CHAPTER 37

Teratomas and Other Germ Cell Tumors

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Pediatric germ cell tumors are rare tumors that are unique due to their varied clinical presentation and locations. Approximately 20% of pediatric germ cell tumors are malignant, and they represent 1% to 3% of all malignant tumors in childhood and adolescence.[1,2] Three features distinguish these childhood tumors from many other malignancies as well as their counterparts: In children, the extragonadal tumor site is more common than the gonadal site, whereas in adults, only 10% are at extragonadal sites; yolk sac tumor is the predominant malignant histology, and a serum marker (alpha fetoprotein, AFP) exists to follow response to therapy and monitor for recurrent disease; and the introduction of modern chemotherapy with cisplatin and bleomycin significantly increased survival for affected children and has allowed neoadjuvant therapy with vital organ preservation in initially unresectable cases.

Abnormal or arrested migration of primordial germ cells results in deposition of cells in the sacrococcygeal region, retroperitoneum, mediastinum, and pineal gland of the brain, resulting in the potential of extragonadal germ cell tumors at these sites. Whereas in adults 90% of germ cell tumors are at gonadal locations, in childhood, the extragonadal site is more common until puberty, at which time the gonadal sites are more common. The totipotential nature of these cells results in a wide variety of histologic patterns, and in addition, one quarter of pediatric tumors have more than one histologic component.[2] The management of these tumors is dependent upon complete surgical resection at diagnosis or after neoadjuvant therapy, accurate and thorough histologic examination, and selective use of chemotherapy. Prior to the late 1970s, the survival of advanced-stage tumors was dismal; however, Einhorn's introduction of cisplatin, vinblastine, and bleomycin for disseminated testicular cancer in 1977 changed the treatment of all germ cell tumors with dramatic results.[3] Subsequent studies validated the use of chemotherapy in a neoadjuvant fashion, thus allowing vital organ preservation in advanced cases with frequent massive tumor shrinkage. The role of the surgeon in determining resectability and performing a proper staging operation is vital.

Current therapy within the Children's Oncology Group (COG) is risk based: with surgery alone for stage 1 testes and ovary tumors and all immature teratomas, with anticipated survival of 95% to 100%; surgery and chemotherapy for all remaining gonadal tumors (except stage IV ovary) and low-stage (I-II) extragonadal, with anticipated survival of 90% to 100%; and surgery and intensive chemotherapy for high-risk (stage III-IV) extragonadal and stage IV ovary, with survival between 75% and 90%, depending on site and stage.

Embryology and Classification

Primordial germ cells arise near the allantois of the embryonic yolk sac endoderm and are evident at the fourth fetal week. They migrate along the midline dorsal mesentery to the genital ridge, arriving by the end of the sixth fetal week. The migration of the germ cells appears to be mediated by the c-KIT receptor and stem cell factor; the latter is expressed in increasing levels from the yolk sac to the genital ridge.[4,5] Arrested migration is presumed to account for the extragonadal locations in the normal path of the germ cells (retroperitoneum), whereas aberrant migration results in cells at other extragonadal sites (pineal, sacrococcygeal).

CLASSIFICATION

Teilum[6] proposed the germ cell origin of gonadal tumors, and the pathway of differentiation is listed in Figure 37-1. Seminoma (or dysgerminoma) is a primitive germ cell tumor that lacks the ability for further differentiation. It is unusual in childhood and occurs most frequently in the mediastinum, pineal gland, and at the gonadal sites during the adolescent years. Embryonal carcinoma is composed of cells capable of further differentiation into embryonic or extraembryonic tumors. Teratomas are the most common germ cell tumor and are composed of elements from one or more of the embryonic germ layers and contain tissue foreign to the anatomic site of origin.[7,8]

Mature and immature teratomas are considered benign lesions. It is, however, imperative to have a thorough and accurate pathologic review, because 25% of germ cell tumors in childhood are mixed tumors with more than one histologic

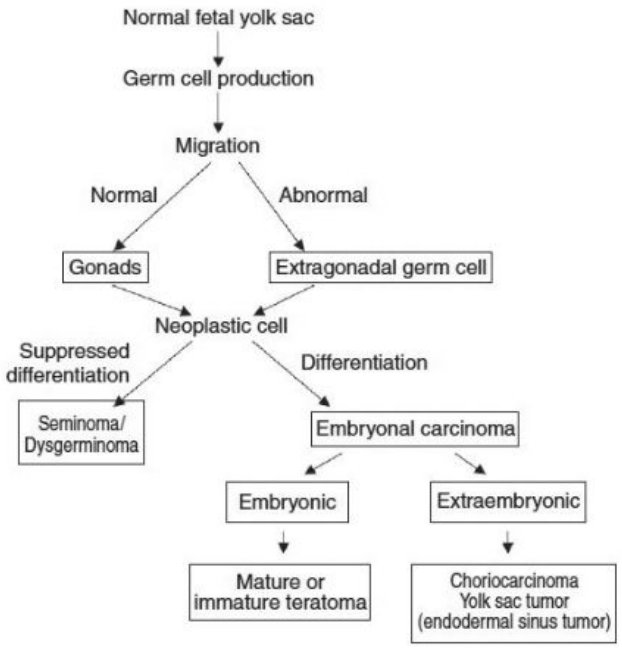

FIGURE 37-1 Classification system for development of germ cell tumors.

component.[2] Certain sites are more likely to have mixed tumor histology, with ovary (46%) and mediastinal (61%) the most common.[9,10] Mature teratomas contain well-differentiated tissue, whereas immature teratomas contain neuroectoderm and are graded between 1 and 3 based on the number of low-power fields of primitive neuroepithelium.[11] There has been debate about the treatment of immature teratomas. Many adult reports of ovarian tumors have considered grade 3 lesions malignant, and these patients have been treated with chemotherapy. A review of childhood immature teratomas demonstrated an association between high-grade immaturity and the presence of microscopic foci of endodermal sinus tumor,[12] with malignant foci observed in 83% of grade 3 immature teratomas as the only risk factor for recurrence.[13]

Yolk sac tumors (endodermal sinus) and choriocarcinoma are well-differentiated, highly malignant tumors. Yolk sac is the more common histology in childhood and occurs primarily in the sacrococcygeal region, ovary, and prepubertal testes.

Genetics and Risk Factors

Germ cell tumors demonstrate a bimodal age distribution with peaks at 2 and 20 years of age. Pediatric germ cell tumors differ in several aspects from their adult counterparts. Pediatric yolk sac tumors are more likely to have DNA ploidy, whereas adolescent and adult germ cell tumors are usually aneuploid.[14] In children younger than 4 years of age, the primary malignant germ cell tumor is yolk sac, and these are diploid or tetraploid; the teratomas are diploid with normal karyotypes and are benign.[15–17] Childhood yolk sac tumors have also demonstrated deletion of chromosomes 1p and 6q in 50% of specimens.[18] In addition, a smaller percentage demonstrates amplification of c-MYC. The isochromosome i (12p), which noted in malignant ovarian germ cell tumors but not in ovarian immature teratomas.[19]

The presence of intersex disorders is a known risk factor for gonadoblastoma, an in-situ germ cell tumor with the ability to differentiate into dysgerminoma, immature teratoma, yolk sac tumor, or choriocarcinoma.[20] One risk group includes testosterone deficiency, androgen insensitivity syndromes, and 5-alpha-reductase deficiency, which are androgen-deficient males. The presence of any portion of a Y chromosome is considered a risk factor in these children.[21] Risk of malignancy in androgen insensitivity is 3.6% at age 20 and 22% at age 30[22]; in view of this, gonadectomy usually in adolescence, is recommended. Gonadal dysgenesis is associated with a risk of malignancy of 10% at age 20 and 19% at age 30.

Undescended testes have an increased risk of malignancy, with the rate highest for intraabdominal testes. Approximately 0.4% of all males have undescended testes, however, it is observed in 3.5 to 12% of the testicular cancer population.[23] One study noted that although intraabdominal testes only account for 14% of undescended testes, they account for nearly 50% of tumors in the undescended testes group. The effect of orchiopexy on the risk of testes cancer is not known, and 20% of the tumors in patients with undescended testis occur in the descended testis.[24] Seminomas occur in a higher percentage of undescended testes (60%) compared with the descended testes tumors (30% to 40%),[25] and one study observed that orchiopexy decreases the incidence of seminoma.[26] The early identification of these children is important, because a recent report noted a 2-year-old boy with a large yolk sac tumor in an intraabdominal testis with lymph node involvement.[27] Surgery and chemotherapy yielded a successful outcome.

Risk-Based Therapy

The survival of patients with advanced-stage germ cell tumors was poor prior to the introduction of modern chemotherapy, with most survivors having had low-stage surgically excised tumors. Surgery and chemotherapy consisting of vincristine, actinomycin, cyclophosphamide, and doxorubicin was the primary therapy in the 1960s and 1970s.[28] In 1975, Samuels and colleagues[29] introduced bleomycin with vinblastine for advanced-stage testicular tumors, and in 1977, Einhorn and Donohue[3] reported success with cisplatin, vinblastine, and bleomycin in disseminated testicular cancer. This therapy dramatically transformed the treatment of germ cell tumors. Even after the introduction of cisplatin-based regimens, the early results in children were poor. A report from the Children's Cancer Group (CCG) of children treated between 1978 and 1984, using cisplatin and bleomycin alternating with other agents (cyclophosphamide, dactinomycin, and doxorubicin), reported 4-year survival and event-free survival (EFS) of 54% and 49%, respectively, with ovarian tumors higher at 67% and 63%, respectively, and extragonadal tumors at 48% and 42%, respectively.[30] The lower survival in the early study may have been due to the inclusion of less effective chemotherapy that lengthened the intervals between the courses of the more effective cisplatin and bleomycin.

The subsequent CCG/Pediatric Oncology Group (POG) intergroup studies conducted between 1990 and 1996 used

testes and 88.9% for stage III-IV gonadal and stage I-IV extragonadal.[31–33] The higher-risk group (stage III-IV gonadal and stage I-IV extragonadal) were stratified to either standard or high-dose cisplatin, and the overall survival was not different between the groups, but the toxicity was higher with the high-dose cisplatin, and it has therefore not been incorporated in the current study.

Based on these past studies, the current COG protocol for malignant germ cell tumors is risk based (Fig. 37-2). The overall goal is to maintain the excellent survival from the past intergroup study while decreasing the toxicity of the chemotherapy. Mature teratoma is considered to be a benign lesion, and these tumors are not entered on the current protocol. Immature teratomas at all sites are treated with surgery and observation. The 3-year survival for immature teratomas on the last study was 93% among 73 patients with immature teratoma, and four of the five recurrences were salvaged with platinum-based chemotherapy.[13,34] Stage I ovarian and testes tumors are treated with surgery and observation, although this portion of the protocol is currently suspended (see Ovary section). Stage II-III ovary and stage II-IV testes currently receive three cycles of PEB administered during 3 days compared with four cycles during 5 days on the prior study, thus resulting in significantly less total chemotherapy. Higher-risk tumors (stage IV ovary and stage III-IV extragonadal), are currently not a part of a protocol but would received PEB.

Low risk	
Stage 1 ovary	
Stage 1 testes	Surgery alone
Immature teratoma	COG, AGCT 0132
Intermediate risk	
Stage II–III ovary	
Stage II–IV testes	Surgery and Chemo-PEB x 3
Stage I–II extragonadal	COG, AGCT 132
High risk	
Stage III–IV extragonadal	Surgery and
Stage IV ovary	PEB

FIGURE 37-2 Low- and intermediate-risk–based scheme for pediatric germ cell tumors. Children's Oncology Group AGCT 0132, opened November 2003.

Testes

CLINICAL PRESENTATION AND INITIAL EVALUATION

Testicular germ cell tumors in children are one of the rarer germ cell tumor types, with an incidence of 0.5 to 2.0 per 100,000.[35] The bimodal age distribution of testes tumors, with a small peak in the first 3 years of life and a much larger peak in young adults, suggests a difference in the tumors of these age groups. The malignant germ cell tumors in the younger group are predominantly yolk sac tumors, whereas most adolescent and adult testes tumors are seminomas and mixed tumors. Several other factors provide evidence of differences between pediatric and adult testes tumors. Intratubular germ cell neoplasia (ITGCN), which is a carcinoma in situ, is commonly identified in adults with malignant germ cell tumors but does not occur in association with prepubertal yolk sac tumor. Adult testes tumors usually have a chromosomal gain of the short arm of chromosome 12p (isochromosome 12p), whereas this is not seen in prepubertal yolk sac tumors.

Testicular tumors are rare in boys prior to puberty, and during this time non–germ cell Sertoli tumors and paratesticular rhabdomyosarcomas are more common, whereas germ cell tumors predominate in pubertal and adult males. Paratesticular neuroblastoma has also been reported arising from an embryonic adrenal rest along the spermatic cord.[36,37] Although it is difficult to determine the incidence of malignancy in prepubertal testes tumors, several reports would suggest that it is less common than in adults. In one large series,[38] 74% of all tumors were benign, with teratoma accounting for 48% and yolk sac tumors only 5%. This has affected the initial sur-

Most testicular tumors present as a painless scrotal mass. In the intergroup CCG/POG study (1990 to 1996)[31] of malignant testes tumors, 76% of the stage 1 boys presented with a testicular mass and 17% with generalized scrotal swelling. The preoperative diagnosis was tumor in 79%, hydrocele in 11%, hernia in 3%, and acute scrotum or torsion in 3%.

Preoperative workup includes a thorough physical examination, looking for signs of androgenization as well as metastatic disease. Metastatic disease is relatively uncommon in prepubertal testes cancer, but if present, is usually in the retroperitoneum or chest. Testicular ultrasonography is useful to identify extratesticular lesions and may be useful to identify or raise the suspicion of a teratoma. Benign testes tumors tend to be well circumscribed with sharp borders and decreased blood flow on Doppler studies.[39] Preoperative AFP levels should be obtained, and this level was elevated in 98% of the children with malignant tumors in the most recent study.[31] If the preoperative diagnosis is a testicular malignancy (elevated AFP), it is reasonable to obtain an abdominal computed tomography (CT) scan, because the presence of enlarged nodes after an inguinal exploration can be due to either a reactive or malignant process.

OPERATIVE MANAGEMENT

The standard approach consists of an inguinal incision, with initial control of the vessels at the level of the internal inguinal ring with subsequent mobilization of the testes. A preoperative elevation of AFP indicates the presence of yolk sac tumor and thus precludes consideration of testes-sparing surgery, and a radical orchiectomy is performed with ligation of the cord at the internal ring. If the AFP is normal, there is a much greater chance that the mass represents a benign lesion, and in these instances, the field can be draped off and the tunica opened. Enucleation is often possible, leaving a large amount of residual normal testes.[40] If frozen section analysis reveals a benign lesion, the tunica is closed, and if malignant, an orchiectomy is completed. Unfortunately, this is not always possible, and in a recent review from the U.K. Children's Cancer Group, 48 of 53 boys with mature or immature teratoma

Stage	Extent of disease
I	Limited to testis (testes), completely resected by high inguinal orchiectomy; no clinical, radiographic or histologic evidence of disease beyond the testes.
II	Transscrotal biopsy; microscopic disease in scrotum or high in spermatic cord (<5 cm from proximal end). Tumor markers fail to normalize or decrease with an appropriate half-life.
III	Retroperitoneal lymph node involvement, but no visceral or extraabdominal involvement. Lymph nodes > 4 cm by CT; or > 2 cm and < 4 cm with biopsy proof.
IV	Distant metastases, including liver.

FIGURE 37-3 Current Children's Oncology Group staging system for childhood testes cancer.

has been reported for testes teratoma.[42] A more recent report noted no atrophy or recurrence with enucleation in a large group of benign testes tumors.[43]

POSTSURGICAL TREATMENT

Testicular teratomas are benign lesions and are treated with enucleation, if possible, and then postoperative observation. Testicular immature teratomas are also benign germ cell tumors, and surgery alone (enucleation if possible) is definitive treatment. Higher-grade immature teratomas are, however, associated with yolk sac tumors. In a (CCG/POG) review, grade 1 and 2 immature teratomas were not associated with yolk sac tumors, whereas 2 of 3 grade 3 lesions were associated with yolk sac tumors.[13]

Yolk sac tumor is the primary malignant prepubertal testes cancer. The current staging is noted in Fig. 37-3. The role of surgery alone for stage I testes tumors was reported in the 1980s[44] and confirmed in an initial small series.[45] The U.K. Children's Cancer Study Group[46] and the Testicular Tumor Registry of the Section of Urology of the American Academy of Pediatrics,[47] in larger series (73 and 181 children, respectively), confirmed the safety of surgery alone for stage I malignant testes tumors.

The intergroup trial of testes cancer (CCG/POG; 1990–1996)[31] confirmed the excellent outcome with stage 1 testes tumors treated with surgery alone (Table 37-1). This study of 63 boys (median age 16 months) reported AFP elevation in 98%. In patients with the preoperative diagnosis of tumor, the surgical guidelines were followed in 84% of boys but were followed in only 27% with a nontumor diagnosis. Although overall adherence to surgical guidelines did not affect outcome, scrotal violation was associated with a 75% recurrence rate compared with 15.5% in those without scrotal violation. All recurrences were successfully treated with surgery and chemotherapy.

Stage 2 boys on the CCG/POG study included only 17 patients, and 11 were stage II because of a transcrotal procedure.[32] Survival was excellent (see Table 37-1) with surgery and chemotherapy. Higher-stage 3 and 4 boys received surgery and were then randomized to standard or high-dose cisplatin, both with etoposide and bleomycin.[33] Sixteen were recurrences from stage 1 disease (median age 3.1 years), and the

TABLE 37-1
Survival for Testes Cancer, POG/CCG 9048/8891; 9049/8882, 1990-1996

Stage	N	*Treatment*	*6-Year EFS (%)*	*6-Year Survival (%)*
I	63 S	78.5	100	
II	17	S + PEB × 4	100	100
III	17	S + HDP/EB vs. PEB	94.1	100
IV	43	S + HDP/EB vs. PEB	88.3	90.6

CCG, Children's Cancer Group; EB, etoposide and bleomycin chemotherapy; EFS, event-free survival; HDP, high-dose platinum chemotherapy; PEB, platinum, etoposide, and bleomycin chemotherapy; POG, Pediatric Oncology Group; S, surgery.

excellent (see Table 37-1). The toxicity with high-dose cisplatin was significant without added benefit, and it has therefore been eliminated from current protocols.

The current protocol of the Children's Oncology Group is designed to reduce the total dose and days of chemotherapy (Fig. 37-2). As noted in the staging, if the retroperitoneal nodes are greater than 4 cm in size, it is assumed to be due to tumor, whereas nodes between 2 and 4 cm require biopsy to confirm status. There is no role for retroperitoneal lymph node dissection in prepubertal yolk sac tumors at diagnosis and simple biopsy is adequate.

Ovary

CLINICAL PRESENTATION AND EVALUATION

Ovarian tumors are the most common site for germ cell tumors in children and adolescents. Eighty to 90% percent of all ovarian masses are benign (epithelial cyst, mature teratoma), often with predominant cystic components.[10,48] Presenting symptoms often include pain and gradual onset of lower abdominal fullness. Approximately 10% present with an acute abdomen secondary to torsion or tumor rupture.[10] Of all girls presenting with ovarian torsion, only 1.8% to 3% are malignant tumors; however, 33% are benign tumors, including teratoma and cystadenoma.[48]

In nonacute cases, preoperative evaluation should include assessment of AFP and beta-HCG, as well as ultrasonography and usually abdominal and pelvic CT scan. Unfortunately, reliable tumor markers are absent in many tumors. Germinoma is present in one third of malignant tumors, and they have normal markers or mild elevation of beta-HCG, and embryonal carcinomas have normal markers.[2] Benign lesions are primarily cystic, and a 2% risk of malignancy in cystic lesions is frequently quoted based on adult series.[49–51] This, however, is also unreliable, because in the recent intergroup study from the Children's Oncology Group (COG), 57% of malignant tumors had cystic components.[10] A recent study attempting to identify risk factors noted that markers were elevated in only 54% of malignant tumors. The best predictors were a mass with solid characteristics and a mass greater than 8 cm in diameter.[52] They also noted as, in other series, that girls between 1 and 8 years have the greatest incidence of malignancy. In view of these observations, great care should be

1. Collect ascites or peritoneal washings for cytology
2. Examine peritoneal surface and liver; excise suspicious lesions
3. Unilateral oophorectomy
4. Examine contralateral ovary and biopsy if suspicious lesion
5. Examine omentum and remove if adherent or involved
6. Inspection of retroperitoneal lymph nodes, biopsy of enlarged nodes

FIGURE 37-4 Operative procedure for malignant ovarian germ cell tumor.

Stage I: Limited to ovary (ovaries) peritoneal washings negative; tumor markers normal after appropriate half-life decline (AFP 5 days, HCG 16 hours).

Stage II: Microscopic residual; peritoneal washings negative for malignant cells, tumor markers positive or negative.

Stage III: Lymph node involvement; gross residual or biopsy only; contiguous visceral involvement (omentum, intestine, bladder); peritoneal washings positive for malignant cells; tumor markers positive or negative.

Stage IV: Distant metastases, including liver.

FIGURE 37-5 Children's Oncology Group ovarian staging system. AFP, alpha fetoprotein; HCG, human chorionic gonadotropin.

The staging procedure endorsed by COG is listed in Figure 37-4 and the current staging system in Figure 37-5. The importance of an accurate and complete staging procedure and accurate pathologic evaluation cannot be overemphasized. The recent COG intergroup study of 131 girls reported positive ascites/peritoneal fluid in 23 of 100 girls, and 5 of these would have otherwise been stage I tumors.[10] This is particularly relevant, because the current low- and intermediate-risk COG study manages stage I girls with surgery alone.

The survival rates of children in the most recent intergroup study is listed in Table 37-2. The current therapy for ovarian malignant tumors is noted in Figure 37-2. In the most recent study,[33] the results for stage IV ovarian tumors did not allow them to be included in the current low- and intermediate-risk COG study (AGCT 0132) using reduced chemotherapy.

Some tumors are noted with invasion into surrounding structures, and in these cases, recommendations are for initial biopsy, neoadjuvant chemotherapy, and delayed resection. Bilateral ovarian tumors were observed in 8% of girls on the recent study, and 4 of the 11 contralateral tumors were benign teratomas. The current recommendation for bilateral tumors is to attempt ovarian preservation, if possible, on the least involved side, attempting to find a plane of demarcation between the tumor and normal ovarian tissue. The larger tumor should be removed and sent for frozen section. If the first side is malignant and the contralateral side is greater than 10 cm, it should also be removed.

The treatment algorithm for malignant ovarian tumors is surgery and observation for stage I and surgery and chemotherapy for higher-stage tumors (see Fig. 37-2). The surgery-only arm was based on a German and French series of a total of 39 girls with stage I tumors treated with surgery alone who experience a 67% EFS with salvage of 12 of 13 recurrences with chemotherapy for an overall survival of 97.4%.[53,54] The CCG/POG intergroup study noted excellent results in girls with stage I immature teratoma, with microscopic yolk sac tumor

TABLE 37-2
Event-free Survival (EFS) and Survival in Pediatric Ovarian Germ Cell Tumors, POG/COG Intergroup Study 1990-1996

Stage	N	*Treatment*	*6-Year EFS (%)*	*6-Year Survival (%)*
I	41	S + PEB	95	95.1
II	16	S + PEB	87.5	93.8
III	58	S + HDP/EB vs. PEB	96.6	97.3
IV	16	S + HDP/EB vs. PEB	86.7	93.3

CCG, Children's Cancer Group; EB, etoposide and bleomycin chemotherapy; HDP, high-dose cisplatin chemotherapy; PEB, cisplatin, etoposide, and bleomycin chemotherapy; POG, Pediatric Oncology Group; S, surgery.

treated with surgery alone as well as stage I girls treated with surgery and PEB.[55] The current low-risk arm of the study has been closed because of a higher than expected recurrence rate in stage I ovarian tumors. These girls had a less than 70% three-year EFS, thus leading to suspension of the trial; however, with salvage chemotherapy, they have an overall survival of over 95%.[56]

Laparoscopy has been widely used for ovarian cystic disease, and the application of this for malignant procedures has been controversial. The primary concern is adequate completion of the staging procedure (potential understaging) and avoidance of intraperitoneal spill or tumor rupture, which could upstage a stage I to a stage II tumor. The COG germ cell committee and others[10,57] recommend laparotomy for known malignancy; however, this is difficult to determine preoperatively, although preoperative elevated markers and a large solid mass are very suggestive of malignancy. A recent French study suggested that size greater than 7.5 cm or predominately solid components predicted malignancy and thus required laparotomy.[57]

Most primarily cystic lesions, some of which are large, are benign, and a laparoscopic approach is appropriate. One option to avoid spill is to either excise the cyst, as a cystectomy or oophorectomy, and then place it in a retrieval bag, which is then delivered out of the umbilical opening, allowing decompression of the cyst while in the bag without spill and then removal of the bag and cyst. A second option is to glue a bag to the cyst through a small laparotomy, using one of the adhesives, such as cyanoacrylate, as described by Shozu and colleagues.[58] The cyst is incised by cutting through the center of the bag–cyst interface, allowing removal of the fluid without spill, and the decompressed cyst is then delivered from the abdominal cavity. The cyst can then be separated from the normal ovary as a cystectomy, or if not possible or if there is concern for malignancy, an oophorectomy.

Sacrococcygeal Tumors

CLINICAL PRESENTATION AND INITIAL EVALUATION

Tumors of the sacrococcygeal region, referred to as sacrococcygeal teratomas (SCTs) in most reports, generally present in two distinct fashions: neonates with large predominantly external lesions, which are detected in utero or at birth and are rarely malignant (Fig. 37-6); and older infants and children

who present with primarily hidden pelvic tumors with a much higher rate of malignancy (Fig. 37-7). Sacrococcygeal teratomas are the most common extragonadal tumor in neonates, accounting for up to 70% of all teratomas in childhood. A 3 to 4:1 female to male ratio is generally reported.[59] Newborns typically present with a mass protruding from the sacral region, and many are detected with prenatal ultrasonography. Abdominal delivery should be considered if the external mass is greater than 5 cm, to avoid dystocia and rupture.[60] In-utero shunting can lead to fetal hydrops, which is associated with high mortality. Adzick and colleagues[61] performed the first successful fetal resection in a fetus that developed placentomegaly and polyhydramnios and, at 25 weeks, underwent fetal resection of a 400-g immature teratoma. After delivery at 29 weeks, the child underwent exploration, with no residual tumor identified.

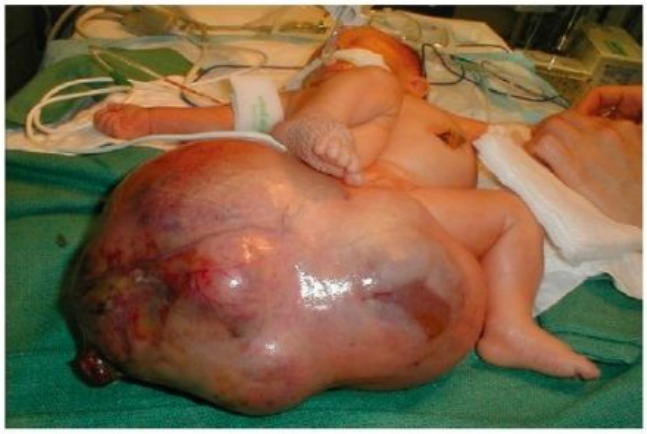

FIGURE 37-6 A newborn with a large ruptured sacrococcygeal teratoma.

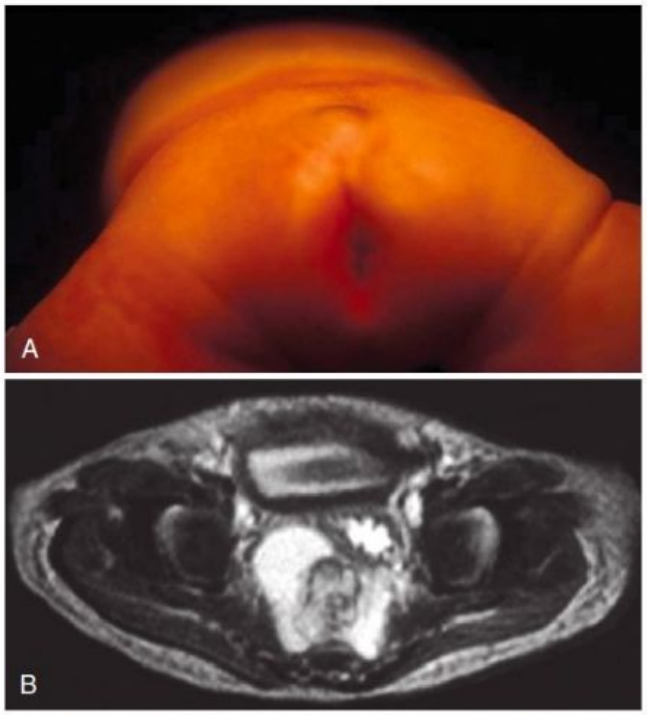

FIGURE 37-7 **A,** Three-month-old boy with a small external mass noted since birth. **B,** Underlying presacral mass noted on magnetic resonance imaging.

Makin and colleagues[62] reported a 77% survival among 41 antenatally diagnosed SCTs but noted survival of 50% in those undergoing fetal interventions and survival of only 14% if the intervention was for hydrops. Intervention included nonresection procedures, such as cyst drainage, laser ablation, or alcohol sclerosis. Another study of prenatally detected lesions noted the highest survival (100%) in lesions less than 10 cm with predominantly cystic tumors, whereas survival was only 48% in tumors greater than 10 cm and in those with increased vascularity, vascular steal syndrome, or rapid growth.[63] This is a difficult group, and the University of California San Francisco experience with fetal resection noted a survival of 20%.[64]

Older infants and children typically present with symptoms related to compression of the bladder or rectum. If a mass has been noted at birth and left in place, an increased rate of malignancy has been noted.[65] AFP levels, which can be normally elevated in newborns, should be obtained and then followed to ensure that they return to normal by 9 months of age. An association of the triad of presacral teratoma, anal stenosis, and sacral defects was first reported by Ashcraft and Holder, who also confirmed the autosomal dominant nature of the condition.[66] Currarino proposed that adhesions between the endoderm and ectoderm form, causing a split notochord that results in this association, and the triad now bears his name.[67]

CLASSIFICATION AND ASSOCIATION WITH MALIGNANCY

Altman and colleagues[68] developed the classification system of SCTs based on a survey of the Surgical Section of the American Academy of Pediatrics (Fig. 37-8). In this study, the malignancy rate increased with the more hidden (type III and IV) lesions. This survey also noted the low rate of malignancy in neonates and young infants (≤2 months of age, 7% girls and 10% boys have malignant tumors) and the higher rates in older infants and children (≥2 months of age, 48% girls and 67% boys have malignant tumors). Several subsequent studies have confirmed this and noted malignancy rates as high as 90%.[65,69]

SURGICAL MANAGEMENT

In neonates presenting with large external masses, the degree of pelvic and abdominal involvement should be assessed preoperatively with either ultrasonography, CT, or magnetic resonance imaging (MRI), and these studies may also offer a clue as to the characteristics of the vascular supply. An open or laparoscopic abdominal exploration may be required to mobilize the pelvic portion and to divide the middle sacral artery.

The neonatal type I and II lesions can usually be approached with the child in the prone position (Fig. 37-9). Removal of the coccyx is an essential step, because Gross and colleagues[70] reported a 37% recurrence rate if it was not removed. In view of the anterior displacement caused by the large mass, the rectum is often brought back to a more posterior location at the time of closure. Fishman and colleagues[71] described a buttocks contouring closure bringing

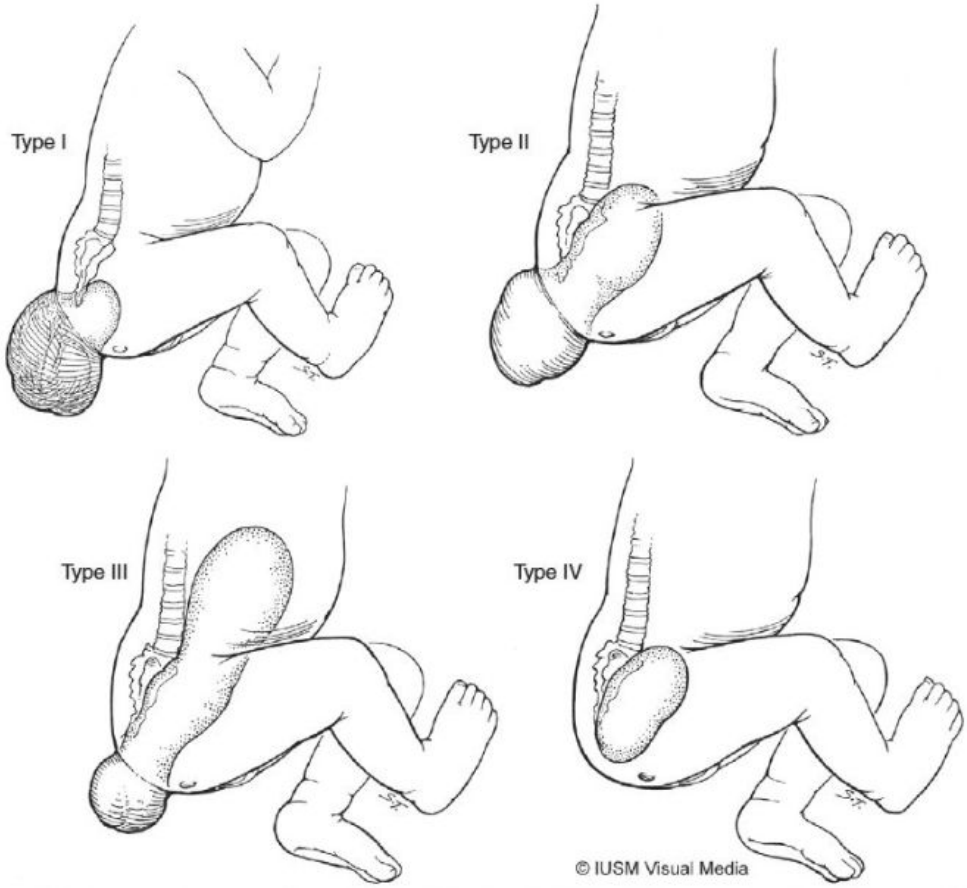

FIGURE 37-8 Classification of sacrococcygeal teratomas based on Altman's study: Type I (46.7% of reported cases) predominantly external, type II (34.7%) external with intrapelvic extension, type III (8.8%) visible externally but predominantly pelvic and abdominal, type IV (9.8%) entirely presacral. (Adapted from Altman RP, Randolph JG, Lilly JR: Sacrococcygeal teratoma: American Academy of Pediatric Surgical Section Survey—1973. J Pediatr Surg 1974;9:389-398.)

the ventral portion of the lateral flaps to a more central posterior location, thus resulting in a transverse posterior incision and two vertical incisions in the midportion of each buttock. The operative approach in older infants and children is similar; however, due to the presence of malignancy in many of these cases with invasion of adjacent structures or massive size, initial resection is not possible, and an initial biopsy followed by neoadjuvant chemotherapy is the best mode of management (Fig. 37-10). In the CCG/POG Intergroup study, there was no survival difference between initial and delayed rejections, supporting surgical delay in these cases.[72]

POSTOPERATIVE MANAGEMENT

The staging system for extragonadal tumors is noted in Figure 37-11. Most neonatal tumors are mature or immature teratomas that can be managed by surgery and postoperative observation. Recurrent tumors are noted in 10% to 20% of initially benign tumors, and 50% of these are malignant recurrences.[65,73] The recurrence may be due to a sampling error of the original tumor, incomplete resection of a malignant focus, or transformation of a small benign remnant into a malignant lesion. The large size of the neonatal tumors and frequent cystic components can often result in rupture during resection. Follow-up of these neonates should include serial AFP levels to ensure return to normal by 9 months of age and rectal examination every 3 months until 3 years of age, because the latest reported recurrence has been at 33 months.[65]

The management of the older infants with malignant tumors has been influenced by the chemosensitive nature of these yolk sac tumors. In the intergroup study of 74 infants and children (median age 21 months; 62 girls, 12 boys), 59% had metastatic disease at diagnosis, and the initial procedure was biopsy in 45 patients and resection in 29 patients.[72] All patients received chemotherapy, and postchemotherapy resection was accomplished in all but three patients. Definitive resection required a sacral approach in 63% and a combined abdominal-sacral approach in 35%. The 4-year EFS and survival was 84 ± 6% and 90 ± 4%, respectively, with no significant difference noted between timing of resection or presence of metastatic disease. In view of these results, it is strongly recommended to avoid resection of normal structures at initial exploration.

Long-term follow-up of the newborns and older children is necessary, because neuropathic bladder or bowel abnormalities have been reported in 35% to 41% of survivors.[74,75] A recent report from the U.K. Children's Cancer Group noted that 10 of 95 survivors of sacrococcygeal tumors had a neuropathic bladder, and two had leg weakness.[41] In a large survey of

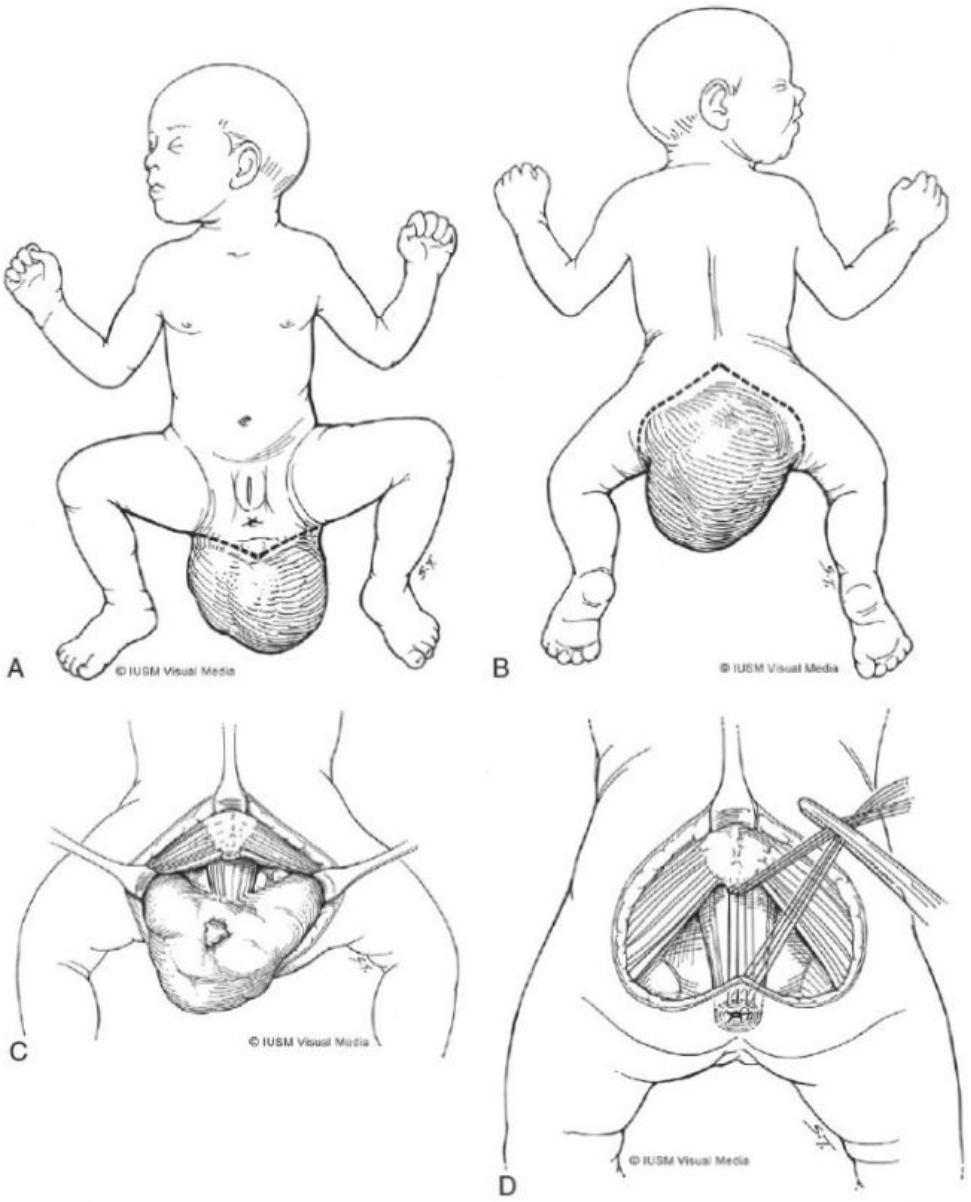

FIGURE 37-9 **A** and **B,** Operative excision of sacrococcygeal teratoma in a neonate with an inverted-V incision. **C** and **D,** The tumor along with the coccyx is excised with careful preservation of the rectum.

79 patients from the Netherlands, 9.2% reported involuntary bowel movements, 13.2% suffered from soiling, 16% had constipation, and 30% reported difficulty with urinary control,[76] with all of these correlating with decline in their quality of life. Interestingly, the Altman classification of the tumor did not correlate with the occurrence of these long-term complications.

Mediastinal Germ Cell Tumors

Mediastinal tumors are relatively common in childhood and adolescence and are more common in boys than girls. Germ cell tumors compromise approximately 6% to 18% of mediastinal tumors,[77] and of these, 86% are benign.[78] Mediastinal germ cell tumors are typically located in the anterior mediastinum. Younger children present predominantly with respiratory symptoms. The most common symptoms during adolescence include chest pain, precocious puberty, or facial fullness related to superior vena caval obstruction. Klinefelter's syndrome is also observed in the adolescent group as are hematologic malignancies. The histology of the malignant mediastinal germ cell tumors is more heterogeneous than other sites. In the intergroup study of 38 children, yolk sac was seen in boys less than 5 years of age and in all girls; the older boys had mixed malignant tumors in greater than 50%.[9] Reflective of this, the AFP was elevated in 29 cases and beta-HCG in 16 cases.

Anterior mediastinal tumors pose significant anesthetic risks because of airway compression and may affect the anesthetic from compression as well as the weight of the tumor