by definition are 100% seminoma, whereas most NSGCTs are a mixture of two or more of the five types of germ cell tumors: seminoma, embryonal carcinoma, teratoma, yolk sac tumor, and choriocarcinoma. A tumor that contains any elements of embryonal carcinoma, teratoma, yolk sac tumor, or choriocarcinoma is considered to be an NSGCT even if most of the tumor is seminoma. Because seminomas do not produce α-fetoprotein (AFP), patients who have an elevated AFP level have a NSGCT by definition regardless of the histopathology.

Diagnosis and Differential Diagnosis

Whenever a testis tumor is suspected, transscrotal ultrasound should be performed; if a mass suspicious for cancer is seen, the standard diagnostic procedure is an inguinal orchiectomy. Transscrotal orchiectomy or biopsy is contraindicated because of the risk of seeding the tumor in the scrotum and altering the pattern of spread. Differential diagnosis includes testicular lymphoma, torsion, epididymo-orchitis and other benign scrotal lesions.

Clinical Presentation

Testis cancer most often manifests as testicular enlargement, mass, or induration. It may or may not be painful or tender, and the presence of pain does not exclude a diagnosis of cancer. Testicular atrophy, gynecomastia, back pain, and thromboembolic disease are less common presentations.

Staging the cancer requires measuring postorchiectomy levels of serum AFP, human chorionic gonadotropin (β-HCG), and LDH as well as assessing for nodal and organ metastases, which should be done with a CT scan of the abdomen and pelvis and either chest CT or a chest radiography. The testes drain to the retroperitoneal lymph nodes, and retroperitoneal nodal spread constitutes stage II disease. In practice, testis cancer is divided into three categories: stage I (localized), with no evidence of spread to lymph nodes or beyond; stage II (regional), with enlarged retroperitoneal lymph nodes but no distant metastases; and disseminated disease. Disseminated disease includes stage I or II disease in which serum AFP and/or β-HCG levels are persistently elevated after orchiectomy, bulky stage II disease, and all stage III disease. Metastases to other organs or to pelvic or other nonretroperitoneal lymph nodes represents stage III disease, as does spread to retroperitoneal nodes in the setting of highly elevated serum tumor markers. Disseminated disease is divided into three categories: good-risk, intermediate-risk, and poor-risk disease; treatment differs for the different risk groups.

Treatment

Stage I seminomas and NSGCTs are usually managed with surveillance after surgery. The risk of relapse is about 18% for seminomas and 30% for NSGCTs. Alternatives to surveillance are single-agent carboplatin chemotherapy or radiation therapy for seminomas and bleomycin and etoposide and cisplatin (BEP) chemotherapy or retroperitoneal lymph node dissection (RPLND) for NSGCTs. Long-term disease-specific survival for stage I disease is 99% regardless of which of these approaches is used.

Stage II seminomas are usually treated with radiation, but chemotherapy (with bleomycin, etoposide, and cisplatin [BEP] or etoposide plus cisplatin [EP]) is used when the disease bulk is greater than 5 cm and sometimes for less bulky tumors. Management of stage II NSGCTs depends on the disease bulk and the levels of serum AFP and β-HCG. If either marker is elevated, then chemotherapy is preferred regardless of disease bulk. If no nodes are bigger than 2 cm and there are fewer than six enlarged nodes, then RPLND or close observation is appropriate. For bulkier disease, chemotherapy is administered, although RPLND may be used in carefully selected cases.

Treatment of stage III disease depends on the sites of metastases and the levels of serum tumor markers. For good-risk disease, the treatment is three cycles of BEP or four cycles of EP chemotherapy. For intermediate- and poor-risk disease, the treatment is four cycles of BEP chemotherapy (or etoposide, ifosfamide, and cisplatin [VIP] chemotherapy). In NSGCT, all residual masses should be resected after chemotherapy if feasible. In cases of seminoma, residual masses are typically observed unless they show increased uptake on 8-fluorodeoxyglucose (FDG) positron emission tomography (PET scan). Patients with pure seminomas and residual masses after chemotherapy are the only testis cancer patients who should be considered for PET scans.

Relapsed disease after chemotherapy is treated with salvage chemotherapy given either at standard doses or at high doses with hematopoietic stem cell support.

Prognosis

Overall, the long-term disease-specific survival rate for testis cancer is 95%. By stage, the survival rates are 99% for stage I, 96% for stage II, and 73% for stage III. By disseminated disease risk category, survival is about 90% for good-risk disease, about 80% for intermediate-risk disease, and about 50% for poor-risk disease.

For a deeper discussion on these topics, please see Chapters 197, "Tumors of the Kidney, Bladder, Ureters, and Renal Pelvis," 200, "Testicular Cancer," and 201, "Prostate Cancer," in Goldman-Cecil Medicine, *25th Edition.*

SUGGESTED READINGS

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