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following patients as they are treated with various forms of therapy. Asymptomatic patients do not require treatment regardless of the size of the gland, while those with an inability to urinate, gross hematuria, recurrent infection, or bladder stones require evaluation and treat ment. In patients with symptoms, uroflowmetry can identify those with normal flow rates who are unlikely to benefit from treatment, and bladder ultrasound can identify those with high postvoid residuals who may need intervention. Pressure-flow (urodynamic) studies detect pri mary bladder dysfunction. Cystoscopy is recommended if hematuria is documented and to assess the urinary outflow tract before surgery. Imaging of the upper tracts is advised for patients with hematuria, a history of calculi, or prior urinary tract problems.

Symptomatic relief is the most common reason patients seek treat ment for BPH, and therefore, symptomatic relief is usually the goal of therapy for BPH. α-Adrenergic receptor antagonists are thought to treat the dynamic aspect of BPH by reducing sympathetic tone of the blad der outlet, thereby decreasing resistance and improving urinary flow. 5ARIs are thought to treat the static aspect of BPH by reducing prostate volume and having a similar, albeit delayed effect. 5ARIs have also proven beneficial in the prevention of BPH progression, as measured by prostate volume, the risk of developing acute urinary retention, and the risk of having BPH-related surgery. The use of an alpha-adrenergic receptor antagonist and a 5ARI as combination therapy seeks to provide symptomatic relief while preventing progression of BPH. PART 4 Oncology and Hematology Another class of medications that has shown improvement in LUTS secondary to BPH is phosphodiesterase-5 (PDE5) inhibitors, used currently in the treatment of erectile dysfunction. All four of the PDE5 inhibitors available in the United States—sildenafil, vardenafil, tadalafil, and avanafil—appear to be effective in the treatment of LUTS secondary to BPH. The use of PDE5 inhibitors is not without con troversy, however, given the fact that short-acting phosphodiesterase inhibitors such as sildenafil need to be dosed separately from alpha blockers such as tamsulosin because of potential hypotensive effects. Symptoms due to BPH often coexist with symptoms due to overac tive bladder, and the most common pharmacologic agents for the treat ment of overactive bladder symptoms are anticholinergics. This has led to multiple studies evaluating the efficacy of anticholinergics for the treatment of LUTS secondary to BPH. Surgical therapy is now considered second-line therapy and is usu ally reserved for patients after a trial of medical therapy. The goal of surgical therapy is to reduce the size of the prostate, effectively reduc ing resistance to urine flow. Surgical approaches include TURP, trans urethral incision, or removal of the gland via a retropubic, suprapubic, or perineal approach. Also used are transurethral ultrasound–guided laser-induced prostatectomy (TULIP), stents, and hyperthermia. ■ ■FURTHER READING Bergengren O et al: 2022 Update on prostate cancer epidemiology and risk factors: A systematic review. Eur Urol 84:191, 2023. Deek MP et al: Multi-institutional analysis of metastasis-directed ther apy with or without

androgen deprivation therapy in oligometastatic castration-sensitive prostate cancer. Eur Urol Oncol 7:1403, 2024. Donovan JL et al: Patient-reported outcomes 12 years after localized prostate cancer treatment. NEJM Evid 2:EVIDoa2300018, 2023. Erra tum in: NEJM Evid 2:EVIDx2300122, 2023. Eastham JA et al: Clinically localized prostate cancer: AUA/ASTRO Guideline. J Urol 208:505, 2022. Fendler WP et al: Assessment of 68Ga-PSMA-11 PET accuracy in localizing recurrent prostate cancer: A prospective single-arm clinical trial. JAMA Oncol 5:856, 2019. Haile ES et al: Medical management of benign prostatic hyperplasia. Cleve Clin J Med 91:163, 2024. Hamdy FC et al: Fifteen-year outcomes after monitoring, surgery, or radiotherapy for prostate cancer. N Engl J Med 388:1547, 2023. Hugosson J et al: Prostate cancer screening with PSA and MRI fol lowed by targeted biopsy only. N Engl J Med 387:2126, 2022. Hussain M et al: Survival with olaparib in metastatic castration-

resistant prostate cancer. N Engl J Med 383:2345, 2020.

Kasivisvanathan V et al: MRI-targeted or standard biopsy for

prostate-cancer diagnosis. N Engl J Med 378:1767, 2018. Merseburger AS et al: Genomic testing in patients with metastatic castration-resistant prostate vancer: A pragmatic guide for clinicians. Eur Urol 79:519, 2021. Morgan TM et al: Salvage therapy for prostate cancer: AUA/ASTRO/ SUO guideline part I: Introduction and treatment decision-making at the time of suspected biochemical recurrence after radical prostatec tomy. J Urol 211:509, 2024. Pinsky PF, Parnes H: Screening for prostate cancer. N Engl J Med 388:1405, 2023. Roach M 3rd et al: Prostate cancer, race, and health disparity: What we know. Cancer J 29:328, 2023. Sartor O et al: Lutetium-177-PSMA-617 for metastatic castrationresistant prostate cancer. N Engl J Med 385:1091, 2021. Virgo KS et al: Initial management of noncastrate advanced, recurrent, or metastatic prostate cancer: ASCO guideline update. J Clin Oncol 39:1274, 2021. David J. Vaughn

Testicular Cancer Testicular germ cell tumors (GCTs) represent 95% of all testicular neo plasms. Non-GCTs of the testis are much less common. Approximately 5% of GCTs arise in extragonadal locations including the mediastinum, retroperitoneum, and pineal gland. Treatment for testicular GCTs is determined by pathology and stage. The development of effective chemotherapy for this disease represents a landmark achievement in oncology. About 95% of newly diagnosed patients with testicular GCTs will be cured. For this reason, testicular cancer has been called “a model for a curable neoplasm.” INCIDENCE AND GLOBAL CONSIDERATIONS In 2023, ~9200 cases of testicular GCTs will be diagnosed in the United States, with 470 deaths. The incidence of testicular GCTs appears to be increasing worldwide. The disease has the highest incidence in Scandinavia, Western Europe, and Australia/New Zealand. Africa and Asia have the lowest incidence. The incidence in the United States and the United Kingdom is intermediate. While a distinct biology related to geography is not apparent, several countries have reported a migration to earlier stage disease in part related to public awareness and earlier diagnosis. ■ ■EPIDEMIOLOGY Testicular GCT is the most common malignancy diagnosed in adoles cent and young adult males (defined as age 15–39 years). The incidence in patients over 50 is increasing. Testicular GCT is most commonly diagnosed in Caucasians. The disease is much less commonly seen in African Americans. Testicular GCTs have an estimated heritability of almost 50%. Interestingly, the risk of GCT is higher in male siblings than in offspring of the patient. Although epidemiologic studies have been performed attempting to identify a relationship with environmental exposures, no conclusive causal links have been

established. Risk Factors The strongest risk factors for testicular GCT include a prior history of the disease, cryptorchidism, and a history of testicular germ cell neoplasia in situ. Patients with a prior history of testicular GCT have a 1–2% risk of developing a contralateral GCT. These are

more commonly metachronous than synchronous. Men with crypt orchidism have approximately a four- to sixfold increased risk of developing testicular GCT. Orchidopexy before puberty decreases but does not eliminate this risk. Interestingly, the contralateral descended testis is also at risk for this disease. Men undergoing infertility evalu ation in which a testicular biopsy demonstrates germ cell neoplasia in situ have a significant risk of developing GCT. Although scrotal ultrasound of patients with testicular GCT may demonstrate testicular microcalcifications that may be related to germ cell neoplasia in situ, the significance of testicular microcalcifications in the general popula tion is unclear. ■ ■BIOLOGY The primordial germ cell is the cell of origin for GCTs. Most malignant GCTs arise from in situ neoplasia. The molecular events that result in the development of germ cell neoplasia in situ and subsequent malig nant GCT have not been fully determined. However, genetic analysis of GCTs has demonstrated an excess copy number of isochromosome 12p (i[12p]) in most cases. Several genome-wide association studies have identified multiple independent loci associated with testicular GCT risk. The strongest of these is the KITLG (KIT ligand) locus on chromosome 12. These loci contribute significantly to the heritable risk of this disease. ■ ■PATHOLOGY GCTs are either seminomas or nonseminomas. For a tumor to be considered a seminoma, it must be 100% seminoma. Any mixed GCT should be approached as a nonseminomatous GCT. Seminomas repre sent ~50% of cases. Seminomas arise most commonly in patients in the fourth decade of life. Seminomas may contain syncytiotrophoblastic cells, which may secrete β-human chorionic gonadotropin (hCG). Seminomas do not secrete α-fetoprotein (AFP). Seminomas are exqui sitely sensitive to both chemotherapy and radiation therapy. Nonsemi nomatous GCTs are most commonly diagnosed in the third decade of life. The histologic subtypes include embryonal carcinoma, yolk sac tumor, choriocarcinoma, and teratoma. Embryonal carcinoma is the most undifferentiated nonseminomatous GCT subtype with the poten tial to differentiate into the other subtypes. Embryonal carcinoma may secrete AFP, hCG, both, or neither. Yolk sac tumor often secretes AFP. Choriocarcinoma is an aggressive subtype, often secreting hCG at very high levels. These nonseminomatous GCT subtypes are all considered chemotherapy sensitive. Teratoma is composed of somatic cell types that are derived from two or more germinal layers (endoderm, meso derm, and ectoderm). Teratomas are classified as mature, in which cell types resemble normal adult somatic tissue; immature, in which cell types resemble fetal somatic tissue; and malignant, in which the cell types have undergone malignant transformation into the malignant counterpart of the somatic tissue. Teratomas are chemotherapy resis tant and must be treated surgically. ■ ■INITIAL PRESENTATION Signs and Symptoms Although a painless testicular mass is pathognomonic of a GCT, most patients present with testicular swell ing, firmness, discomfort, or a combination of these. The differential diagnosis may include epididymitis or orchitis, and a trial of antibacte rials may be considered. Patients with retroperitoneal metastases may complain of back or flank pain. Patients may have cough, shortness of breath, or hemoptysis because of lung metastases. In patients with elevation of serum hCG, gynecomastia may be present. Diagnostic delay is not uncommon and may be associated with a more advanced stage at diagnosis. Physical Examination Careful examination of the affected testis and the contralateral normal testis should be performed. Many tumors will have a hard consistency to palpation. Some patients may show testicular atrophy. Evaluation for supraclavicular lymphadenopathy, gynecomastia, and abdominal mass should be performed. Inguinal

lymphadenopathy is rare. Most patients with lung metastases will have normal auscultation of the lungs.

Diagnostic Testing If a firm testicular mass is identified, a scrotal ultrasound should be performed. Patients with suspected epididymitis or orchitis who do not respond to antibiotics should also undergo scrotal ultrasound. Scrotal ultrasound should include both testicles. On ultrasound, a testicular GCT is hypoechoic and may be multifocal. A solid mass identified on ultrasound should be considered malignant until otherwise proven. Transscrotal aspiration or biopsy of a testicular mass should never be performed. Such scrotal violation may result in tumor seeding of the scrotum or inguinal lymph nodes. Serum Tumor Markers Serum AFP, hCG, and lactate dehydro genase (LDH) should be measured in patients suspected of testicular GCT. AFP is elevated in ~60–70% of patients who present with non seminomatous GCTs. Seminomas never secrete AFP. A patient with a seminoma with elevation of AFP should be approached as having a nonseminomatous GCT. The half-life of AFP is 5–7 days. A falsely elevated AFP may be seen in patients with hepatic disease or a condi tion called hereditary persistence of AFP, in which patients may have baseline AFP levels that are mildly elevated. hCG may be elevated in both nonseminomatous GCTs as well as seminomas. Patients with cho riocarcinoma may have markedly elevated levels of hCG. The half-life for hCG is 24–36 h. False-positive elevation of hCG may be seen sec ondary to hypogonadism, marijuana use, or because of interfering sub stances measured by the assay. LDH is a nonspecific marker for GCT. Its principal use is to help in the assessment of the risk classification of a patient with metastatic disease. Although elevation of serum tumor markers supports the diagnosis of a testicular GCT, most patients with seminoma and up to a third of patients with nonseminomatous GCTs do not have elevated levels. Serum microRNA (miR)-371a-3 has been identified as a promising biomarker for GCT, and validation studies are ongoing. CHAPTER 93 Testicular Cancer ■ ■INITIAL MANAGEMENT Inguinal Orchiectomy Prompt referral to urology should be performed if a testicular GCT is suspected. The initial treatment for most patients suspected of having a testicular GCT is radical ingui nal orchiectomy with removal of the testicle and spermatic cord to the level of the internal inguinal ring. In patients who present with metastatic disease and the diagnosis of GCT is certain, orchiectomy may be deferred until completion of chemotherapy. Although some institutions perform testis-sparing surgery in select patients, the gold standard remains radical inguinal orchiectomy. Pathologic examina tion of the entire testicle is important, since testicular GCTs may be multifocal. Given the rarity of this cancer, review by an experienced pathologist is essential for accurate tumor classification. Serum tumor markers should be obtained before and after orchiectomy. Staging The staging of testicular GCT is based on an understanding of the pattern of spread. The initial spread is by the lymphatic route to the retroperitoneal lymph nodes. A left-sided testicular GCT spreads first to the primary landing zone of left paraaortic lymph nodes inferior to the left renal vessels. A right-sided testicular GCT spreads first to the primary landing zone of the aortocaval nodes inferior to the right renal vessels. Nodal metastases may extend into the iliac regions. If scrotal violation occurred, inguinal lymph node metastases may be seen. Subsequent lymphatic spread is to the retrocrural, mediastinal, and supraclavicular lymph nodes. Hematogenous spread to the lung is the next most com mon site of metastasis. Metastases to the liver, bone, and brain are less common. Patients with newly diagnosed testicular GCTs should undergo computed tomography (CT) scan of the abdomen and pelvis. Chest x-ray should be performed. CT scan of the chest is performed if retroperitoneal metastases are present or if lung nodules are identified on chest x-ray. Bone scan and magnetic resonance imaging (MRI) of the brain are not routinely performed unless clinically indicated. Positron emission tomography (PET)

has little role in the initial staging of testicular GCTs.

The American Joint Committee on Cancer tumor-node-metastasis (TNM) staging classification is used. There are three main stages of testicular GCT. Stage I is limited to the testis; stage II involves the ret roperitoneal lymph nodes; and stage III includes lymph node involve ment beyond the retroperitoneum and/or distant metastatic disease.

■ ■STAGE-BASED MANAGEMENT Treatment of testicular GCT is based on two factors: (1) whether the tumor is seminoma or nonseminomatous GCT and (2) the stage of the patient. This is summarized in Fig. 93-1. Stage I • SEMINOMA About 70% of newly diagnosed patients with seminoma present with stage I disease. This is defined as no evidence of metastatic disease on imaging of the chest, abdomen, and pelvis. Approximately 15% of patients with stage I seminoma have metastatic disease at the microscopic level, usually in the retroperito neum. Historically, patients with stage I seminoma were treated with a course of adjuvant radiation therapy to the paraaortic lymph nodes. While still an option, this is not usually performed because of concerns for late radiation-induced secondary malignancies. Active surveillance is the most common approach elected by these patients following orchiectomy. With active surveillance, interval physical examination and CT scan of the abdomen are performed. For the 15% of patients who develop metastatic disease during active surveillance, treatment is curative in nearly all. A third option for clinical stage I seminoma is adjuvant chemotherapy with carboplatin monotherapy for one or two cycles. While effective in decreasing the risk of recurrence, most patients are cured by orchiectomy alone, and therefore, the additional treatment is unnecessary. In addition, long-term data on toxicity are not available. PART 4 Oncology and Hematology NONSEMINOMATOUS GCTS About 40% of newly diagnosed patients with nonseminomatous GCTs present with stage I disease. Because nonseminomatous GCTs have an increased potential for invasion and metastasis, spread to the retroperitoneum and beyond is more com mon than with seminoma. If pre-orchiectomy serum tumor markers are elevated, these must normalize after orchiectomy to be considered stage I. Patients with persistently elevated or rising serum tumor mark ers after orchiectomy have stage IS disease and should be treated with cisplatin-based chemotherapy. If the tumor is limited to testis without lymphovascular invasion, the risk of recurrence is approximately 20%. However, if the tumor has high-risk features including lymphovascular invasion, invasion of the spermatic cord, or invasion of the scrotum, the risk of recurrence is ~50% or higher. Historically, a prophylactic retroperitoneal lymph node dissection (RPLND) was performed. This surgery is not only diagnostic but also therapeutic. In fact, most patients who undergo prophylactic RPLND will never require chemo therapy. While still an option, this approach subjects many patients to unnecessary major abdominal surgery. RPLND is also associated with a small risk of retrograde ejaculation due to nerve injury, and nerve-sparing techniques have been developed. Active surveillance is frequently performed especially for patients without lymphovascular invasion. Most patients who relapse will be treated with cisplatin-based chemotherapy and achieve cure rates approaching 100%. Active sur veillance can also be employed for patients with higher risk features, although the risk of progression is significantly higher. For this rea son, some advocate adjuvant cisplatin-based chemotherapy with BEP (bleomycin, etoposide, cisplatin) for one cycle for these patients. Other centers favor a prophylactic RPLND. Almost all patients who present with stage I nonseminomatous GCTs will achieve cure. Stage II • SEMINOMA Approximately 15–20% of newly diag nosed patients with seminoma present with stage II disease. Patients are subgrouped into IIA, IIB, or IIC based on the size of the retroperi toneal nodes (≤2 cm, >2 to 5 cm, or >5 cm, respectively). Patients with

stage IIA disease are usually treated with “dogleg” radiation therapy (referring to the shape of the radiation field), which includes the para aortic and ipsilateral iliac nodes. Cisplatin-based chemotherapy may also be considered. Stage IIB disease is treated with cisplatin-based chemotherapy or, in select patients, radiation therapy. Most patients

treated with radiation therapy who relapse will subsequently be cured with cisplatin-based chemotherapy. RPLND has been considered in select patients with stage IIA and nonbulky stage IIB seminoma in an effort to avoid chemotherapy and radiation therapy. For patients with stage IIC disease, cisplatin-based chemotherapy should be used. NSGCTS Approximately 15% of newly diagnosed patients with non seminomatous GCTs present with clinical stage II disease. Patients with stage IIA disease may be treated with primary RPLND. Alternatively, these patients may be treated with cisplatin-based chemotherapy. Patients with stage IIB and IIC disease are best initially managed with cisplatin-based chemotherapy. Stage III Patients who present with stage III GCT (seminoma or nonseminomatous GCT) are treated with cisplatin-based chemother apy. These patients are classified into good-, intermediate-, or poor-risk categories using the International Germ Cell Consensus Classification system, which is based on clinical factors including histology, site of primary, the presence of nonpulmonary visceral metastatic disease, and the level of postorchiectomy serum tumor markers (Table 93-1). Most patients with stage III GCT present with good-risk disease and

> 90% will be cured. The remainder present with intermediate-risk or poor-risk disease associated with 5-year survival rates of ~80% and 50%, respectively. Select patients with rapidly progressive metastatic disease and life-threatening symptoms such as hemoptysis in whom there is a high clinical suspicion of GCT should emergently initiate cisplatin-based chemotherapy, even without a tissue diagnosis. Chemotherapy The development of cisplatin-based chemotherapy represents an important advance in cancer medicine. Through a series of carefully performed clinical trials with the aim of maximizing cure while minimizing the extent of treatment, the chemotherapy approach to the treatment of these patients has been standardized. Patients with good-risk metastatic GCT are treated with either three cycles of BEP or four cycles of etoposide and cisplatin (EP). Patients with intermediate- and poor-risk metastatic disease are treated with either four cycles of BEP or four cycles of etoposide, ifosfamide, and cisplatin (VIP). Maintain ing dose and schedule is important, as dose modifications and delays have been associated with inferior outcomes. Serum tumor markers should be monitored throughout treatment and should normalize during or after treatment. Cisplatin-based chemotherapy is associated with myelosuppression, nausea and vomiting, and alopecia. Cisplatin may result in nephrotoxicity, ototoxicity, and peripheral neuropathy. Bleomycin may result in pulmonary toxicity, and risk factors for this include age >40, renal failure, tobacco use, and the cumulative dose of bleomycin received. For patients at increased risk of bleomycininduced pneumonitis, non–bleomycin-containing regimens as noted above may be given. Cisplatin-based chemotherapy is also associated with sterility. Approximately 30% of newly

> diagnosed testicular GCT patients have severe oligospermia or azoospermia. For the remainder with normal baseline spermatogenesis who receive cisplatin-based chemotherapy, all will be azoospermic at the completion of therapy. Approximately 80% of these patients will recover spermatogenesis over a period of several years. For this reason, prechemotherapy sperm banking should be offered to all patients treated with chemotherapy. Postchemotherapy Surgery Upon completion of cisplatin-based chemotherapy, many patients with normalized serum tumor markers will have radiographic evidence of residual masses. In approximately half of patients with nonseminomatous GCT, the residual mass is composed of necrosis and/or fibrosis. About 40% will have residual teratoma, and only 10% will have residual viable nonteratomatous GCT. Unfortunately, radiographic imaging cannot accurately differen tiate between these entities. For this reason, nonseminomatous GCT patients with residual masses after chemotherapy undergo resection of all sites of disease. This most commonly includes a postchemotherapy RPLND. However, thoracotomy and neck dissection are required in some patients. Given the complexity of this surgery, patients should be referred to highly experienced centers. If the patients are found to have residual necrosis or teratoma, no additional therapy is required.

Testis Seminoma NSGCT Stage IA Testis only, no lymphovascular invasion Active surveillance; or Adjuvant carboplatin × 1 or 2 cycles; or Adjuvant para-aortic RT Stage IB Testis only, with lymphovascular invasion or invasion of spermatic cord or scrotum Active surveillance; or Adjuvant carboplatin × 1 or 2 cycles; or Adjuvant para-aortic RT Stage IS Elevated serum tumor markers postorchiectomy BEP × 3 cycles; or EP × 4 cycles BEP × 3 cycles; or EP × 4 cycles A Lymph nodes Seminoma NSGCT Stage IIA N1: nodes ≤ 2 cm Para-aortic and ipsilateral iliac RT; or BEP × 3 cycles or EP × 4 cycles; Nerve-sparing RPLND in select patients Stage IIB N2: nodes > 2 to 5 cm BEP × 3 cycles or EP × 4 cycles; or Para-aortic and ipsilateral iliac RT BEP × 3 cycles or EP × 4 cycles +/– postchemotherapy RPLND Stage IIC N3: nodes > 5 cm BEP × 3 cycles or EP × 4 cycles BEP × 3 cycles or EP × 4 cycles +/– postchemotherapy RPLND B FIGURE 93-1 Stage-based management of testicular germ cell tumor.

Stage 1 CHAPTER 93 Active surveillance; or Nerve-sparing RPLND; or Adjuvant BEP × 1 cycle Active surveillance; or Adjuvant BEP × 1 cycle; or Nerve-sparing RPLND Testicular Cancer Stage 2 Testis Nerve-sparing RPLND; or BEP × 3 cycles or EP × 4 cycles

Stage 3 Lungs Liver Lymph nodes Testis PART 4 Oncology and Hematology Seminoma NSGCT Stage IIIA (good-risk) BEP × 3 cycles; or EP × 4 cycles BEP × 3 cycles; or EP × 4 cycles; +/– Postchemotherapy surgery Stage IIIB (intermediate-risk) BEP × 4 cycles; or VIP × 4 cycles BEP × 4 cycles; or VIP × 4 cycles +/– Postchemotherapy surgery Stage IIIC (poor-risk) N/A BEP × 4 cycles; or VIP × 4 cycles +/– Postchemotherapy surgery Abbreviations: BEP, bleomycin, etoposide, cisplatin; EP, etoposide, cisplatin; N/A, not applicable; NSGCT, nonseminomatous germ cell tumor; RPLND, retroperitoneal lymph node dissection; RT, radiation therapy; VIP, etoposide, ifosfamide, cisplatin. C FIGURE 93-1 (Continued) TABLE 93-1 International Germ Cell Consensus Classification System RISK GROUP SEMINOMA NSGCT Good Any primary site; and normal AFP, any hCG, any LDH;

and nonpulmonary visceral metastases absent Gonadal or retroperitoneal primary; and nonpulmonary visceral metastases absent; and AFP <1000 ng/mL; and hCG <5000 mIU/mL; and LDH <1.5 × ULN Intermediate Any primary site; and normal AFP, any hCG, any LDH; and nonpulmonary visceral metastases present Gonadal or retroperitoneal primary; and nonpulmonary visceral metastases absent; and one of the following: AFP 1000–10,000 ng/mL HCG 5000–50,000 mIU/mL LDH 1.5–10 × ULN Poor N/A Mediastinal primary; or nonpulmonary visceral metastases present; or one of the following: AFP >10,000 ng/mL HCG >50,000 mIU/mL LDH >10 × ULN Abbreviations: AFP, α-fetoprotein; hCG, human chorionic gonadotropin; LDH, lactate dehydrogenase; N/A, not applicable; NSGCT, nonseminomatous germ cell tumor; ULN, upper limit normal. Nonpulmonary visceral metastases include liver, bone, and brain. Source: Reproduced with permission from International Germ Cell Cancer Collaborative Group: International Germ-Cell Consensus Classification: A prognostic factor based staging system for metastatic germ cell tumors. J Clin Oncol 15:594, 1997.

Brain Bone However, for patients with residual viable nonteratomatous GCT, two additional cycles of chemotherapy may be considered. It should be noted that in most centers, patients with minimal residual tumors defined as retroperitoneal lymph nodes of ≤1 cm forego postchemo therapy RPLND. Patients who experience normalization of serum tumor markers with first-line chemotherapy but have enlarging tumors, most often cystic masses in the retroperitoneum, may have “growing teratoma syndrome.” These patients are best approached with surgery. For patients with metastatic seminoma, most residual masses are necrotic and do not harbor viable tumor. Patients with residual masses of 3 cm or less may be observed without surgery. For patients with residual masses >3 cm, fluorodeoxyglucose (FDG)-PET may be used to distinguish necrosis from viable seminoma and identify patients who should be considered for postchemotherapy surgery or short interval imaging. ■ ■RELAPSED DISEASE Approximately 20–30% of patients with metastatic GCTs treated with cisplatin-based chemotherapy will not achieve durable disease control. Most of these patients will experience disease progression within 2 years following completion of chemotherapy. The International Prognostic Factors Study Group developed a risk stratification classification sys tem for patients in first relapse. Contributors to a worsened prognosis include NSGCT histology, extragonadal primary, incomplete response to first-line chemotherapy, time to relapse of 3 months or less, level of serum tumor markers at relapse, and the presence of nonpulmonary visceral metastatic disease.

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