

Testicular Tumors 2

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SUMMARY

Testicular Tumors

Testicular tumors are the most common cause of painless testicular enlargement. They occur with increased frequency in undescended testis and in males with gonadal dysgenesis. Germ cells are the source of 95% of testicular tumors, and the remainder arise from Sertoli or Leydig cells. Germ cell tumors may be composed of one histologic pattern (60% of cases) or mixed patterns (40%). They are often preceded by in situ lesions. The most common single histologic patterns of testicular tumors are seminoma, embryonal carcinoma, yolk sac tumors, choriocarcinoma, and teratoma. Mixed tumors contain more than one element, most commonly embryonal carcinoma, teratoma, and yolk sac tumors. Clinically testicular tumors can be divided into two groups: seminomas and nonseminomatous tumors. Seminomas remain confined to the testis for a long time and spread mainly to para-aortic nodes—rarely to distant sites. Nonseminomatous tumors tend to spread earlier both by lymphatics and blood vessels. hCG is produced by syncytiotrophoblasts and is always elevated in choriocarcinomas and in those seminomas that have syncytiotrophoblasts. AFP is made by yolk sac cells and is elevated in yolk sac tumors. Most nonseminomatous tumors have mixed patterns and hence elevation of both hCG and AFP.

Yolk sac tumors:

Yolk sac tumors, also termed endodermal sinus tumors, are the most common primary testicular neoplasm in children younger than 3 years of age. In adults, yolk sac tumors are most often seen admixed with embryonal carcinoma. In the histogenetic scheme noted previously, yolk sac tumors represent endodermal sinus differentiation of totipotent neoplastic cells. Grossly, these tumors are often large and may be well demarcated. Histologic examination discloses low cuboidal to columnar epithelial cells forming microcysts, sheets, glands, and papillae, often associated with eosinophilic hyaline globules. A distinctive feature is the presence of structures resembling primitive glomeruli, the so-called Schiller-Duval bodies. α -fetoprotein (AFP) can be demonstrated within the cytoplasm of the neoplastic cells by immunohistochemical techniques.

Choriocarcinomas represent differentiation of pluripotent neoplastic germ cells along trophoblastic lines. Grossly, the primary tumors are often small, nonpalpable lesions, even with extensive systemic metastases. Microscopically, choriocarcinomas are composed of sheets of small cuboidal cells irregularly intermingled with or capped by large, eosinophilic syncytial cells containing multiple dark, pleomorphic nuclei; these represent cytotrophoblastic and syncytiotrophoblastic differentiation, respectively (18-8). Well-formed placental villi are not seen. The hormone hCG can be identified with appropriate immunohistochemical staining, particularly within the cytoplasm of the

syncytiotrophoblastic elements.

Teratomas represent differentiation of neoplastic germ cells along somatic cell lines. These tumors form firm masses that on cut surface often contain cysts and recognizable areas of cartilage. Histologically, three major variants of pure teratoma are recognized. Mature teratomas contain fully differentiated tissues from one or more germ cell layers (e.g., neural tissue, cartilage, adipose tissue, bone, epithelium) in a haphazard array. Immature teratomas, in contrast, contain immature somatic elements reminiscent of those in developing fetal tissue. Teratomas with somatic-type malignancies are characterized by the development of frank malignancy in preexisting teratomatous elements, usually in the form of a squamous cell carcinoma or adenocarcinoma. Pure teratomas in prepubertal males are usually benign. In adults, teratomas metastasize in as many as 37% of cases. As with other germ cell tumors, testicular teratomas in adults often contain other malignant germ cell elements and therefore should be generally regarded as malignant neoplasms.

Mixed germ cell tumors, as noted, account for approximately 40% of all testicular germ cell neoplasms. Combinations of any of the described patterns may occur in mixed tumors, the most common of which is a combination of teratoma, embryonal carcinoma, and yolk sac tumors.

Embryonal carcinoma. In contrast to the seminoma the embryonal carcinoma is a hemorrhagic mass.

Clinical Features

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Clinically, it is best to consider testicular germ cell tumors under two broad categories: Seminomas and non-seminomatous tumors. As will be evident from the discussion that follows, these two groups of tumors have somewhat distinctive clinical presentation and natural history.

Embryonal carcinoma shows sheets of undifferentiated cells as well as primitive glandular differentiation. The nuclei are large and hyperchromatic.

Yolk sac carcinoma. in, Low-power photomicrograph demonstrating areas of loosely textured, microcystic tissue and a papillary structure resembling

a developing glomerulus. B, Higher power photomicrograph demonstrating characteristic hyaline droplets within the microcystic areas of the tumor. α -fetoprotein is present within the droplets.

Choriocarcinoma shows cytotrophoblastic cells with central nuclei and syncytiotrophoblastic cells with multiple dark nuclei embedded in eosinophilic cytoplasm. Hemorrhage and necrosis are prominent.

Individuals with testicular germ cell neoplasms present most frequently with painless enlargement of the testis. However, some tumors, especially nonseminomatous germ cell neoplasms, may have widespread metastases at diagnosis, in the absence of a palpable testicular lesion. Seminomas often remain confined to the testis for prolonged intervals and may reach considerable size before diagnosis. Metastases are most commonly encountered in the iliac and para-aortic lymph nodes, particularly in the upper lumbar region. Hematogenous metastases occur later. In contrast, nonseminomatous germ cell neoplasms tend to metastasize earlier, by both lymphatic and hematogenous routes. Hematogenous metastases are most common in the liver and lungs. Metastatic lesions are typically histologically identical to the primary testicular tumor; rarely they may contain other germ cell elements. Testicular germ cell neoplasms are staged as follows:

Stage I: Tumor confined to the testis
Stage II: Regional lymph node metastases only
Stage III: Nonregional lymph node and/or distant organ metastases

Assay of tumor markers secreted by tumor cells is important in the clinical evaluation and staging of germ cell neoplasms. hCG, produced by neoplastic syncytiotrophoblastic cells, is always elevated in patients with choriocarcinoma. As noted, other germ cell tumors, including seminoma, may also contain syncytiotrophoblastic cells without cytotrophoblastic elements and hence may elaborate hCG. Approximately 10% to 25% of seminomas elaborate hCG. AFP is a glycoprotein normally synthesized by the fetal yolk sac and several other fetal tissues. Nonseminomatous germ cell tumors containing elements of yolk sac (endodermal sinus) often produce AFP; in contrast to hCG, the presence of AFP is a reliable indicator of the presence of a nonseminomatous component to the germ cell neoplasm, because yolk sac elements are not found in pure seminomas. Because mixed patterns are common, most nonseminomatous tumors have elevations of both hCG and AFP. In addition to their role in the primary diagnosis and staging of testicular germ cell tumors, serial determinations of hCG and AFP are useful for monitoring patients for persistent or recurrent tumor after therapy. It should be noted, however, that AFP is also elevated in hepatocellular carcinoma.

The treatment of testicular germ cell neoplasms is considered a success story of chemotherapy. Although roughly 8000 new cases of testicular cancer occur in the United States yearly, fewer than 400 men are expected

to die of the disease. In fact, after being treated for testicular cancer, Lance Armstrong won the Tour de France bicycle race a record seven times! The treatment is determined by both the histologic pattern of the tumor and the stage of disease at the time of diagnosis. Seminomas are exquisitely radiosensitive, and they also respond well to chemotherapy. The prognosis of many nonseminomatous germ cell tumors has improved dramatically with the introduction of platinum-based chemotherapy regimens.

Teratoma. Testicular teratomas contain mature cells from endodermal, mesodermal, and ectodermal lines. Pictured here are four different fields from the same tumor containing (A) neural (ectodermal), (B) glandular (endodermal), (C) cartilaginous (mesodermal), and (D) squamous epithelial elements.

Summary of Testicular Tumors

Tumor
Peak Age (yr)
Morphology
Tumor Markers

Seminoma
40-50
Sheets of uniform polygonal cells with cleared cytoplasm; lymphocytes in the stroma
10% have elevated hCG

Embryonal carcinoma
20-30
Poorly differentiated, pleomorphic cells in cords, sheets, or papillary formation; most contain some yolk sac and choriocarcinoma cells
90% have elevated hCG or AFP or both

Yolk sac tumor

Poorly differentiated endothelium-like, cuboidal, or columnar cells
90% have elevated AFP

Choriocarcinoma (pure)

20-30

Cytotrophoblast and syncytiotrophoblast without villus formation

100% have elevated hCG

Teratoma

All ages

Tissues from all three germ-cell layers with varying degrees of differentiation

50% have elevated hCG or AFP or both

Mixed tumor

Variable, depending on mixture; commonly teratoma and embryonal carcinoma

90% have elevated hCG and AFP

AFP, α -fetoprotein; hCG, human chorionic gonadatropin.