CHAPTER 103
TERATOMAS

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Introduction

The term teratoma, derived from the Greek *teraton* meaning "a monster", was coined by Virchow in 1869 for a tumour originating in the sacrococcygeal region. Teratomas are composed of multiple tissues foreign to the organ or site in which they arise. Although teratomas are sometimes defined as having the three embryonic layers (endoderm, mesoderm, and ectoderm), recent classifications also include monodermal types.

The term germ cell tumour (GCT) is also frequently used to describe these tumours, although this term encomprises a larger group including the mature and the immature teratomas, germinomas, embryonal carcinomas, yolk sac tumours, and choriocarcinomas. The germ cell tumours may arise in the gonads or in extragonadal sites, including the brain, face, neck, mediastinum, retroperitoneum, and sacrococcygeal region.

Aetiology

Three theories are postulated for the aetiology of teratomas. The first theory supports the origin from the totipotent primordial germ cells. These cells develop among the endodermal cells of the yolk sac near the origin of the allantois and migrate to the gonadal ridges during weeks 4 and 5 of gestation. Some cells may miss their target destination and give rise to a teratoma anywhere from the brain to the coccygeal area, usually in the midline. The second theory has teratomas arising from remnants of the primitive node. During week 3 of gestational development, midline cells at the caudal end of the embryo divide rapidly, giving rise to all three germ layers of the embryo. By the end of week 3, the primitive streak shortens and disappears. This theory would explain the more common occurrence of teratomas in the sacrococcygeal region. The third theory has teratomas as an incomplete twinning.

Classification

Teratomas are anatomically classified as gonadal (testis or ovary) or extragonadal (brain, face, neck, mediastinum, retroperitoneum, and sacrococcygeal region). Histologically, teratomas are classified as mature or immature on the basis of the presence of the immature neuroectodermal elements within the tumour. Mature teratomas comprise only mature elements, such as the skin, hair, fat tissue, cartilage, bone, and glands. Immature teratomas contain immature elements, such as neuroepithelial tissue and immature mesenchyme. The presence of microscopic foci of the yolk sac tumour, rather than the histological grade of immaturity, is a valid predictor of recurrence. The grading of immature teratomas is unnecessary in children because the management is not altered by the grade.

Teratomas may also contain or develop foci of malignancy; and a malignant germ cell tumour may be found in sites typical for teratomas, such as the mediastinum or sacrococcygeal area. Whether the lesion was malignant from the onset or the malignant cells destroyed and replaced the benign teratoma component is often difficult to differentiate. The most common malignant component within a teratoma is a yolk sac tumour. Malignancy at birth is uncommon, but increases with age and with incomplete resection. An apparently mature teratoma may recur several months or years after resection as a malignant yolk sac tumour, illustrating the difficulties in histologic sampling of large tumours and the need for close follow-up.

Tumour Markers

Alpha-fetoprotein (AFP) is a tumour marker secreted by most yolk sac tumours and some embryonal carcinomas. It can be measured in the serum and noted in cells by immunohistochemistry. This marker is particularly useful for assessing the presence of residual or recurrent disease. AFP levels are normally very high in neonates and decrease with time. The postoperative half-life is about 6 days. Persistently high levels may be an indication of the need for further surgical procedures or chemotherapy. Other markers that may be elevated are β-human chorionic gonadotropin (β-hCG), produced by choriocarcinomas, and, rarely, carcinoembryonic antigen. The lactate dehydrogenase (LDH) isomer of LDH-1 is present in many tumours with the histologic features of an endodermal sinus tumour, yolk sac tumour, dysgerminoma, and choriocarcinoma.

Genetics

The genetic basis for teratomas is not well understood, and the clinical usefulness of chromosome mapping for teratomas is unclear. Deletions on chromosomes 1 and 6 were reported in children but noted on chromosome 12 in adults. N-myc gene expression was noted in immature teratomas, but not in the mature group.

Associated Anomalies

Teratomas are mainly isolated lesions but may form part of the Currarino triad (anorectal malformation, sacral anomaly, and a presacral mass) as the presacral mass. Other associated anomalies reported are urogenital (hypospadias, vesicoureteral reflux, and vaginal or uterine duplications); congenital dislocation of the hip; central nervous system lesions (anencephaly, trigonocephaly, Dandy-Walker malformations, spina bifida, and myelomeningocele); Klinefelter syndrome (strongly associated with mediastinal teratoma); and the very rare associations with trisomy 13, trisomy 21, Morgagni hernia, congenital heart defects, Beckwith-Wiedemann syndrome, pterygium, cleft lip and palate; as well as such rare syndromes as the Proteus and Schinzel-Giedion syndromes.

Tumour Sites

Testicular Teratoma

Teratomas of the testes are the most common type of benign neoplasms, usually occurring in boys under 3 years of age. These tumours can be managed successfully with radical orchiectomy and do not require any adjunctive treatment. Small encapsulated cystic teratomas may also be enucleated much like their ovarian counterpart (see the next subsection); the cord should be occluded atraumatically until a frozen section confirms the benign nature of the lesion. However, for the purpose of treatment, all testicular tumours should be assumed malignant unless proven otherwise on histopathology.

The operation is performed through a groin incision.

1. The external inguinal ring is identified and the inguinal canal incised to identify the internal ring.

2. The cremasteric bundle is opened, the spermatic cord is carefully mobilised at the internal inguinal ring, and it is controlled by an occlusive vascular clamp. This prevents lymphatic and haematogenous spread of the tumour during manipulation.

3. The testis is delivered into the wound, and if the mass is solid, a radical orchiectomy is completed with ligation of the spermatic cord at the level of the internal ring.

4. If the malignant tumour was biopsied through the scrotum before referral, a hemiscrotectomy is generally performed, although recent evidence suggests that chemotherapy could adequately treat tumour seeding.

Ovarian Teratoma

Mature teratoma, a benign neoplasm, is the single most common ovarian tumour, representing approximately 40% of all ovarian tumours. It may be cystic, solid, or mixed with calcification (noted in 50% of cases on plain abdominal radiograph).Ten percent are bilateral.

Abdominal pain, the presence of a mass, and occasionally an acute abdomen as a result of torsion or rupture of the tumour are known clinical presentations. Some are discovered incidentally with imaging. Tumours that are predominantly cystic (dermoid cysts) may be safely excised, preserving a rim of normal ovarian tissue. Controversy exists about the safety of laparoscopic excision because rupture of the cyst often occurs, leading to potential peritoneal implantation of cells. Solid teratomas are more often immature, and the treatment of choice is salpingo-oophorectomy. Chemotherapy is reserved for tumours with a higher grade of immaturity. Serum AFP levels may be elevated preoperatively and should be monitored after operation. In such cases, careful sectioning of the specimen may reveal microscopic foci of a yolk sac tumour; this does not alter management as long as AFP levels return to normal.

Sacrococcygeal Teratoma

Sacrococcygeal teratoma is the most common congenital tumour, accounting for 35–60% of all teratomas. The estimated incidence is 1 per 35,000 to 40,000 live births, with a female-to-male ratio of 4:1. Altman et al. have classified these tumours into four types:

- Type I tumours are predominantly external with a minimal presacral component—this is the most common type.
- Type II tumours are external but have a significant intrapelvic component.
- Type III tumours are external but pelvic and extend significantly into the abdomen.
- Type IV tumours are entirely presacral.

Recently, an increasing number of sacrococcygeal teratomas have been detected by antenatal ultrasonography (US) examination of the fetus. Prenatal US is useful in making a differential diagnosis between sacrococcygeal teratoma, myelomeningocele, and other tumours. Antenatal US helps to establish tumour extension into the pelvis and the presence or absence of polyhydramnios, foetal hydrops, and intratumoural haemorrhage. Massive haemorrhage into the tumour may occur spontaneously in utero, resulting in anaemia and hypoproteinaemia followed by foetal hydrops.

In countries where prenatal US is not readily available, a sacrococcygeal teratoma is seen as a visible mass at birth, making the diagnosis obvious (Figure 103.1). Although many neonates with sacrococcygeal teratomas do not have symptoms, some require intensive care because of prematurity, high-output cardiac failure, disseminated intravascular coagulation, and tumour rupture or bleeding within the tumour. Lesions with a large intrapelvic component may cause urinary obstruction. Besides looking for signs of a myelomeningocele, the physical examination should always include a rectal examination to evaluate any intrapelvic component. The most useful imaging is a US scan looking for intrapelvic extension and meningomyelocoele. The diagnosis of purely intrapelvic teratomas is often delayed. Children have constipation, urinary retention, an abdominal mass, or symptoms of malignancy such as failure to thrive.

Age is a predictor of malignancy in sacrococcygeal teratomas. The risk of malignancy is <10% at birth but >75% after the age of 1 year for sacrococcygeal tumours (Figure 103.2), with the exception of familial presacral teratomas. The risk of malignancy also is high for incompletely excised lesions. Complete excision of the tumour with the coccyx should be carried out as soon as the neonate is stable enough to undergo the procedure. An abdominoperineal approach may be necessary for tumours with pelvic extension. Serum markers (AFP and β-hCG) should be determined before the operation for later comparison.

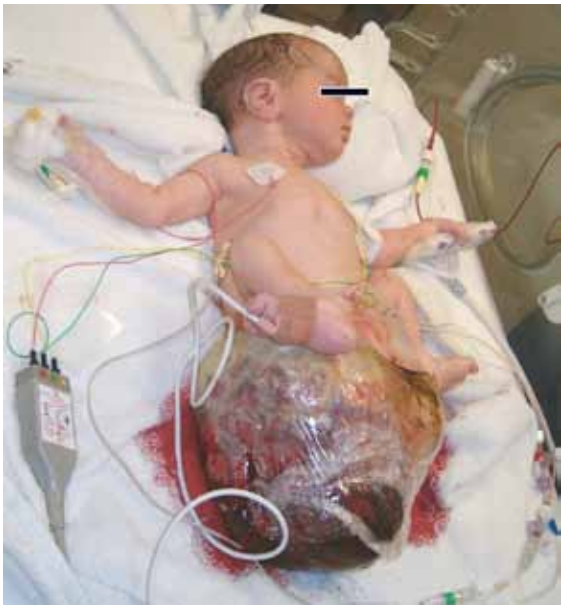

Figure 103.1: Giant ruptured sacrococcygeal teratoma.

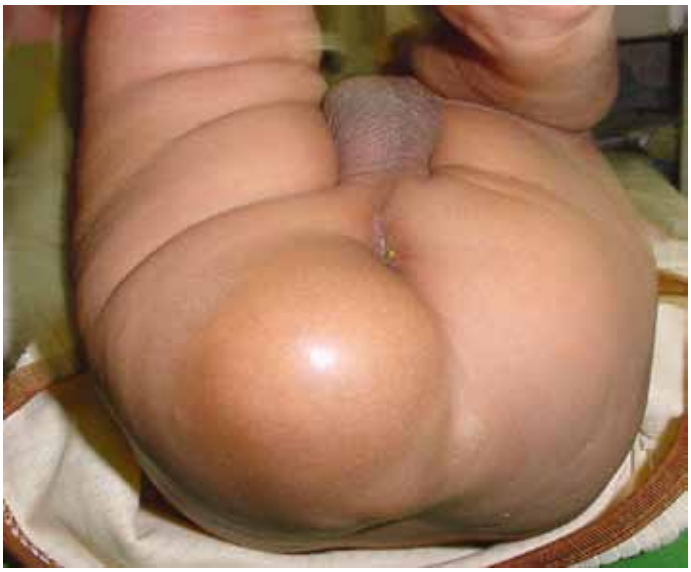

Figure 103.2: Malignant sacrococcygeal teratoma presenting at 3 months of age.

Postoperatively, it is important to monitor all patients with physical examination, including rectal examination and serum markers, every 2 or 3 months for at least 3 years, because most recurrences occur within 3 years of operation.

In older patients, treatment of malignant tumours involves excision, chemotherapy, and monitoring with imaging studies and serum markers. For unresectable tumours, biopsy and chemotherapy are followed by excision of the primary tumour after adequate reduction has been obtained. Radiation therapy is usually reserved for local recurrence of malignant tumours. Patients with malignant tumours should be enrolled in a paediatric cooperative study or treated according to their guidelines.

Poor prognosis is noted in prenatal hydrops, dystocia, tumour rupture, prematurity, highly vascular lesions, and lesions >10 cm. In the absence of severe prematurity and intrapartum complications, the prognosis is dependent on the presence of malignancy and is therefore related to age at operation, completeness of resection, tumour type, and tumour stage.

Functional results in survivors are excellent in most patients, with the exception of reports of faecal and urinary continence problems as well as lower limb weakness in some series.

Mediastinal Teratoma

The mediastinum is the second most frequent site of extragonadal teratomas. Mediastinal teratomas occur in newborns to adolescents, and arise predominantly in the anterior mediastinum, occasionally in the posterior mediastinum, and rarely in the pericardial and intracardiac region. Mediastinal teratomas typically manifest on computed tomography (CT) scans as a heterogeneous mass containing soft tissue, fluid, fat, or calcification. Some patients are asymptomatic, and diagnosis is made incidentally on chest x-ray. However, affected children usually manifest symptoms such as dyspnea, cough, or chest pain. When the tumour causes severe respiratory distress in neonates, mimicking congenital diaphragmatic hernia, emergency surgery to relieve lung compression and postoperative care supporting respiration are required. Surgical approaches to mediastinal teratomas are either lateral thoracotomy or median sternotomy; the latter is necessary in some patients with large, bilaterally invasive lesions. Small lesions have been resected by using video-assisted thoracic surgery (VATS). Large lesions may cause airway compromise and require intubation and care in the intensive care unit. Many of these large tumours are best managed with initial biopsy, neoadjuvant chemotherapy, and delayed complete resection.

Other sites for thoracic teratomas are intrapericardial, cardiac, and pulmonary.

Gastric Teratomas

Gastric teratomas (Figure 103.3) are rare tumours, accounting for less than 2% of abdominal teratomas and 1% of all teratomas. They occur mainly in neonatal boys and are almost always benign in nature with an excellent prognosis. The tumour is predominantly exogastric (67%). The endogastric type (33%) grows into the lumen of the stomach and erodes mucosa, causing gastric outlet obstruction, haematemesis, and melaena. The exogastric type is an exophytic mass in the lesser curvature or posterior wall of the stomach; the entire stomach may be involved. The exogastric variant may present with respiratory distress and abdominal distention. Diagnostic modalities include plain radiograph, US, CT scan, and serum markers. Plain radiograph may show a soft tissue mass with calcification in the upper abdomen. Surgical excision is curative. Recurrence and malignancy are rare, despite local infiltration or nodal metastasis. Periodic follow-up, including AFP measurements, is important.

Other rare sites of abdominal teratomas include liver, gallbladder, pancreas, kidney, intestine, bladder, prostate, uterus, mesentery, omentum, abdominal wall, and diaphragm.

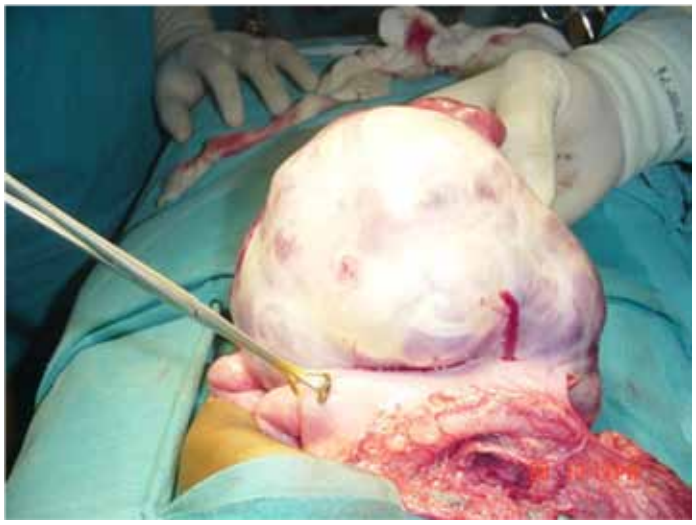

Figure 103.3: Gastric teratoma.

Retroperitoneal Teratomas

Retroperitoneal teratomas represent 5% of all childhood teratomas and occur outside the pelvis in the suprarenal location.The tumour presents as an abdominal mass with symptoms of vomiting and constipation. Diagnosis is made by imaging with calcification on plain radiograph, US, CT scan, and serum markers. Surgical excision is often easily performed, and malignancy is uncommon. The retroperitoneum site is the most common for the foetus in foetu malformations.

Intracranial Teratomas

Intracranial teratomas generally present with symptoms of space-occupying lesions. These lesions account for only 2–4% of all teratomas, but they represent nearly 50% of brain tumours in the first 2 months of life. Most are benign in neonates but malignant in older children and young adults. These teratomas can appear in utero and cause massive hydrocephalus. The pineal gland is the most common site of origin, but intracranial teratomas may be seen in different areas, such as the hypothalamus, ventricles, cavernous sinus, cerebellum, and suprasellar region.

Cervical Teratomas

Cervical teratomas represent up to 8% of all teratomas. Large tumours can be seen in utero with US. These tumours are initially seen as a partly or completely cystic neck mass, which may compromise the airway and require immediate intubation or tracheostomy. Extension of the tumour to the mediastinum or displacement of the trachea may cause pulmonary hypoplasia and increase respiratory morbidity and mortality. The tumour is usually well defined and may contain calcifications. The differential diagnosis includes cystic hygroma, congenital goiter, foregut duplication cyst, and branchial cleft cyst. Investigation should include plain radiographs, US, and measurement of AFP and β-hCG, as well as urinary catecholamine metabolites. CT and magnetic resonance imaging (MRI) may be useful to establish the diagnosis and to define the anatomic relations.

Craniofacial Teratomas

Craniofacial teratomas include a spectrum of lesions that may be life threatening. The spectrum includes epignathus (teratoma from palate), orbital, pharyngeal, oropharyngeal, and middle ear teratomas.

Miscellaneous Sites

Teratomas have been reported in other sites, such as the skin, parotid, vulva, perianal region well away from the coccyx, spinal canal, umbilical cord (possibly associated with omphalocele), and placenta.

Key Summary Points

1. Teratomas comprise multiple tissues foreign to the organ or site in which they arise.
2. Most teratomas are benign and have excellent surgical outcomes.
3. Sacrococcygeal teratoma is the most common neonatal tumour with a worst prognosis in delayed presentation and recurrence.
4. Serum tumour markers assist in the diagnosis of recurrent tumours.

References

Altman RP, Randolph JG, Lilly JR. Sacrococcygeal teratoma: American Academy of Pediatrics Surgical Section survey. J Pediatr Surg 1974; 9:389–398.

Azizkhan RG, Haase GM, Applebaum H, Dillon PW, Coran AG, King PA, King DR, Hodge DS. Diagnosis, management, and outcome of cervicofacial teratomas in neonates: a Children's Cancer Group study. J Pediatr Surg 1995; 30:312–316.

Basu S, Rubello D. PET imaging in the management of tumours of testis and ovary: current thinking and future directions. Minerva Endocrinol 2008; 33:229–256.

Bernbeck B, Schneider DT, Bernbeck B, Koch S, Teske C, Lentrodt J, Harms D, Göbel U, Calaminus G, on behalf of the MAKE Study Group. Germ cell tumours of the head and neck: report from the MAKEI Study Group. Pediatr Blood Cancer 2008; 52:223–226.

Certo M, Franca M, Gomes M, Machado R. Liver teratoma. Acta Gastroenterol Belg 2008; 71:275–279.

Chaganti RSK, Rodriguez E, Mathew S. Origin of adult male mediastinal germ-cell tumours. Lancet 1994; 343:1130–1132.

Chen Y, Xu H, Li Y, Li J, Wang D, Yuan J, Liang Z. Laparoscopic resection of presacral teratomas. J Minim Invasive Gynecol 2008; 15:649–651.

Gupta DK, Carachi R, eds. Pediatric Oncology—Surgical and Medical Aspects. Jaypee Brothers, 2007.

Gupta DK, Kataria R, Sharma MC. Prepubertal testicular teratomas. Eur J Pediatr Surg 1999; 9:173–176.

Gupta DK, Sharma S. Granulosa cell tumour of the ovary. In: Gupta DK, Carachi R, eds. Pediatric Oncology—Surgical and Medical Aspects. Jaypee Brothers, 2007, Chap 30, Pp 308–316.

Gupta DK, Sharma S, Carachi R. Neonatal tumours. In: Gupta DK, Carachi R, eds. Pediatric Oncology—Surgical and Medical Aspects. Jaypee Brothers, 2007. Chap 11, Pp 48–57.

Herman TE, Siegel MJ. Congenital gastric teratoma. J Perinatol 2008; 28:786–787.

Ikeda H, Tsuchida Y. Germ cell tumours. In: Gupta DK, Carachi R, eds. Pediatric Oncology—Surgical and Medical Aspects. Jaypee Brothers, 2007, Chap 27, Pp 271–286.

Ishiguro T, Tsuchida Y. Clinical significance of serum alpha-fetoprotein subfractionation in pediatric diseases. Acta Paediatr 1994; 83:709–713.

Kaplan GW, Cromie WC, Kelalis PP, Silber I, Tank ES. Prepubertal yolk sac testicular tumours: report of the Testicular Tumour Registry. J Urol 1988; 140:1109–1112.

Noudel R, Vinchon M, Dhellemmes P, Litré CF, Rousseaux P. Intracranial teratomas in children: the role and timing of surgical removal. J Neurosurg Pediatr 2008; 2:331–338.

Rintala R, Lahdenne P, Lindahl H, Siimes M, Heikinheimo M. Anorectal function in adults operated for a benign sacrococcygeal teratoma. J Pediatr Surg 1993; 28:1165–1167.

Shimizu K, Nakata M, Hirami Y, Akiyama T, Tanemoto K. Teratoma with malignant transformation in the anterior mediastinum. J Thorac Cardiovasc Surg 2008; 136:225–227.

Swamy R, Embleton N, Hale J. Sacrococcygeal teratoma over two decades: birth prevalence, prenatal diagnosis and clinical outcomes. Prenat Diagn 2008; 28:1048–1051.

Treiyer A, Blanc G, Stark E, Haben B, Treiyer E, Steffens J. Prepubertal testicular tumours: frequently overlooked. J Pediatr Urol 2007; 3:480–483.