**Germ Cell Tumors**

1. A 14-year-old postmenarchal girl presents with abdominal pain and distension and secondary amenorrhea. Physical examination reveals a large pelvic mass, hirsutism, and facial hair. The parents also report that the girl’s voice is deeper. Imaging studies show a mass arising from the left ovary.

What is the most likely diagnosis?

A. Dysgerminoma

B. Ovarian carcinoma

C. Choriocarcinoma

D. Sertoli-Leydig tumor

E. Yolk sac tumor

**Explanation**

Stromal sex-cord tumors (Sertoli-Leydig and juvenile granulosa cell tumors) must be included in the differential diagnosis of ovarian solid masses, particularly for postpubertal female patients. Sertoli-Leydig tumors are typically associated with elevated levels of testosterone causing secondary amenorrhea and virilization. Inhibin levels also usually are elevated and are a good marker for diagnosis and follow-up.

2. A 28-month-old girl presents with abdominal and lower back pain and urinary retention. Imaging studies show a midline pelvic mass with retroperitoneal nodal enlargement and multiple lung and bone metastases. Alpha-fetoprotein (AFP) serum concentration is 320,000 ng/mL. A biopsy of the primary mass is performed, and pathology is pending.

What is the most likely histology?

A. Embryonal carcinoma

B. Germinoma

C. Yolk sac tumor

D. Immature teratoma

E. Choriocarcinoma

**Explanation**

This is a typical presentation of a stage IV sacrococcygeal germ cell tumor originating from an untreated sacrococcygeal teratoma. The most common histology in this scenario is yolk sac tumor. The high AFP serum concentration is consistent with this diagnosis. Choriocarcinoma is typically associated with elevated beta-HCG, and germinomas, embryonal carcinomas, and immature teratomas are typically associated with normal (or only mildly elevated) serum AFP.

3. A 15-year-old boy presents with chest pain and respiratory distress. A chest CT reveals a large anterior mediastinal mass. Alpha-fetoprotein (AFP) serum concentration is 12,000 ng/mL, and beta-HCG is 75 ng/mL.

What clinical syndrome could be associated with this presentation?

A. Klinefelter syndrome

B. DICER-1 syndrome

C. Isochromosome 12p

D. Cowden syndrome

E. Gardner syndrome

**Explanation**

This patient has a mediastinal mixed malignant germ cell tumor, probably with yolk sac and choriocarcinoma components. Patients with gonadal dysgenesia such as Klinefelter syndrome are at elevated risk of malignant germ cell tumors. Isochromosome 12p is a common genetic abnormality found in malignant germ cell tumors in adolescents and young adults, but this is a somatic event, not a germline defect. DICER-1 syndrome is associated with pleuropulmonary blastoma, cystic nephroma, and Sertoli-Leydig tumors, among others. Patients with Cowden syndrome typically develop hamartomas of the mucosal membranes and are at risk of developing breast, thyroid, and endometrial cancer. Patients with Gardner syndrome are at risk of colon carcinoma and hepatoblastoma.

4. A 14-year-old postmenarchal girl presents with large abdominal mass and a 4-month history of secondary amenorrhea. Physical examination reveals a large pelvic mass, hirsutism, and facial hair. Imaging studies show a mass probably arising from the left ovary.

As you document family history, what malignancy would you expect to find in other family members?

A. Adrenocortical carcinoma

B. Retinoblastoma

C. Pleuropulmonary blastoma

D. Yolk sac tumor

E. Malignant peripheral nerve sheath tumor

**Explanation**

This patient has a virilizing ovarian mass, consistent with a testosterone-producing stromal sex-cord tumor such as Sertoli-Leydig cell tumor, which is associated with germline DICER-1 mutations in 50% of the cases. The DICER-1 syndrome is characterized by a very broad phenotype. The most common malignancy is pleuropulmonary blastoma. Other malignancies described in the syndrome include cystic nephroma, stromal sex-cord tumors, uterine cervix embryonal rhabdomyosarcoma, Wilms tumor, cervical primitive neuroectodermal tumor, ciliary body medulloepithelioma, medulloblastoma, and seminoma.

5. A 2-year-old boy presents with a right scrotal mass. Ultrasound of the scrotum shows a right testicular mass; additional imaging studies show no evidence of retroperitoneal lymph node enlargement, and chest CT is negative. Laboratory evaluation shows serum alpha-fetoprotein (AFP) levels of 230,000 ng/mL and beta-HCG of 3 ng/mL. A right orchiectomy is performed, and in subsequent weeks the AFP levels normalize. Pathology indicates a yolk sac tumor. You are meeting with the family to discuss the next steps in care.

What would be the most appropriate next step in treatment?

A. Adjuvant therapy with four cycles of cisplatin, etoposide, and bleomycin

B. Retroperitoneal lymph node dissection

C. Observation

D. Retroperitoneal lymph node dissection followed by four cycles of cisplatin, etoposide, and bleomycin

E. Two cycles of single-agent cisplatin

**Explanation**

With normalization of the AFP, this patient has stage I testicular malignant germ cell tumor, which has an excellent prognosis with surgery and observation. Adjuvant chemotherapy is not recommended in this scenario. Retroperitoneal lymph node dissection, a procedure that is commonly prescribed in the management of seminoma in adults, is not recommended as initial treatment of pediatric testicular germ cell tumors.