neoplasia. Testicular CIS appears to develop from fetal gonocytes and is characterized histologically by seminiferous tubules containing only Sertoli cells and malignant-appearing germ cells.

If encountered in the contralateral testis, CIS is associated with the development of contralateral testicular cancer in 50% of patients at 5 years of follow-up.11 CIS will be found in approximately 5% of contralateral testes (approximately the same rate as cryptorchid testes).12

The association of testicular microlithiasis with testicular cancer is still of questionable clinical significance.13, 14

Approximately 60% of testicular cancers are localized, 24% are regional, and 14% are distant stage at diagnosis. Although there has been no appreciable change in the stage distribution at diagnosis, advances in treatment have been associated with a 60% decrease in mortality. Testicular cancer is so curable even at advanced stages and there are so few cases that it would be virtually impossible to document a decrease in mortality associated with screening.

Treatment options for CIS include observation, radiation therapy, chemotherapy, and orchiectomy. Although low-dose radiation therapy can preserve Leydig cell function and prevent germ-cell tumor development, a conservative approach of observation may also be warranted. Individuals at high risk (e.g., cryptorchidism, atrophic testis, and intersex conditions) require close observation.

Testicular cancer survivors are at an increased risk of solid tumors for at least 35 years after treatment.15 There is a low cumulative risk of metachronous contralateral testicular cancer and a favorable overall survival of patients diagnosed with metachronous contralateral testicular cancer.16

Most testicular cancers are first detected by the patient, either unintentionally or by self-examination. Some are discovered by routine physical examination. However, no studies have been done to determine the effectiveness of testicular self-examination or clinical testicular examination in reducing mortality from testicular cancer. The benefit of testicular self-examination is unknown.

Screening would be very unlikely to decrease mortality substantially because therapy is so effective, even for advanced stages of disease. However, early detection may have a practical impact on therapy. There is an increase in both the number of courses of chemotherapy and the extent of surgery required for treatment of advanced disease that results in higher morbidity. Patients diagnosed with localized disease require less treatment and have lower morbidity.17

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