Rare Tumors

28

Hugo A. Heij

Definition

When is a tumor called rare? From a practical point of view we will use the definition in this chapter that a tumor is considered "rare" if there is no treatment protocol available. One can derive a very long "list of rarities" from the pediatric pathology literature [1–3], which allows the following subdivided definitions:

1. Rare tumors independent of age.
2. Adult-type tumors in children[1].
3. Rare but typical childhood tumors.
4. Common pediatric tumors with rare histologic features.
5. Common pediatric tumors in rare locations.
6. Seemingly common but in fact rare tumors.
7. Rarely recognized occurrences of common tumors.

In view of the surgical character of this book it seems appropriate to discuss the rare tumors arranged according to their anatomical regions, with special emphasis on the abdominal cavity. The aim of this chapter is not to provide an exhaustive list of all rare tumors, but rather to focus on solid tumors that require surgical treatment. Where possible, guidelines for management will be derived from the available literature. To that purpose, literature searches have been performed in Medline (PubMed) using the type of tumor as MESH term, focusing on reviews. Also, cross references and hand searches of the literature have been done.

[1]Ethical issues may arise in families with a genetic predisposition for malignant tumor. Recently a discussion was published by the committee on bioethics of the American Academy of Pediatric on the pro's and con's of genetic testing of children for adult-type tumors, like familial adenomatous polyposis and breast cancer (Caga-anan et al., *Pediatric* 2012;129:163–7).

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IPSO Rare Tumor Registry

Ten years ago, a registry of rare tumors was instituted by the International Society for Pediatric Surgical Oncology (IPSO). The aims of this registry are to collect data and tissue for research, and to provide information and guidance on the management of patients with rare tumors.

The entries provide an impression (but nothing more exact than an impression) of the epidemiology. For the epidemiology and incidence: see also [2]. Table 28.1 provides an overview of the spectrum of tumors registered.

Benign (Pseudo)Tumors

These are essentially benign tumors and the reason to present them here is because of the confusion that may arise with malignant tumors (Laffan EE. Pediatric soft tissue tumors .., *Radiographics* 2009;e36)

Inflammatory Myofibroblastic Tumor

Inflammatory myofibroblastic tumor (IMT) was first described in the lung in 1937, and since then has been reported at various sites. Histopathologically, IMT is a benign solid tumor, mainly composed of spindle-shaped cells, and has a chronic inflammatory component [4]. Synonyms are: inflammatory pseudotumor, pseudosarcomatous myofibroblastic proliferation, plasma cell tumor, xanthomatous pseudotumor, fibroxanthoma, and histiocytoma [4, 5].

The presentation varies according to the location: respiratory symptoms and clubbing in pulmonary IMT; abdominal pain, fever, and weight loss in abdominal IMT [6].

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Table 28.1 Overview of the spectrum of tumors registered with IPSO

Tumor spectrum	
Adrenocortical carcinoma	30
Hamoudi (Frantz) tumor	11
Carcinoid	3
GIST	3
Pancreaticoblastoma	3
Aggressive fibromatosis	3
Pulmonary blastoma	2
Pheochromocytoma	2
Lipoblastoma	2
Chorioncarcinoma liver	2
Desmoplastic tumor abdomen	2
Single entries (n = 25)	
Transitional cell carcinoma	
Spindle epithelial tumor with thymus-like differentiation (SETTLE)	
Seminoma	
Renal cell carcinoma	
Mullerian papilloma	
Mucoepidermoid bronchial carcinoma	
Metanephric adenofibroma	
Mesenchymal hamartoma	
Malignant trophoblastic tumor placental site	
Malignant fibrohistiocytoma	
Malignant nonchromaffinic paraganglioma	
Inflamm. myofibroblastic tumor – pt known with neurofibromatosis	
Infantile fibromatosis	
Hemangiopericytoma (infantile type)	
Granulosa-Theca cell tumor	
Gonadoblastoma	
Follicular thyroid ca (lft)	
FNH (focal nodular hyperplasia)	
Embryonic pancreatic tumor	
Ductal adenocarcinoma of pancreas/hepatoblastoma (fetal type)	
Chondroblastoma	
Chemodectoma	
Angiomyolipoma (Tuberous sclerosis)	
Angiomatoid fibrous histiocytoma	
Adenocarcinoma colon	

With acknowledgement to Dr. D.C. Aronson

Large fibrous inflammatory pseudo-tumors may occur in the mesentery, duodenum, jejunum, pancreas, spleen, and liver [4, 5, 7–9].

Malignant transformation of IMT has been described in a 13-year old boy with NF-1 presenting with a pelvic tumor with liver metastases. Despite resection and chemotherapy, the tumor recurred (Ernst et al., *JBR BTR* 2011)

The most frequent finding is a palpable mass in the abdomen [4, 9–11]. Jaundice was the presenting sign in a 6-year-old boy with IMT in the hilum of the liver [7].

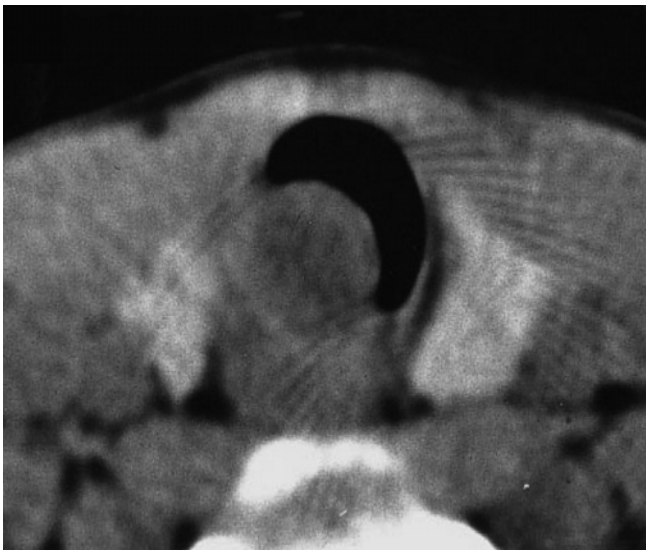

Fig. 28.1 I.M.T. of the trachea. Inflammatory pseudotumor of the trachea (From Bumber et al. [5])

Thoracic IMT has been reported in the heart [12], lung [4], mediastinum, and trachea [5]. A 14-year-old boy with IMT of the trachea underwent successful CO_2-laser excision [5] (Fig. 28.1). Successful diagnosis of IMT by fine needle aspiration cytology (FNAC) with ancillary studies towards ALK and actin expression has been reported (Stoll & Li). ALK expression may also be of prognostic significance as Fragoso et al. (ref) describe seven cases with ALK-negative IMT and a benign course.

The treatment of IMT is complete resection, which may require sacrifice of blood vessels and other vital structures [7, 13]. There are scarce data on recurrence rate, but the available evidence suggests it may be higher than 10 %. Tumors that have ill-defined margins and therefore cannot be resected completely have a higher risk of recurrence [8]. Although usually histologically benign, radiation and cytotoxics have been successfully used in unresectable and recurrent IMT. Corticosteroids have also been advocated under these circumstances [11]. Good response to adjuvant chemotherapy was reported for an unresectable IMT in a 10-year old boy with multiple abdominal tumors (Bertocchini, *JPS* 2011)

Xanthogranulomatous Pyelonephritis

Xanthogranulomatous pyelonephritis (XPN) is a rare destructive inflammatory process. This condition can be mistaken for a Wilms' tumor; however, the radiographic presence of infection and calculi often help to make a preoperative diagnosis of XPN. Treatment is nephrectomy and antibiotic coverage [14].

Juvenile Xanthogranuloma

Juvenile xanthogranuloma (JXG) is a member of the group of histiocytic proliferative disorders. JXG is a usually benign self-limiting disorder presenting as nodular skin lesions. It occurs mainly in the head and neck region and is present at birth in 5–17 % of the cases [15]. In the hand, JXG may arise from the tendon sheath and is called giant cell tumor of the tendon sheath [16].

Disseminated JXG in contrast may involve liver, lungs and CNS, and in young children has a poor prognosis. Various treatments, including surgical resection, have been attempted. Dölken et al. report a 7-month-old girl with life-threatening systemic JXG, including multiple CNS lesions, that responded well to chemotherapy according to the Langerhans cell histiocytosis protocol [17]. The association of JXG and mastocytosis was described recently in a 3-year old girl (Gruber et al., *Int J Dermatol*)

Langerhans' Cell Histiocytosis

Histiocytic and dendritic neoplasms in children are rare. They arise from antigen-processing phagocytes (histiocytes) and antigen-presenting dendritic cells, which are derived from the hemopoietic stem cells. The WHO classification distinguishes six entities, of which Langerhans' cell histiocytosis is the most common. Other types are: Langerhans' cell sarcoma and histiocytic sarcoma. These tumors have been described in the vertebral bodies, responding to irradiation, but later metastasizing to the lung [18]; but also as primary pulmonary cystic lesions with fatal outcome despite chemotherapy [19]; as facial swelling [20] (Fig. 28.2); and as cervical lymphadenopathy, with a favorable response to chemotherapy [21].

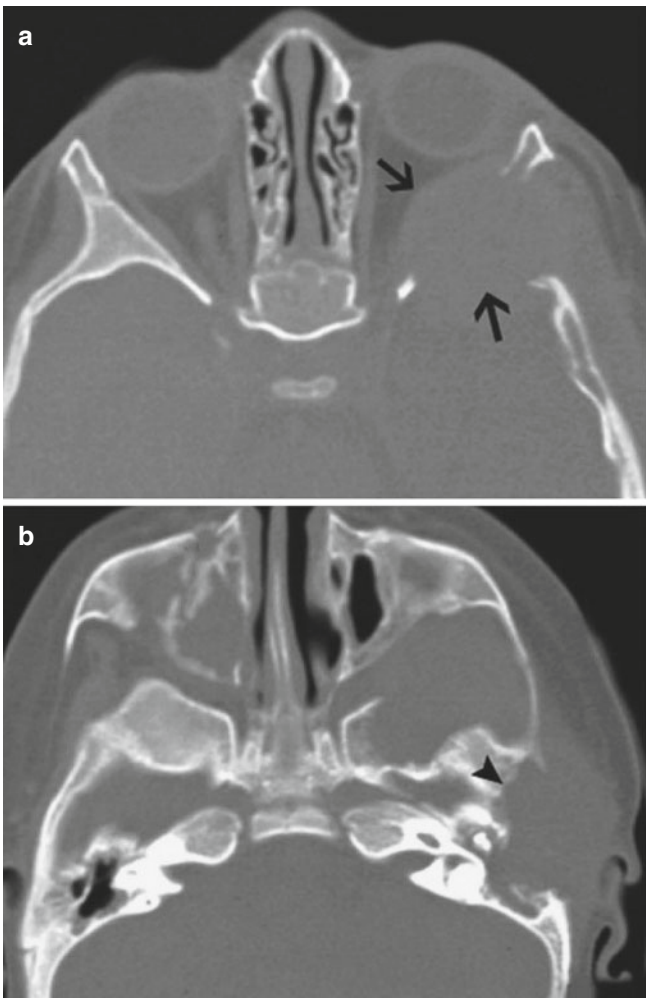

Fig. 28.2 Langerhans cell histiocystosis (**a**) CT scan shows a lytic lesion of the frontal and sphenoid bones (*arrows*) (**b**) CT scan shows destruction of the temporal bone (*arrowhead*)

Association of Malignancy and Langerhans' Cell Histocytosis

A case of simultaneous occurrence of malignant histocytosis and primary gonadal germ cell tumor was reported in an 18-year-old male by Margolin and Tarweek [22]. The testicular cancer was a stage 1 teratocarcinoma with endodermal sinus tumor elements with malignant histocytosis. The patient died despite treatment with chemotherapy.

Two case reports described the association of histocytosis and germ cell tumors. A 14-year-old boy developed fatal malignant histiocytosis of the spleen during cytotoxic treatment for mediastinal immature teratoma which had been excised 11 months before [23]. A 15-year-old boy presented with chest pain and was diagnosed with a mediastinal germ cell tumor and simultaneous histiocytioc sarcoma of the spleen [24]. Recently more report have been published on the association of LCH with nephroblastoma in a 2 years old girl (Narui, *PBC* 2009); neuroblastoma in a 5 year old boy (Rayburg, *PBC* 2009); Broncho- Alvaeolar Carcinoma in a 15-year old male with colonic polyposis (von der Thusen, *JCO* 2011)

Fibromatosis

Fibromatosis in children comprise a wide spectrum of conditions. A fibroblastic stem cell, called collagenoblast with many oncogenic potentials, has been postulated as the common origin of fibromatoses [25].

Infantile digital fibromatosis (Reye tumor) is a benign condition with a tendency to spontaneous regression. Calcifying aponeurotic fibroma is equally benign and requires conservative excision. In newborns, plantar nodules

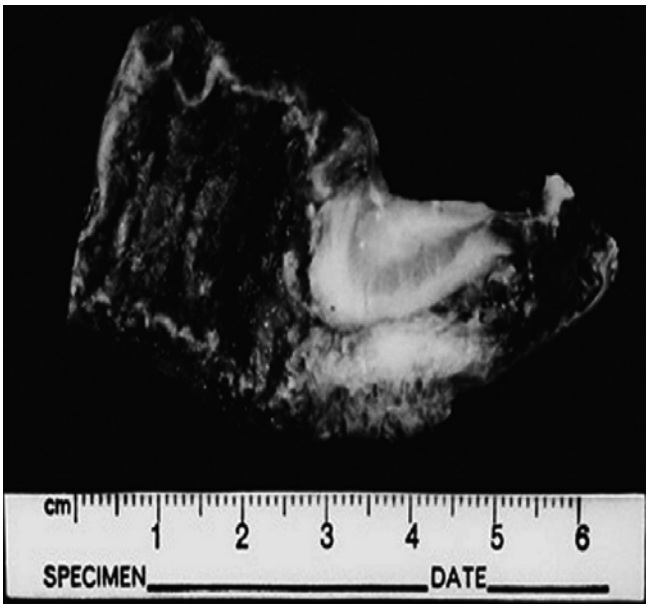

Fig. 28.3 Intestinal fibromatosis. Congenital solitary intestinal fibromatosis (With kind permission from Numanoglu et al. [28]). Review For an overview of the role of imaging, particularly MRI in fibromatosis (see Laffan et al. (2009))

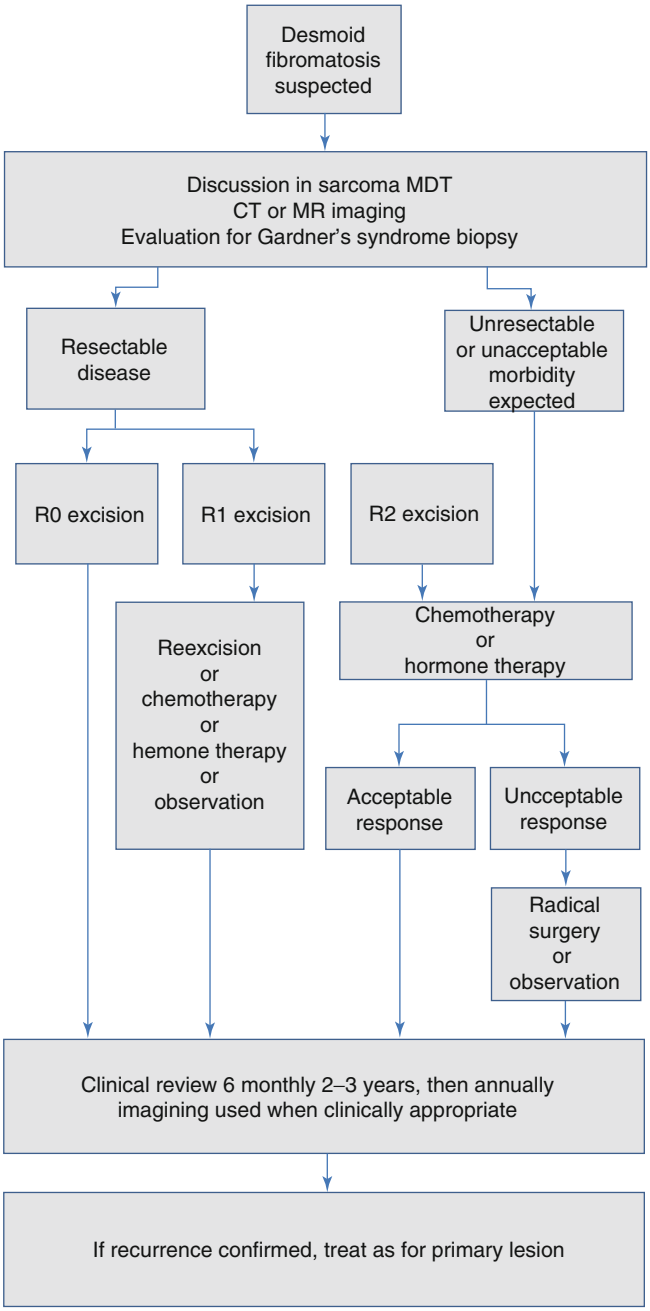

Fig. 28.4 Wilks et al. present a treatment algorithm for facial pediatric desmoids tumors (From *JPRAS* 2011)

have been reported, that are classified as precalcaneal congenital fibrolipomatous hamartoma [26, 27]. At the other end of the spectrum are lesions like: low-grade myofibroblastic sarcoma, plexiform fibrohistiocytic tumor, and congenital and infantile fibrosarcoma that require complete (radical) excision [16].

Congenital intestinal fibromatosis has been reported to cause obstruction (Fig. 28.3) [28]. Aft er excision, the prognosis is good [28, 29].

Aggressive fibromatosis (AF), also called desmoid tumor, arises form the connective tissue of muscles and overlying fascia. The histological features are benign and they do not metastasize, but show local invasiveness and have a tendency to recur. The age distribution peak of pediatric AF is at 8 years (range 0–19). The majority occurs sporadically, but they can be associated with Familial Adenomatous Polyposis (FAP) and Gardner syndrome. The recurrence risk after complete excision is significantly lower than in the case of positive surgical margins [30, 31]. If complete excision is not feasible, as in intra-abdominal, mesenteric tumors, NSAIDs and tamoxifen may be effective [32]. The role of cytotoxic agents (a combination of vincristin, actinomycin-D, and cyclophosphamide, VAC) and radiotherapy, although advocated in cases of positive resection margins, is not defined [31]. Prognostic factors have been described by Salas et al. (*JCO* 2011) and particularly for children by Meazza (*Minerva Pediatr* 2011) and encompass: age, size, site (girdle or intra-abdominal localization) incomplete resection, and beta-catenin activating mutations. Similar findings in pediatric aggressive fibromatosis of head and neck were reported by Sharma et al. Wilks et al. present an algorithm for facial pediatric desmoids tumors (*JPRAS* 2011) (Fig. 28.4).

Mesenteric fibromatosis has been reported in a 13 year-old boy after irradiation for Hodgkin's disease [33].

Another rare variation in the spectrum is DermatoFibroSarcoma Protuberans, DFSP. The pigmented

version is also known as Bednar Tumor. It is a low grade malignancy but with a high risk of local recurrence. Fibrosarcomatous transformation has been reviewed by Voth et al. A good response to imatinib, allowing complete resection of an initially irresectable tumor, has been reported (Gooskens et al., *PBC* 2010).

Fibromatoses in children are difficult to manage for a variety of reasons. They are rare and their clinical behavior is unpredictable. Most cannot be diagnosed without histologic material. Management must therefore be based on an adequate biopsy followed by a detailed discussion between pathologist and surgeon. Although some recur, those that are not malignant are best treated by conservative, nonmutilating excision, with further excision as recurrence occurs. When malignancy is found on biopsy, excision with a margin of normal tissue is necessary. MRI is helpful in planning these procedures. Appropriate staging, including CT-scan of the chest, is indicated [32].

Vascular Tumors

Malignant Vascular Tumors

Malignant vascular tumors (hemangiosarcoma, malignant hemangioendothelioma, and Kaposi sarcoma) are extremely rare in children.

A case of a 13-year-old girl with malignant hemangioendothelioma has been reported. The tumor was treated by surgical excision of the omentum. However, bloody ascites and multiple peritoneal implants were already present [34].

A series of 18 children were described by the combined Italian and German oncology groups [35]. Surgery is the mainstay of treatment, but even with combined treatment of excision, chemotherapy and radiotherapy the 5-year survival was 30 %. A 2-year old girl with rupture of a angiosarcoma of the spleen and liver metastases came into complete remission after splenectomy, partial liver resection, and treatment with VAI [36].

Kaposi sarcoma (KS) is associated with HIV in children in Africa (Fig. 28.5), but less frequently in children in industrialized countries [37]. In Africa, it is now one of the most frequent tumors in children [38]. The Human Herpes Virus 8 (HHV 8) is involved in the pathogenesis [39]. Thalidomide appears a promising and affordable inhibitor of angiogenesis [40].

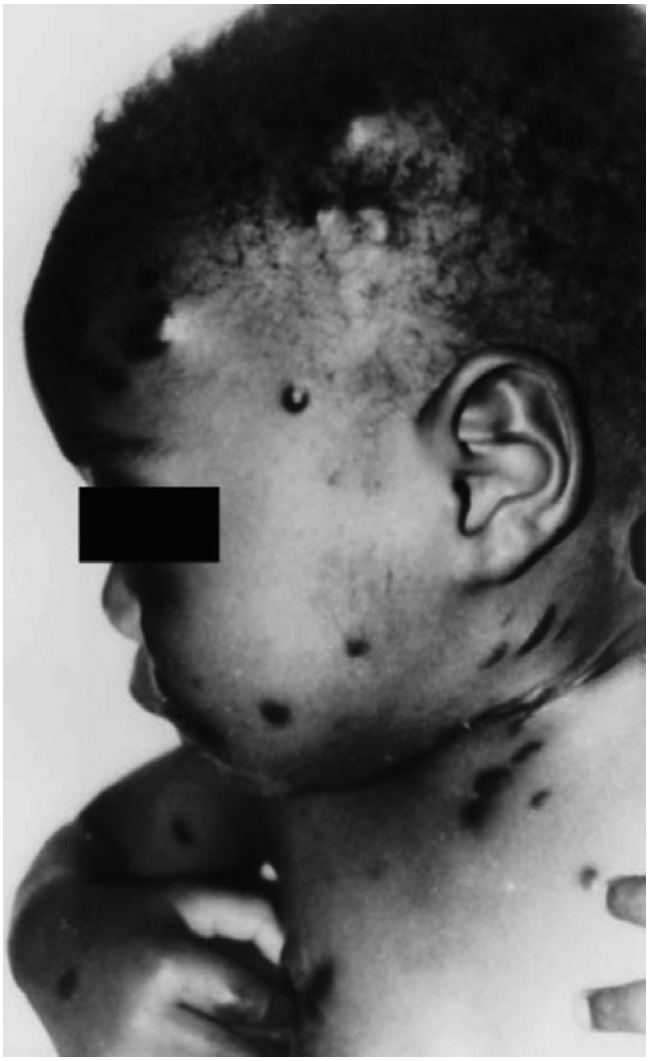

Fig. 28.5 Kaposi's sarcoma (From Manji et al. [38])

Hemangiopericytomas

Hemangiopericytoma (HPC) is a rare tumor that represents 1 % of all vascular tumors and arises not from endothelium but from pericytes, therefore strictly spoken it is not a blood vessel tumor. In children, there are two forms: the infantile (below the age of 12 months) and the adult type. Although histologically this tumor looks aggressive, it behaves in a benign manner. Spontaneous regression has sometimes been observed. HPC can be localized in the heart, lung, retroperitoneum, or the urinary tract and may present as an abdominal mass causing obstructive symptoms. Subcutaneous tumors may not appear vascular. While the tumor is benign, tumor recurrence has been recorded more than 10 years later. Imaging studies may show calcification in the soft tissues. The treatment of choice is complete excision of the tumor, which is followed by complete remission in patients with the infantile type. HPC in older children behaves like the adult type. Adjuvant treatment with VAC and IVA [ifosfamide, vincristine, Adriamycin (doxorubicin)] is advised in patients with irresectable lesions or positive margins [41].

A review from St Jude Children's Hospital (17 children between 1962 and 2009) showed a better clinical behavior than the adult type with chemoresponsiveness and spontaneous regression (Fernandez-Pineda, *JPHO* 2011)

Recently, a malignant Perivascular Epitheloid Cell tumor (PEComa) has been reported in a 2 year old child by Alaggio et al. (*JPS* 2012;47:e31). This family of tumors was first described by Zamboni in 1996, and includes angiomyolipoma, lymphangio-leiomyomatosis, clear cell 'sugar' tumor of the lung, and clear cell myomelanocytic tumor (CCMMT). In this case the tumor was located in the ligamentum teres. After excision, a recurrence showed good response to sirolimus.

Rare Tumors of the Head and Neck

Malignant Mesenchymoma

Malignant mesenchymoma is a rare neoplasm of mesenchymal origin arising in the soft tissues, the extremities, neck, back, sacrum, and occasionally in the mediastinum. See below, the section titled "Ectomesenchymoma."

Brain Metastases in Children

Hematogenous brain metastases are uncommon in children. A literature review revealed an incidence of 4 % in over 2000 reported patients. The incidence varied according to the primary tumor: between 1.3 % in Wilms' tumor, 4.4 % in neuroblastoma, and 13.5 % in germ cell tumor [42]. In the SIOP Wilms' tumor studies between 1971 and 2000, brain metastases were reported in 14 out of 3040 patients (0.5 %). Treatment consisted of multimodal chemotherapy, radiotherapy, and surgery in seven patients. None of the patients survived [43]. In a review of 20 patients reported in the literature, death was recorded in five cases and in the remaining patients survival time of up to 8.5 years was noted [44]. There may be a publication bias in this compiled data since the experience of a single institution with 16 patients with brain metastases from various primary pediatric tumors, reported one survivor at 20 months with alveolar soft part sarcoma [45]. Many of these patients had metastases in multiple organs. In summary, the prognosis of brain metastases from solid tumors in children appears dismal, despite multimodal treatment.

Nasopharyngeal Carcinoma

Epithelial cancers (carcinomas) are the single largest group of rare tumors in children, with an incidence of 2–3 % of all childhood malignancies in the Western population. For most sites incidence increases with age, but nasopharyngeal carcinoma (NPC) has a bimodal age distribution, with an early peak in adolescence. The most common presentation is with cervical lymphadenopathy. The role of surgery is therefore limited to biopsy. Chemotherapy (methotrexate, 5-FU, and cisplatinum) and irradiation achieved a high response rate and sustained remission in 91 % [2]. An increase in the prevalence of squamous cell carcinoma (SCC) in various locations but particularly in the nasopharynx, was reported by Chow et al. Possible causes for this increase are the improved survival of cancer patients who may develop SCC as secondary tumor. (Chow, *JPS* 2007;42:2035–9)

In 1997, Srotjan et al. [46] described five children with nasopharyngeal carcinoma with advanced stage IV tumors that were treated with low irradiation dose adjusted to preradiation neoadjuvant chemotherapy. Tumor control was achieved and acute and long-term morbidity reduced.

Salivary Gland Carcinoma

Carcinoma of the salivary gland is very rare in children [47]. Taylor et al. [48] described 15 such children. The primary site was the parotid gland in 11 cases, submandibular gland in three, base of the tongue in one. Six children were treated with complete excision, one required postoperative radiotherapy, five had partial excision, and four tumors were biopsied only. They concluded that complete excision is the treatment of choice.

Mucoepidermoid carcinoma of the parotid has been reported as secondary malignancy in a 17-year-old boy and a 16-year-old girl, who had been treated for osteosarcoma and Ewing's sarcoma, respectively. Subtotal parotidectomy appeared curative. Mucoepidermoid carcinoma has been reported before as secondary tumor after leukemia or lymphoma treatment, but not in sarcoma patients [49].

Synovial Sarcoma of the Larynx in a Child

Morland et al. [50] reported the first case of synovial sarcoma of the larynx in a child. He was treated with combination chemotherapy and radiotherapy, which led to remission for 3 years. Only six cases have been previously reported.

Rare Tumors of the Chest

Tumors of the Sternum

In addition to malignant bone tumors of the sternum, a deceptive condition called Self Limiting Sternal Tumors of Childhood (SELSTOC) occurs. Te Winkel et al. describe a

series of 14 young children with a rapidly growing sternal mass that disappeared within 6 months. (Te Winkel, *PBC* 2010)

Mediastinum

Thymic lesions consist of tumors, cysts, or hyperplasia. Clinical presentation varies from respiratory symptoms to incidental findings on x-rays. About 30 cases in children have been reported in the literature. Benign thymoma, is, unlike in adults, not always associated with myasthenia or other autoimmune diseases. Complete surgical excision is curative. Multiple localizations have been reported [51]. Malignant thymomas are aggressive and require complete excision.

Stage of the tumor is an independent prognostic factor for survival. Adjuvant chemotherapy and radiotherapy are advocated for invasive tumors [52, 53].

Tracheal and Bronchial Tumors in Children

Primary tumors of the trachea are rare in adults, and even more so in children. Carcinoid represents about one third of the cases, bronchogenic carcinoma one quarter, and mucoepidermoid carcinoma and pleuropulmonary blastoma 9 and 8 %, respectively [54–56].

Diagnosis may be delayed because of lack of awareness. Presentation may be with hemoptysis, pneumonia, and other respiratory symptoms. The diagnosis of carcinoid can be improved by octreotide nuclear scan, as these tumors contain somatostatin receptors. Improved imaging will outline the extent of the tumor and hence guide the surgical treatment, which consists of complete excision, if necessary involving lobectomy or pneumonectomy. Endoscopic treatment of carcinoid is discouraged by most authors [57]. Craig et al. reported on video-assisted thoracoscopic pneumonectomy for bronchial carcinoid affecting the bronchus intermedius in a 14-year-old girl [58].

The outcome of mucoepidermoid carcinoma of the tracheobronchial tree appears good after complete excision [59, 60].

Personal experience

I treated a child with one a couple of years back. It was in the left main bronchus, occluding LLL bronchus totally and wiping out the left lower lobe, but didn't occlude LUL bronchus and extended up into Left main bronchus about 1 cm. I took out the left lower lobe and did a sleeve resection of left main and a bit of LUL bronchus, joining upper lobe bronchus to the residual left main bronchus. Histology was intermediate grade Mucoepidermoid carcinoma, 3 mm clear of all margins, no nodes involved. No chemo or radio therapy and no recurrence now 4 years later.

We tried High Res CT with reconstruction and MRI for follow up, but while they are adequate for nodal or hilar disease, they were not helpful or reliable for mucosal or bronchial wall recurrence. I therefore do regular Bronchoscopies, ceasing at 5 years, which also checks for any stricture formation (none yet). High Res CT subjects them to too much radiation and would only pick up bulky disease in this site, which is a bit late. MRI not really impressive in the bronchus/mediastinum. CXR changes would be too late, so I would encourage you to do Bronchoscopies, probably 3 monthly for a year, 6 monthly for 2 more years then yearly to 5 years. No evidence based support for this, as it is too rare a tumour, but that seems a reasonable protocol. Very curable if recurrence picked up early.

Regards,

Bruce G Currie

Sydney Children's Hospitals Network.

Inflammatory pseudotumor of the trachea has been mentioned above. Cartilaginous neoplasms of the trachea have been described in a child with Mafucci's syndrome, causing obstructive symptoms. Endoscopic laser ablation was successful [61].

Primary Lung Tumors

Primary tumor of the lung is rare in childhood. Yu et al. report the Boston experience with 40 cases in 90 years. The more frequently occurring tumors were: carcinoid (8), IMT (7) and PleuroPulmonary blastoma (6). The mortality was 17.5 % (Yu, *JPS* 2010)

Pleuropulmonary Blastoma

Pleuropulmonary blastoma is a rare malignant primary tumor of the lung in children, but 25 % of cases are extrapulmonary and metastasize mainly to the CNS. A case of extrapulmonary pleuropulmonary blastoma was reported in a child [62]. This tumor is associated with pre-existing cystic lesions of the lung (congenital cystadenomatoid malformation, CCAM). In fact, the extended classification of CCAM (or Congenital Pulmonary Airway Malformation, CPAM) encompasses 5 types, of which type 4 has a histological picture similar to grade 1 PPB. Table 28.2 [63] presents an overview of this classification. The differentiation between PPB and CPAM continues to defy clinicians. There are no reliable characteristic and low-threshold resection of cystic lung lesions is recommended (Oliveira et al., *Eur J Ped Surg* 2011; Nasr et al. *JPS* 2010;45:1086–9).

PPB is also associated with cystic lesions of the kidney: cystic nephroma [64]. Familial cases of this association have been reported [65, 66]. An association with ovarian sex

Table 28.2 An assessment of the expanded classification of congenital adenomatoid malformations and their relationship to malignant transformation

0	1–3 %	Solid; the lungs are small throughout	Bronchial-type airways that have cartilage, smooth muscle, and glands are separated by abundant mesenchymal tissue	Neonates; other malformations; poor prognosis
1	60–70 %	Large cysts (up to 10 cm)	The cysts are lined by pseudostratified ciliated cells that are often interspersed with rows of mucous cells	Presentation may be late; resectable; good prognosis; rare casesshow carcinomatous change
2	10–15 %	Sponge-like composed of multiple small cysts (up to 2 cm) and solid pale tumor-like tissue	The cysts resemble dilated bronchioles separated by normal alveoli; striated muscle in 5 %	Neonates; other malformations; poor prognosis
3	5 %	Solid	There is an excess of bronchiolar structures separated by air spaces that are small, have a cuboidal lining, and resemble late fetal lung	Neonates; poor prognosis
4	15 %	Large cysts (up to 10 cm)	The cysts are lined by a flattened epithelium resting on loose mesenchymal tissue	Neonates and infants; good prognosis

From MacSweeney et al. [63]

cord stromal tumors has been reported by Schultz et al. (*Gynaecol Oncol* 2011). A genetic syndrome has been postulated [67, 68].

The treatment of choice is surgical excision but the prognosis for this type of tumor is poor. Adjuvant chemotherapy has been used successfully in a child with metastatic disease [69]. The registry web site serves as an important resource for physicians and families (http://www.ppbregistry.org).

Cystic Adenomatoid Malformation of the Lung and Malignant Tumors

Apart from PPBs, there are several published cases of other tumors, like mesenchymomas and rhabdomyosarcomas, arising in CCAM [63].

A case of a 22-month-old child with a CCAM who developed rhabdomyosarcoma of the lung was reported by d'Agostino [70]. Among 382 cases of primary pulmonary tumors only 17 had rhabdomyosarcoma, with six of these 17 (35 %) arising in a pre-existing pulmonary cystic malformation [71].

Tumors of the Diaphragm

Primary tumors of the diaphragm are rare, even in adults, with fewer than 200 cases reported. In children these tumors are exceptional, with 41 cases published [72]. The majority [32] was malignant; half of these were rhabdomyosarcomas. A benign Schwannoma was successfully excised in a 13 year old girl. The literature review in this paper focuses on Schwannomas and the diagnosis of diaphragmatic tumors (Hobbs et al., *JPS* 2012) The presentation may be with chest symptoms or with abdominal symptoms. The diagnosis is oft en difficult because of the rarity and localization. The treatment depends on the histological diagnosis. Preoperative chemotherapy may shrink the tumor to allow complete excision [72].

Breast Masses

Epidemiology and Etiology

Malignant tumors of the breast are rare in children and adolescents. In this age group, only one-third arise from primary breast tissue; the rest arise from non-breast tissue (rhabdomyosarcoma) or are metastatic tumors. Predisposing factors are: genetic (BRAC-1 and BRAC-2 mutations, Li-Fraumeni syndrome) or exposure to ionizing radiation, as in survivors of Hodgkin's disease [73]. These patients need careful and frequent follow-up according to a detailed schedule [74].

Sixteen patients under the age of 20 years were seen between 1951 and 1990. Four had benign cystosarcoma phyllodes, one osteosarcoma, and metastatic histocytic lymphoma, one had adenocarcinoma, nine had infiltrating ductal carcinoma, and one had an infiltrating lobular carcinoma in addition to an infiltrating ductal carcinoma. The treatment involved a combination of surgery, radiotherapy, and chemotherapy [75].

Eighteen patients with breast cancer were treated over a 25-year period including 16 females and two males. Primary malignancy presented in two of the patients, metastatic disease in 13, and secondary malignancy in three [76].

Diagnosis

Mammography in young patients is of limited value; ultrasonography, MRI, and PET-scan are more helpful. Fine needle aspiration cytology has a limited role in children because of pain and fear. Excisional biopsies in prepubertal children involves the risk of damage to the breast bud [77].

Treatment

Benign breast masses in adolescent girls are usually fibroadenomas, which may resolve spontaneously. If not excised they should be followed carefully, as ultrasonography cannot

distinguish between fibroadenoma and cystosarcoma phyllodes [77]. Phyllodes is malignant in 25 % of the cases and should be excised completely with a margin of normal tissue [77].

Two young girls with rhabdomyosarcoma of the breast, one primary and one with metastatic, were treated with surgery and chemotherapy respectively [78].

Rare Tumors of the Abdomen

Peritoneum, Omentum, and Mesentery

Primary tumors of these structures are oft en cystic, and benign, with lymphangioma being the most common [79]. Simple surgical excision is the treatment of choice. Peritoneal sarcomas often are very large and pretreatment with neoadjuvant chemotherapy is oft en necessary to render these tumors operable.

Other extremely rare malignant tumors are discussed below.

Peritoneal Mesothelioma

These tumors, although sharing some common histologic features, can vary considerably in biological behavior. Three different types are described: (a) classic, asbestos-related mesothelioma of adults, mainly in the pleural cavity; (b) multicystic mesothelioma, predominantly affecting the pelvic peritoneum of young women and associated with good prognosis [80]; (c) mesothelioma in children, which has an unpredictable behavior [81]. Measuring DNA index by fl ow cytometry can distinguish the cystic (aneuploid) form from the more malignant (diploid) tumors. In only one case, pathologically proven exposure to asbestos fibers has been reported [82].

The treatment of peritoneal mesothelioma depends on the behavior and appearance. Complete surgical removal is often not possible. There are reports that mesothelioma responds to adriamycin alone or in combination with cisplatinum. Intraperitoneal administration of cisplatinum has also been described [81]. Because of the rarity in children, the diagnosis of mesothelioma is rejected even by pathologists in up to 40 % of the cases [83].

Desmoplastic Round Cell Tumors

The group of small, blue cell tumors include neuroblastoma, PNET/Ewing's sarcoma and Desmoplastic Small Round Cell Tumor (DSRCT).

These arise from soft tissues with mesothelial linings, are characterized by male predominance, adolescent onset, and aggressive behavior. The tumors are often intraperitoneal, massive, and tend to metastasize early to lymph nodes, liver, and lungs. The immunohistochemical profile of these tumors is oft en distinctive and reacts to a broad range of antigens. Clinical presentation is usually with a painful mass, but the tumor can also lead to urinary obstruction [84, 85]. Intra-abdominal desmoplastic small round cell tumors may present with retroperitoneal or mesenteric primary with ascites and hepatic metastases. Urogenital involvement has been reported including paratesticular and ovarian localizations [85–87]. Complete surgical excision is usually impossible. Aggressive multidrug chemotherapy can reduce the tumor mass impressively, but the patient remains with residual disease [88].

Kretschmar et al. [89] reported three cases of desmoplastic small cell tumors and reviewed the literature and found 101 cases reported previously which indicated that this tumor is highly malignant and carries a grave prognosis. Only 50 % of cases respond to chemotherapy with a median survival of 17 months.

Molecular genetic studies revealed potential targets for the treatment of DRCT with the PDGF inhibitor SU101 (leflunomide) (Slater and Shipley, *BMJ* 2007)

Lipoblastoma and Liposarcoma

Lipoblastoma is a benign tumor arising from embryonal fat and therefore only occurs in young children. So far, 85 cases have been described, 12 of them presenting with an abdominal mass. The name lipoblastoma may cause confusion with malignant embryonal tumors, and therefore the term infantile lipoma has been proposed [90]. The treatment of choice is excision [91–93].

Only five cases of liposarcoma in childhood have been documented, with two of them arising from the porta hepatis [94–96]. Three of these five children died, one of them developing a recurrence 12 years after an initial favorable response to surgical excision combined with irradiation and chemotherapy.

Gastrointestinal Tract

General

In a recent review, Ladd and Grosfeld [97] presented 58 children and adolescents with gastrointestinal tumors over a 33-year time frame. The average age was 13.8 years; there were 39 malignant and 19 benign tumors. Over half of the children had lymphomas (Burkitt's in 15, and non-Burkitt's, non-Hodgkin's lymphoma in 15). Six patients had colorectal carcinoma, six had neurogenic tumors, four had inflammatory pseudotumors, three presented with Peutz-Jeghers syndrome; there were two children with carcinoid, two with juvenile colonic polyps, two with hemangioma and one each with leukemic infiltrate and gastric leiomyosarcoma.

In a series of 35 patients reported from Turkey, carcinomas of the large bowel and rectum were the most common, comprising about half of this material [98].

In this chapter, malignant and premalignant tumors of the G-I tract will be discussed.

Carcinoma of the Esophagus

Adenocarcinoma of the esophagus has been reported in an 8-year-old boy from India [99]. There was a longstanding history of vomiting, probably due to gastroesphageal reflux. The patient left the hospital without treatment. The authors quote several other case reports of adenocarcinoma in children with Barrett's esophagus.

Smooth Muscle Tumors

In recent years several cases of gastrointestinal smooth muscle tumors, both benign and malignant, have been reported in human immunodeficiency virus (HIV) infected children [100] Another report mentions similar tumors in the lung of a child with clinical HIV infection [101]. Also, abdominal leiomyosarcomas have been described in very long-term survivors of childhood cancer [102].

Leiomyoma and Leiomyoblastoma

These are essentially benign tumors, often occurring at an early age. Symptoms are most commonly caused by complications, such as intestinal obstruction, intussusception, or bleeding. These tumors have been found to occur in the stomach, small intestine, and colon. Usually, excision at the time of treatment of the complication leads to cure [103].

Leiomyosarcoma

Soft tissue sarcoma account for 7 % of all childhood malignancies. Sarcomas with intestinal involvement comprise only 2 % of this latter group. Leiomyoma often invole the stomach, whereas leiomyosarcoma (LMS) are more often found in the jejunum in children [97]. Over half of LMS occur in newborns. Other risk groups are patients with impaired immunity, e.g., after organ transplantation or due to HIV infection [97, 100–102, 104, 105].

LMS is a highly malignant tumor. The Children's Hospital in Boston reported ten; five (50 %) of the children died with metastases. Wide surgical excision is the treatment of choice [106].

Apparently the histological distinction between leiomyosarcoma and leiomyoblastoma is not always easy [107], which could explain why several neonates with "leiomyosarcoma" survived [108, 109].

In total, 27 cases of pediatric intestinal leiomyosarcoma have been reported in the literature. Complete excision and no recurrence after 5 years was achieved. Visceral metastases are atypical [110].

GIST

Gastro Intestinal Stroma Tumor has been recognized as a distinct entity by WHO since 1990. Although predominantly a tumor of adulthood, occurrence in children has been reported by several authors and over 50 pediatric cases can be found in the literature (Hoelwarth ME, personal communication, 2009) [97, 104, 111–113]. Miettinen et al. [114] reported 44 cases of gastric GIST occurring in patients younger than 21 years from the Armed Forces Institute of Pathology.

GIST is a mesenchymal tumor consisting of cells that are very similar to Interstitial Cells of Cajal (ICC), which express the CD 117 antigen, an epitope of the receptor tyrosine kinase KIT, in contrast to smooth muscle tumors like leiomyosarcomas. The great majority of pediatric GIST (88 %) is located in the stomach, but small bowel and colon localizations have been reported [104].

The most common symptoms are pain, anemia due to gastrointestinal bleeding [115], and abdominal masses. The tumor metastasizes to peritoneum, liver, or lymph nodes. Prognostic factors are: mitotic activity, tumor size and tumor site: gastric and colonic tumors have a better outcome than small bowel or mesenteric primaries [110] (Fig. 28.6).

The association of gastric epithelioid leiomyosarcoma (the older name for a GIST), extraadrenal paraganglioma, and pulmonary chondroma was described as Carney's Triad. Two of the triad's components are potentially lethal and it is very important that any patient with any of these tumors should be followed long-term. In 1993, Argos et al. [116] reported on 36 cases of Carney's Triad including their own case of a 12 year-old girl. In Miettinen's series [114] only one out of 44 cases had Carney's triad, but Price found two patients with the triad in the five described [112].

Surgical resection is the mainstay of the treatment of GIST. Complete gross resection is recommended and lymphadenectomy is not warranted [104, 110]. Response to chemotherapy is probably low, but imatinib mesylate, a tyrosine kinase inhibitor has been reported to achieve 50 % response rate [97, 104, 110].

Gastric Teratoma

One hundred and two cases of this usually benign tumor have been reported in the latest review [97]. The majority of the patients are boys, and malignant degeneration has been only rarely described. Abdominal mass, pain, gastric outlet obstruction, or bleeding are presenting symptoms and signs. After complete resection, no recurrences have been described [117] (Fig. 28.7).

Gastric Carcinoma

Fewer than 25 cases of gastric carcinoma in children have been reported [97]. It appears, however, that childhood infection with Helicobacter pylori can play an important causative role in gastric cancer in the adult [118]. Gastric cancer in children has also been described as a secondary tumor aft er treatment for malignant lymphoma [119]. The most common complaints of stomach cancer in childhood are pain and vomiting, along with symptoms suggesting acid peptic disease. Delay in diagnosis is common and can be avoided by

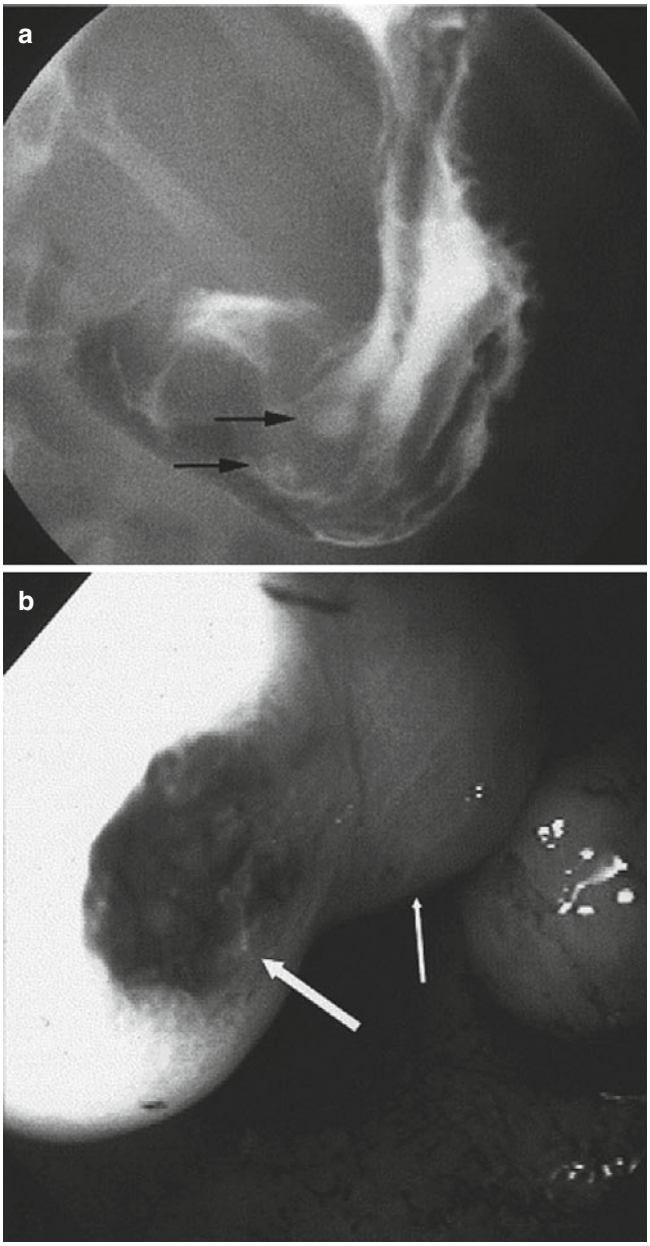

Fig. 28.6 G.I.S.T. Gastrointestinal stromal tumors arising from the stomach (From Durham et al. [110]). (**a**) Upper gastrointestinal series. Distal aspect of stomach shows 2 irregular intragastric filling defects (*arrrows*) in the regio of the antrum of the stomach. (**b**) Upper gastrointestinal endoscopy shows polypoid lesions in the antrum of the stomach with erosion of the surface from a previous episode (*arrows*)

early imaging and endoscopy. Long-term survival is uncommon [120, 121].

The role of chemotherapy and radiation in gastric cancer is still not well defined. Surgery alone may prolong survival. Studies in adults recommend the use of etoposide, doxorubicin (Adriamycin), and cisplatin as primary therapy or combined with surgery and radiation [121]. A 2-year-old boy with pernicious anemia caused by vitamin B12 and iron deficiencies developed atrophic gastritis and gastric carcinoma.

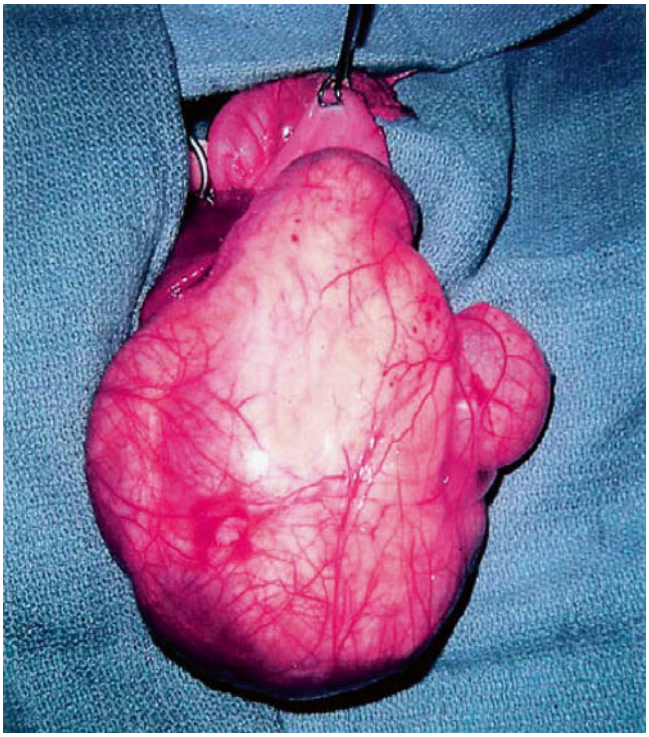

Fig. 28.7 Teratoma of the stomach

This has not been reported previously. Treatment included high subtotal gastrectomy with gastrojejunostomy and resection of associated lymph nodes and omentectomy and 6 months of chemotherapy. Follow-up after 1 year showed no evidence of recurrent disease [122].

Intestinal Polyps and Polyposis Syndromes

Juvenile Polyps

Juvenile polyps are hamartomatous in nature and, although benign, considered by some as a premalignant condition [97]. They occur in about 1 % of children and are usually detected because of complications. Rectal bleeding is most oft en the presenting symptom; however, prolapse of the polyp during defecation or straining may also occur. The majority are single (80 %) and are located in the rectum, but they have also been reported in colon, stomach, duodenum, and ileum [97]. Colonoscopy is recommended for children with unexplained rectal blood loss and normal proctoscopic examination [123, 124]. Solitary polyps should be excised endoscopically. The finding of a solitary rectal polyp is an indication for colonoscopy to exclude polyposis [125].

Generalized Juvenile Polyposis

This uncommon disease is characterized by the development of multiple (50 to more than 200) hamartomatous polyps throughout the intestinal tract, mostly in the large bowel; 85 % of cases occur in children. In half of the cases, there is

a positive family history of polyps or polyposis. The genes involved are SMAD4 on chromosome 18q21.1 or BMPR1A located on the long arm of chromosome 10. The infantile form of this condition is associated with protein-losing enteropathy, anemia, hypoproteinemia, and is often fatal [126]. Eighteen to thirty-five percent of patients with juvenile polyposis develop malignant disease by the age of 35. The treatment of choice is colectomy and an anal sphincter-saving procedure [127].

Peutz-Jeghers Syndrome

Peutz-Jeghers Syndrome (PJS) syndrome is autosomal dominantly inherited with an incidence estimated at 1:120,000. It is characterized by abnormal melanin deposits in the skin, lips, and mucous membranes and the formation of multiple hamartomatous polyps throughout the gastrointestinal tract (Fig. 28.8).

The small bowel is involved in 96 % of cases, the colon in 27 %, the stomach in 24 %, and rectum in 24 %. Labial pigmentation is a reliable clinical marker in 94 % of patients with Peutz-Jeghers syndrome. The causative genetic mutation involves STK11/LKB1 on chromosome 19 [128]. Polyps start to grow in the first decade of life, and 50–60 % of patients will develop symptoms by the age of 20 years.

In a large overview of the material removed by polypectomies in children, Peutz-Jeghers syndrome accounted for 1.73 % of the cases [129]. The complications of bowel obstruction due to intussusception of a polyp and anemia caused by bleeding from these polyps are often noted, sometimes before the typical abnormal pigmentation has developed.

In younger children (below 16 years of age) the gastroduodenal region is frequently the site of the polyps. Apparently these children are at risk for the development of malignant tumors. Two of the 70 patients mentioned earlier developed gastrointestinal adenocarcinoma, perhaps due to degeneration of a polyp, two an ovarian cancer and one a testicular tumor, possibly indicating a genetic disposition. A third case of adenocarcinoma of duodenum and jejunum occuring in an 8-year-old girl with Peutz-Jeghers syndrome was reported later [130]. There is an increased risk of ovarian cancer in relatives of a patient with Peutz-Jeghers syndrome. Whether hamatomatous polyps degenerate into carcinomas (the hamartoma-carcinoma sequence) has been debated. Some investigators consider the polyps as an epiphenomenon to a cancer prone condition [131].

Familial Adenomatous Polyposis (FAP)

This adenomatous autosomal dominant genetic disorder is due to a germline mutation of the APC-gene on chromosome 5q21-22. It is infamous because of its tendency to develop carcinoma of the large bowel, and may cause any

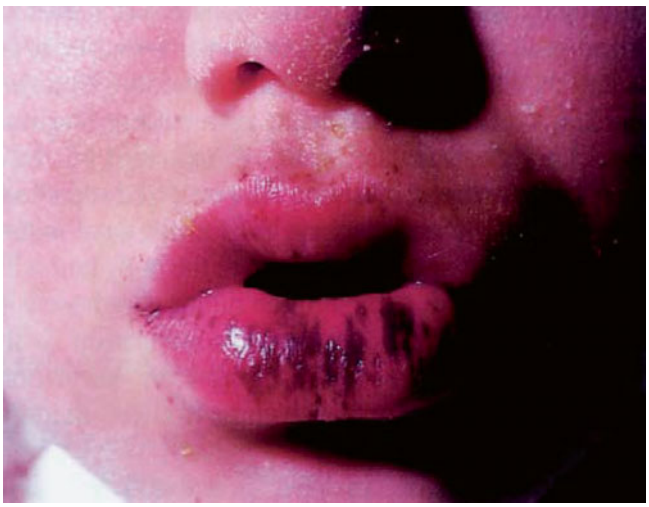

Fig. 28.8 Pigmentations of lips in Peutz Jeghers

significant bowel symptoms during childhood. In families with FAP a colonoscopy is indicated in children before they are 10 years of age [132]. Total colectomy, rectal mucosectomy, and ileoanal anastomosis eliminate the risk for malignant degeneration. Numerous reports have been published on the technical aspects of the ileoanal sphincter-saving operation, which is also applied in patients with ulcerative colitis. Most surgeons prefer the construction of an ileoanal anastomosis, using a "J"-pouch. Early and late complications after these procedures are common and the complication rate can be as high as 41 %. Late complications include inflammation ("pouchitis"), diarrhea, or stasis [133]. These complications occur more often in ulcerative colitis patients, whereas the FAP patients as a general rule fare much better [134].

Children in FAP families also have a tendency towards developing liver tumors (hepatoblastoma) more often than in general population [135]. Another interesting link with familial polyposis is Gardner's syndrome and the familial generalized juvenile polyposis, which by and large probably should be managed in a similar fashion as familal polyposis [136].

Although the risk of colon cancer in children under 15 years of age is very low (6 %), the youngest patient reported was 9 years. Therefore, the timing of colectomy is under debate as dysplasia can be asymptomatic. Vasudevan et al. described a group of 11 children who underwent surgery at a mean age of 13 years. Dysplasia was present in 9 patients (82 %). The authors advocate early operation to prevent malignant degeneration [137].

Colorectal Carcinoma

Uncommon in childhood (less than 1 % of all colonic cancers), this tumor has an extremely poor prognosis. This is due to late detection because of ignoring initial symptoms, a

high percentage of signet ring or anaplastic lesions present, and often regional lymph node metastases (75 % on presentation in the largest published series).

Survival varies from 0 to 25 %. Even in the event of complete resection it would be advisable to give adjuvant therapy with 5-fluorouracil and leucovorinbased cytotoxics in instances of high-grade lesions or regional lymph node involvement [138–140].

Urinary diversion into the sigmoid colon or use of bowel elsewhere in the urinary tract has also been identified as a risk for the development of adenocarcinoma. Although there usually is a time lag of more than 20 years, and therefore the carcinoma will develop beyond childhood, it is a fact to be kept in mind when constructing urinary conduits in children [141]. Experimental evidence suggests that familial polyposis, ulcerative colitis and ureterosigmoidostomies are conditions with an unstable colonic epithelium, which may become dysplastic, and perhaps deteriorate into malignant degeneration [142].

Brown et al. [139] described seven children aged 10–15 years with carcinoma of the colon and rectum. Distant metastases were present in five, and there were no survivors in this series. The youngest patient described was 9 months [97].

Carcinoid Tumors

These tumors appear in the gastrointestinal tract, biliary tree, ovaries, bronchi, lungs, and pancreas. The most common sites are the appendix, followed by small intestine and rectum. In one report a case is described of a carcinoid tumor occurring in a rectal duplication [143]. Appendiceal carcinoid is uncommon in infancy but may occur in late childhood and adolescence. Girls are affected three times as often as boys.

In most patients carcinoid is an incidental finding in the appendix removed for acute or recurrent abdominal pain. Usually the tumor is less than 2 cm in diameter and in 75 % of the cases it is located near the tip of the appendix. Simple appendectomy is curative in these patients. When the tumor is greater than 2 cm in diameter and occurs at the base, or if there is tumor growth beyond the appendix, a more extensive procedure like partial colectomy is indicated [97]. In the largest reported series of 40 cases, no recurrences, metastases, or tumor related deaths were observed [144].

Bile Ducts

Introduction

Two types of tumors occurring in this region deserve mentioning, namely the biliary tract rhabdomyosarcoma and carcinoma arising in the anatomically abnormal bile duct system (Fig. 28.9).

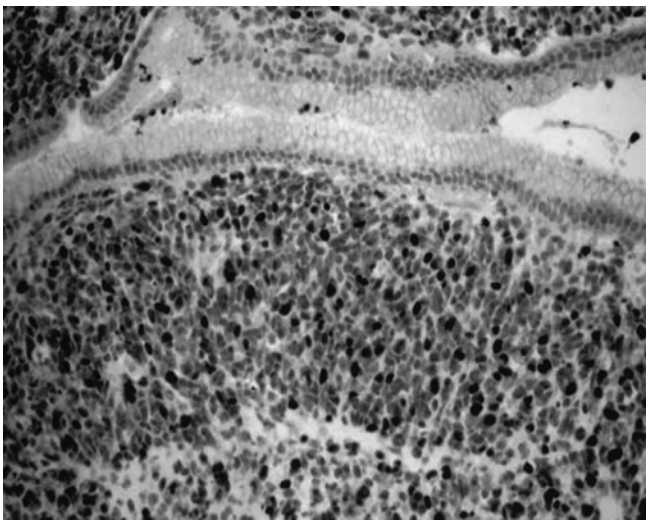

Fig. 28.9 Tumor of CBD. Embryonal rhabdomyosarcoma of the common bile duct mimicking choledochal cyst (From Tireli et al. [145])

Rhabdomyosarcoma

Fewer than 40 cases of rhabdomyosarcoma of the bile ducts have been reported in the literature. The presenting symptom is usually obstructive jaundice [145] (Fig. 28.8).

The diagnosis can be made using abdominal ultrasound, MRI or CT scan. The prognosis for this tumor has been rather poor; 40 % of the cases present with metastases, but local growth is a leading cause of death in most instances [146]. The first large series of ten patients was reported in 1985 [147]. At the time of publication there were four survivors following extensive resection and adjuvant radiation and chemotherapy. An interesting development is a recent report in which after an exploratory operation the patient was treated with chemotherapy which caused a dramatic reduction in tumor size. At a second-look operation complete regression of the tumor was observed. The authors claim that with this approach of aggressive surgery can be prevented [148]. Similar experience was reported by Spunt et al. [149], but this has not been confirmed by other authors [150].

The role of preoperative imaging is uncertain. ERCP was not found to be helpful in the two cases where it was performed [149]. It is not clear whether MRCP is more accurate than CT-scan [150]. Preoperative (PTC) or intraoperative cholangiography can be useful [150].

Carcinoma

The risk of adenocarcinoma developing in a choledochal cyst has been known for many years. A survey of 645 cases of choledochal cyst in Japan treated between 1972 and 1982 disclosed 54 cases (8.4 %) of biliary carcinoma. The incidence varied from 0.3 % in the pediatric population to 15.6 % in the adult cases, indicating that the risk of developing this cancer increases with age [151]. With time, approximately

20–25 % of cases will develop malignancy, which carries a poor prognosis since less than 10 % are resectable [152]. Patients with an anomalous arrangement of the pancreaticobiliary duct system have an increased cellular proliferative activity in the gallbladder mucosa starting in early childhood [153]. It is presumed that complete cyst excision eliminates the risk of malignant degeneration [152].

Pancreaticobiliary maljunction without dilatation of the common duct is very rare, but nevertheless may be associated with carcinoma in later life. Based on experience in a recent series of seven Japanese children with this anomaly, complete excision of common bile duct and gallbladder followed by hepaticojejunostomy is recommended [154].

Pancreas

Introduction

Malignant pancreatic tumors are rare in children. Vossen et al. quote from a Japanese autopsy statistic, that 0.2 % of infant deaths caused by malignant disease are due to pancreatic tumors [155]. A report from Memorial Sloan Kettering describing 17 patients below 21 years in the time period of 33 years between 1967 and 2000, illustrates the spectrum of malignant pancreatic tumors in children. Pancreatoblastoma (5 cases) and solid pseudopapillary or Frantz' tumor (7 cases) were the most frequent. Other tumors were: acinar cell carcinoma (1), nonfunctioning pancreatic endocrine neoplasm (1), malignant VIPoma (1), and PNET (2). The clinical presentation varied: abdominal pain (11), mass (4), anorexia (3). Only three patients were jaundiced [156]. The pancreas may also be the seat of malignant lymphoma, which may be difficult to diagnose [157].

In this section a more detailed description will be given of four types of pancreatic tumors in children:

(a) pancreatoblastoma, (b) solid pseudopapillary or Frantz' tumor, (c) pancreatic ductal Adenocarcinoma, (d) malignant endocrine tumors.

Pancreatoblastoma

Pancreatoblastoma (PB) is a malignant epithelial tumor showing mainly acinar differentiation, but occasionally also containing endocrine and ductal cells. These different cellular elements may derive from a pluripotent "blastomatous" cell. This may also explain the fact that a considerable number of PB express alfafoetoprotein (AFP), and that serum levels are increased in patients with PB. Dhebri et al. have reviewed the literature on 153 cases [158]. Most of the PB occur in early childhood, but 10 % occur in adults. Antenatal diagnosis and successful neonatal management have been reported [159, 160]. The latter patient, and several others in the literature, had the Beckwith-Wiedeman Syndrome (BWS), which is associated with loss of heterozygosity (LOH) on chromosome 11p [161]. The same genetic characteristic has been described in six out of seven patients with PB. Another genetic activation reported in PB is a mutation of the beta-catenin gene [158]. Others have reported multiple chromosomal abnormalities in PB-cells, including MYC-oncogene [162] (Fig. 28.10).

The tumor may arise in any part of the pancreas. The typical mode of presentation is with an abdominal mass, weight loss and pain; jaundice is present in about 10 %. Metastases are present at first diagnosis in 17–35 % of the patients. The diagnosis should be considered on the basis of imaging studies and can be confirmed by fine needle aspiration cytology [163]. The treatment consists of complete resection. If this is not possible, neoadjuvant chemotherapy should be given. Various cytotoxic regimes have been advocated: most contain vincristin and cyclophosphamide or ifosfamide, in combination with either actinomycin-D, cisplatinum, doxorubicin, or bleomycin. Postoperative radiotherapy has been advocated for irresectable or incompletely resected cases. See algorithm in Dhebri et al. [158].

The prognosis in children after complete resection is fairly good, with a reported 5-year survival rate between 50 and 80 % [164].

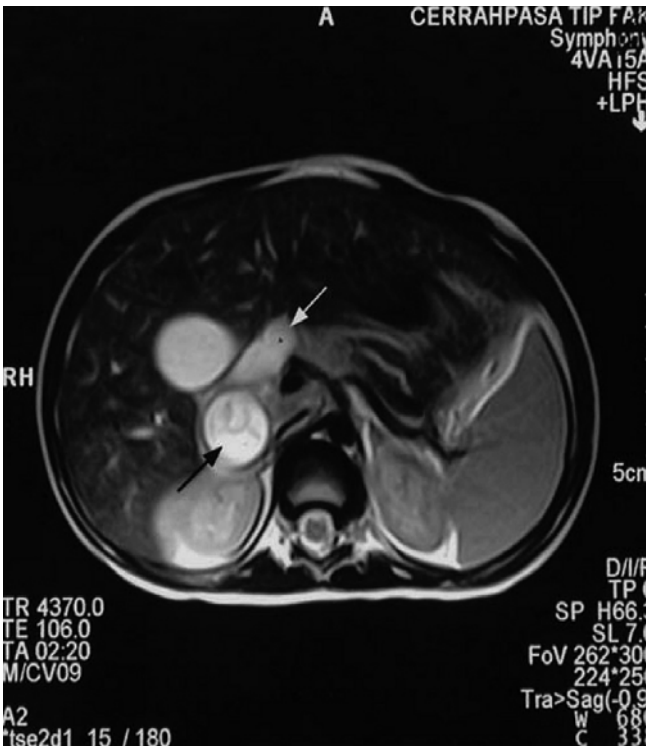

Fig. 28.10 MRI of rhabdomyosarcoma of the common bile duct: *black arrow* points to mass, *white arrow* to CBD (from Tireli [145])

Solid Pseudopapillary Tumor; Papillary Cystic Tumor of the Pancreas; Frantz's Tumor

Solid pseudopapillary tumor of the pancreas (SPTP) is known by several names, including the eponym of the author who first described this tumor in 1959 as a separate entity, V.K. Frantz. Since then, more than 700 cases have been reported in the English literature, their ages ranging between 2 and 85 years, with a mean of 22 years. One hundred sixty-five SPTPs have been reported in children below the age of 18 years. Over 90 % of the tumors occur in females [165, 166]. It has been suggested that SPTP occurs more often in Asians and Africans than in Caucasians [166].

The cell of origin of SPTP is uncertain. Kosmahl et al. [167] performed a comprehensive immunocyto-chemical analysis of 59 tumors and concluded that it is difficult to relate the tumor to epithelial cells, even if a multipotent stem cell origin is considered. On the other hand, SPTP is not a purely endocrine tumor either, both on cytochemical and clinical grounds. The authors postulate that there is a relationship with ovarian rete cells [167]. The tumor may occur in any part of the pancreas, but more often in the tail [167, 168].

The majority of SPTP are localized tumors, particularly in children there are only a few case reports of metastases [169]. Intraperitoneal spread has been observed after abdominal trauma [168]. SPTP is therefore considered as a low-grade malignant tumor.

Most patients present with gastro-intestinal symptoms and a palpable mass. The diagnosis is made by a combination of clinical signs and imaging. Endoscopic ultrasound-guided fine needle aspiration cytology has been advocated, but found conclusive in only a minority of cases [166, 170]. The treatment is complete excision with a margin, but without lymphnode dissection. Intraoperative frozen section is recommended. The prognosis is good in children after complete removal (Fig. 28.11).

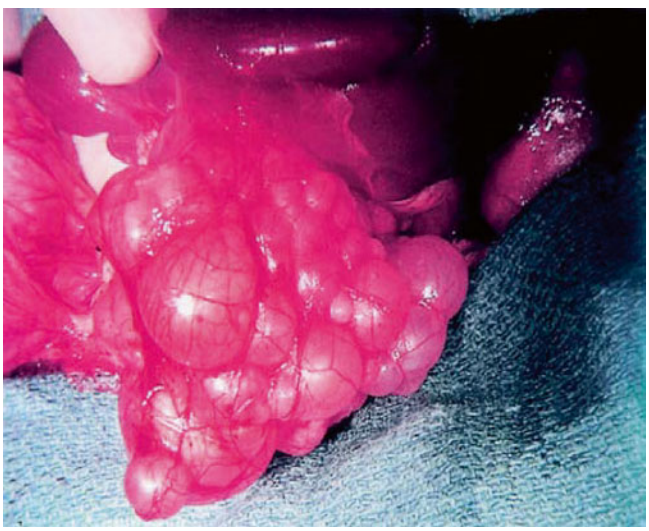

Fig. 28.11 Ectomesenchymoma (From Hajivassiliou et al. [187])

Pancreatic Ductal Adenocarcinoma

Pancreatic ductal adenocarcinoma (PDAC) is a tumor of the elderly that is exceedingly rare in children. Approximately 37 cases have been reported, although some doubt exists whether these were all adenocarcinomas. In a series of 520 pancreatic neoplasms, 404 were PDACs, two occurred in patients younger than 18 years [171]. The presence of an abdominal mass in the epigastrium, abdominal distension, or obstructive jaundice are the common presenting symptoms.

The diagnosis of a panceatic mass can be made with ultrasonography, MRI, or CT scan. Aggressive surgical procedures are recommended when feasible. In the majority of cases pancreatoduodenectomy or distal pancreatectomy are necessary. Even in instances of anaplastic tumors, survival following extirpative resection has been reported. One author claims that all patients in whom a resection was undertaken were long-term survivors, but others found no better outcome in young patients compared to the elderly [171].

Malignant Endocrine Pancreatic Tumors

Whereas in adults, the majority of endocrine pancreatic tumors are insulinomas, which are rarely malignant, in children there is an almost equal distribution of insulinomas and gastrinomas. Unfortunately, most of the insulinomas diagnosed as malignant have already metastasized at diagnosis [155]. Endocrine pancreatic tumors, which are associated with the MEN 1 syndrome, can also be malignant [172]. Malignant endocrine pancreatic tumors have furthermore been reported in children with Tuberous Sclerosis Complex (TSC), an autosomal dominant condition, presenting with epilepsy and mental retardation and known to be associated with benign renal cysts and angiomyolipoma (see also below). TSC1 and TSC2 genes are located on chromosme 9 and 16, respectively. Malignant nonfunctioning islet cell tumors expressing LOH of chromosome 16 (TSC2) were found in two boys [173, 174].

Rare Tumors of the Genitourinary System

Renal Cell Carcinoma

A retrospective analysis of 22 cases of renal cell carcinoma was reported by Aronson et al. [175]. Age, tumor size, location, and histology were found not to be predictors of outcome; tumor stage and complete surgical resection were the only significant prognostic determinants. The overall 5-year survival was 30 %. The survival rate for tumors that were completely resected was 60 % versus 10 % for those lesions incompletely resected.

Attempts to treat these tumors by nephron-sparing surgery have also been reported in children. Cook et al. reported on 15 patients, with a mean age of 7.9 years. Presentation

with hematuria, pain, and polycythemia in 75 %, whereas 25 % were asymptomatic. Treatment consisted of nephrectomy in 10 patients, and partial nephrectomy in five. Excision of metastases was done in 2 patients. Outcome: 13 are in complete remission, and of the three stage IV patients, 1 died and 1 survived with disease. All of the patients with partial nephrectomy are in complete remission. Two editorial comments warn that the long-term outcome of partial nephrectomy in children is unknown, and that the risk of recurrence has to be established in prospective studies.

Renal Cell Carcinoma in Association with Tuberous Sclerosis in Children

Tuberous sclerosis (TS) is an autosomal disorder with incomplete penetrance and variable phenotype (see also section under "Pancreas"). Angiomyolipoma and multiple renal cysts are seen in patients with TS. Cases of renal cell carcinoma in patients with TS are usually multiple and may be bilateral [177].

Transitional Cell Carcinoma of the Bladder

Five boys were reported to have transitional cell carcinoma of the bladder [178] Imaging and urine cytology correlated with cystoscopic and biopsy findings. Ultrasound examination was the most sensitive. A special risk category for bladder tumors are patients with bladder augmentation. Transitional cell carcinoma has been reported in three adults who underwent this procedure for neuropathic bladder [179]. In the discussion of this paper, A.B. Retik states the risk starts to rise after a 10-year lag period, in analogy with the experience in the ureterosigmoidostomy patients.

Cystic Partially Differentiated Nephroblastoma

Cystic partially differentiated nephroblastoma (CPDN) is a rare neoplasm. The tumor consists of well-demarcated cystic lesions of the kidney. Blastemal and other embryonic cells are present in the septa of the cysts; MRI can detect the lesions which are highly suggestive of either CPDN or cystic nephroma [180].

Experience in the NWTSG consists of 21 patients, 13 of whom received cytotoxic drugs whereas eight (all stage I) did not. The outcome was 100 % survival without recurrences. It is concluded that for stage I patients surgical treatment alone is probably sufficient [181].

B Cell Non-Hodgkin's Lymphoma as a Primary Renal Tumor

Primary renal lymphoma is an extremely rare tumor; only about 35 cases are reported in literature. A 6 year-old boy had a unilateral renal tumor which was thought to be a Wilms' tumor. On review of the histology this proved to be a B cell lymphoma [182].

Prostatic Non-Hodgkin's Lymphoma

A T cell non-Hodgkin's lymphoma of the prostate occurred in a child who presented with acute urinary retention and who responded well to treatment with chemotherapy [183].

Testicular Tumors Before Puberty

Twenty-two neonates less than 1 month of age were found to have testis tumors; seven were diagnosed at birth. Cell types included yolk sac tumors in six, and six had gonadal stromal tumors. Six had juvenile granulosa cell tumors, two gonadoblastoma, one teratoma, and one harmartoma. Serum alpha-fetoprotein was normal in ten tested patients. There were no metastases. Seventeen boys were followed up and there was no evidence of disease. Neonatal tumors are rare but should be considered in the differential diagnosis of scrotal masses in the neonate [184].

Testicular tumors are rare in prepubertal children, and the large majority are germ cell tumors. Serum tumor markers should be assessed before operation. If the markers are not elevated and salvageable testis tissue is present on ultrasound, an excisional biopsy with frozen section is advocated. If the tumor is a benign teratoma, the testis can be preserved [185]. Both reports originate from the Prepubertal Testis Tumor Registry (PTTR) created by the Section of Urology of the American Academy of Pediatrics in 1980.

A recent review on testicular and paratesticular tumors in prepubertal boys describes the full spectrum of benign and malignant tumors with recommendations for the management. (Ahmed et al., *The Lancet Oncol* 2010;11:476–83). A more specific overview on sex-cord stromal tumors of testis and ovary in children presents important principles on the surgical management of these tumors (Schultz KAP et al., *J Pediatr Hematol Oncol* 2012;34:S55–63)

Ectomesenchymoma

Ectomesenchymoma is a malignant nonepithelial tumor containing two or more cell-types from ectodermal and mesenchymal origin (Fig. 28.12). Synonyms are: malignant Triton tumor (MTT) and primary osteochondrorhabdomyosarcoma. It is considered a variant of the Malignant Peripheral Nerve Sheath Tumor (MPNST) that contains rhabdomyoblasts [186]. This tumor is associated with Neurofibromatosis type 1 (NF1) and usually develops in these patients before the age of 35 years. It is rare in children, with only 24 cases reported, more than half of them in NF1 patients [186]. Predilection sites are: head and neck, trunk, and extremities.

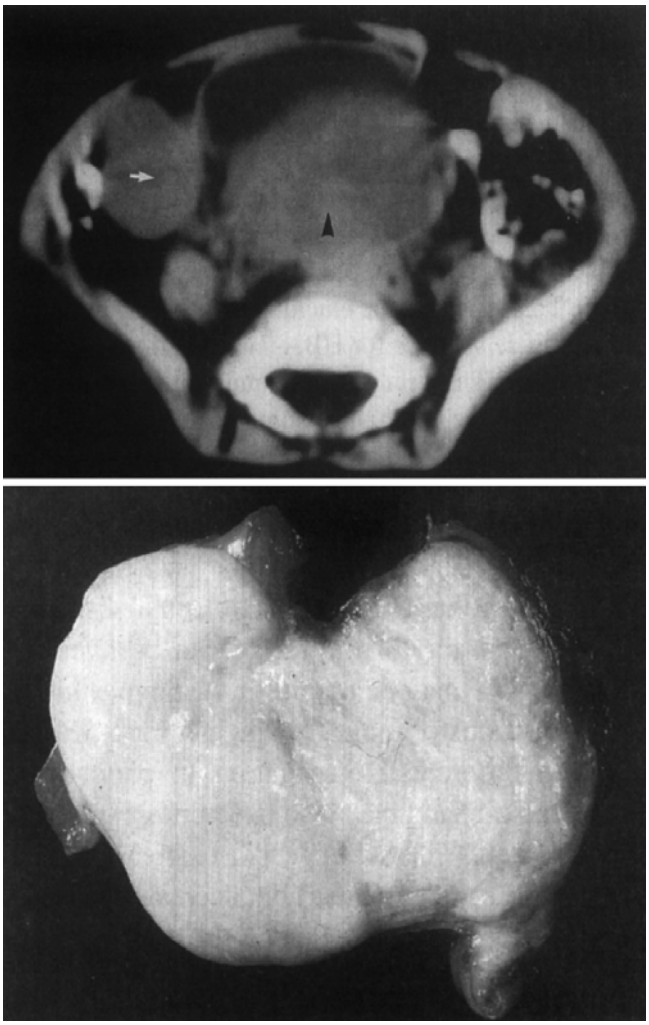

Fig. 28.12 Ectomesenchymoma. Upper picture shows CT-scan with different components (*black and white arrows*), lower picture show cut surface with different differentiations (from Hajivailiou, Figs. 1 and 3)

Hajivassiliou et al. reported a case in a child (gangliorhabdomyosarcoma) with cutaneous nevus syndrome. Review of the literature revealed 35 similar cases [187].

The treatment of MTT consists of wide local excision, the role of chemotherapy is uncertain. The prognosis is grim, with a 5-year survival of 26 % [186].

Malignant ectomesenchymoma of the bone is even more rare. Two children were reported: one 10-year old girl with a tumor of the fibula, and a 15-year-old girl with a tumor of the proximal humerus. A combination therapy of intensive cytotoxics (osteosarcoma protocol) and wide local excision resulted in complete remission in both cases [188–190].

Malignant Melanoma in Children

Malignant melanoma is rare in children, representing 1–3 % of all pediatric malignancies. Two percent of malignant melanomas occur in patients younger than 20 years. Most of pediatric melanomas are seen in adolescents with only 0.3 % in prepubertal children. The incidence is two per million children (below age 15 years), but is rising [191–193].

Certain (skin) conditions predispose to malignant melanoma. Risk factors in addition to exposure to sunlight [193] are:

1. Giant congenital melanocytic nevi (CMN), 5–15 % risk
2. Familial atypical mole/melanoma (FAMM), 100 % risk
3. Treatment with chemotherapy for malignant disease
4. Retinoblastoma
5. Xeroderma pigmentosum, (2000 × increased risk)

Malignant melanoma does occur in prepubertal children. Mones and Ackerman [194] describe a group of 11 children between 1 and 10 years of age, (6 younger than 5 years) with melanoma arising de novo. The diagnosis was missed in all cases, both by the clinician and by the pathologist, and all metastasized. One child died. The melanomas were growing fast, and very thick at the time of diagnosis. Confusion with benign Spitz nevus may arise, and the authors point out that the histopathological criteria for melanoma in young children are not different from those in adults.

Approximately half of melanomas in children arise in association with a pre-existing lesion: about 30 % within giant CMN and 20 % in association with other lesions, like acquired melanocytic nevi or small- or medium-sized CMN [192, 195, 196]. More than half of all melanomas that arise within giant CMNs do so before puberty, whereas melanomas that develop in smaller CMNs often occur after puberty [192]. Prophylactic excision of all giant CMNs, defined as covering 1 % body surface in head and neck and 2 % elsewhere on the body, is therefore recommended [197]. If a nevus changes in size or aspect, starts bleeding or itching, suspicion should arise. In children where melanoma developed in association with a pre-existing nevus, only 7 % of the patients had no signs or symptoms. As the clinical diagnosis is erratic and benign Spitz nevus may be confused with melanoma, the next step is to perform an excisional biopsy of the lesion. If the lesion is smaller than 15 mm, a margin of 1–2 mm is sufficient. It is important to excise the full thickness for adequate staging. Staging depends on the level of penetration (Clarke) or thickness of the lesion (Breslow), and the presence or absence of regional lymphnode and distant metastases. Children (<20 years) were found to have more frequent lymph node metastases than young adults (20–24 years of age), even in non-ulcerated melanoma with <2 mm thickness (Mu et al. *Cancer* 2012;118:2700–7).

The TNM classification of the American Joint Committee on Cancer is shown in Table 28.3 [3]. For adequate staging of lymphnodes, sentinel node biopsy has been advocated [198].

Treatment guidelines are based on the experience in adults. See American Association of Dermatology online guidelines; National Comprehensive Cancer Network Melanoma Panel. Treatment consists of radical excision, with adequate margins. For lesions less than 1 mm

Table 28.3 Staging of melanomas

Primary tumor (T)			
pTX	Primary tumor cannot be assessed		
pTO	No evidence of primary tumor		
pTis	Melanoma in situ		
pTl	Tumor 0.75 mm or less in thickness, or Clark		
	Level II		
pT2	Tumor greater than 0.75 mm but no more than		
	1.5 mm in thickness, or Clark Level III		
pT3	Tumor greater than 1.5 mm but no more than 4 mm in thickness, or Clark Level IV		
pT4	Tumor greater than 4 mm in thickness, or Clark		
	Level V, or satellites present within 2 cm of primary tumor.		
Regional lymph nodes (N)			
NX	Regional lymph nodes cannot be assessed		
NO	No evidence of regional lymph node metastasis		
Nl	Metastasis 3 cm or less in greatest dimension in any regional lymph node or nodes		
N2	Metastasis greater than 3 cm in greatest dimension in any regional lymph node or nodes and/or in transit metastasis.		
Distant metastasis (M)			
MX	Presence of distant metastasis cannot be assessed		
MO	No evidence of distant metastasis		
M 1	Distant metastasis present		
Stage grouping			
Stage 1	pTI	NO	MO
	PT2	NO	MO
Stage 2	pT3	NO	MO
Stage 3	pT4	NO	MO
	Any pT	Nl, N2	MO
Stage 4	Any pT	Any N	MO

From Corpron and Andrassy [3]
From Beahrs et al. [199], with permission. I

thickness, 1-cm margin is considered adequate; if 1–4 mm thickness: 2-cm margins, and 3-cm margin for lesions with more than 4 mm depth [3]. Enlarged lymphnodes should be removed by formal regional dissection. Elective lymphnode dissection is of no advantage in lesions of <1 mm thickness nor in lesions of >4 mm depth. For those between 1 and 4 mm, sentinel node biopsy with routine histopathology and immunohistochemistry is advocated. If the sentinel node is positive, a complete regional node dissection is recommended [192].

Although there is no evidence that chemotherapy is useful in adults, there are some encouraging experiences with a combination of vincristin, cyclophosphamide, and dactinomycin in children [192]. Immunotherapy with Interferon alpha 2b has been found effective. The prognosis is determined by the stage, and there is no evidence that children have a different outlook than adults [3, 192, 195, 196].

References

1. Harms D, Schmidt D. Rare tumors in childhood: pathological aspects. Experience of the Kiel pediatric tumor registry. Med Pediatr Oncol. 1993;21:239–48.
2. Walker DA. Rare tumours. In: Voute PA, Barrett A, Stevens MCG, Caron HN, editors. Cancer in children: clinical management. 5th ed. Oxford: Oxford University Press; 2005. p. 396–420.
3. Corpron CA, Andrassy RJ. Melanomas and other rare tumors. In: Andrassy RJ, editor. Pediatric surgical oncology. Philadelphia: WB Saunders Company; 1997. p. 349–64.
4. Karnak I, Senocak ME, Ciftci AO, et al. Inflammatory myofibroblastic tumor in children: diagnosis and treatment. J Pediatr Surg. 2001;36:906–12.
5. Bumber Z, Jurlina M, Manoilovic S, Jakic-Razumovic J. Inflammatory pseudotumor of the trachea. J Pediatr Surg. 2001; 36:631–4.
6. Stringer MP, Ramori P, Yeung K, Capps S, Kieley E, Spitz L. Abdominal inflammatory myofi broblastic tumors in children. Br J Surg. 1992;79:1357–60.

7. Kaneko K, Ando H, Watanabe Y, et al. Aggressive preoperative management and extended surgery for inflammatory pseudotumor involving the hepatic hilum in a child. Surgery. 2001;129:757–60.
8. Janik JS, Janik JP, Lovell MA, Hendricksonn RJ, Bensard DD, Greffe BS. Recurrent inflammatory pseudotumor in children. J Pediatr Surg. 2003;38:1491–5.
9. Sakai M, Ikeda H, Suzuki N, et al. Inflammatory pseudotumor of the liver: case report and a review of the literature. J Pediatr Surg. 2001;36:663–6.
10. DiFiore JW, Goldblum JR. Inflammatory myofi broblastic tumor of the small intestine. J Am Coll Surg. 2002;14:502–6.
11. Vaughan KG, Aziz A, Meza MP, Hackam DJ. Mesenteric inflammatory pseudotumor as a cause of abdominal pain in a teenager: presentation and literature review. Pediatr Surg Int. 2005;21:497–9.
12. Li L, Cerilli LA, Wick MR. Inflammatory pseudo-tumor (myofibroblastic tumor) of the heart. Ann Diagn Pathol. 2002;6:116–21.
13. Mergan F, Jaubert F, Sauvat T, et al. Inflammatory myofibroblastic pseudotumor in children: clinical review with anaplastic lymphoma kinase, Epstein-Barr virus, and human herpes virus 8 detection analysis. J Pediatr Surg. 2005;40:1581–6.
14. Parida SK, Azmy AF, Hollman AS, Wilkinson L, Beattie TJ. Xanthogranulomatous pyelonephritis. Pediatr Rev Commun. 1992;6:247–51.
15. Hagman C, El-Bahrawy M, Stamp G, Abel RM. Juvenile xanthogranuloma: a case report of a preterm baby. J Pediatr Surg. 2006;41:573–5.
16. Chinyama CN, Roblin P, Watson SJ, Evans DM. Fibromatosis and related tumours of the hand in children. Hand Clin. 2000;16:625–35.
17. Dölken R, Weigel S, Schröders H, et al. Treatment of severe disseminated juvenile systemic xanthogranuloma with multiple lesions in the central nervous system. J Pediatr Hematol Oncol. 2006;28:95–7.
18. Buonocore S, Valente AL, Nightingale D, et al. Histiocytic sarcoma in a 3-year old male: a case report. Pediatrics. 2005;116(2):e322–5.
19. Al-Trabalsi HA, Alshehri M, Al-Shomrani A, et al. Primary pulmonary Langerhans cell histiocytosis in a two year-old child. J Pediatr Hematol Oncol. 2006;28:79–81.
20. Khanna G, Sato Y, Smith RJH, et al. Causes of facial swelling in pediatric patients: correlation of clinical and radiologic findings. Radiographics. 2006;26:157–71.
21. Jain M, Nangia A, Bajaj P. Malignant histiocytosis in childhood. Diagn Cytopathol. 1999;1:359–61.
22. Margolin K, Traweek T. The unique association of malignant histocytosis and a primary gonadal germ cell tumor. Med Pediatr Oncol. 1992;20:162–4.
23. Sasou S, Nakamura SI, Habano W, Takano T. True malignant histiocytosis developed during chemotherapy for mediastinal immature teratoma. Hum Pathol. 1996;27:1099–103.
24. Song SY, Ko YH, Ahn G. Mediastinal germ cell tumor associated with histiocytic sarcoma of the spleen: case report of an unusual association. Int J Surg Pathol. 2005;13:299–303.
25. Hardy JD. The ubiquitous fibroblast. Ann Surg. 1987;205:445–55.
26. Ortega-Monzo C, Molina-Gallardo I, Monteagudo-Castro C, et al. Precalcaneal congenital fibrolipomatous hamartoma: a report of four cases. Pediatr Dermatol. 2000;17:429–31.
27. Jacob CI, Kumm RC. Benign anteromedial plantar nodules of childhood: a distinct form of plantar fibromatosis. Pediatr Dermatol. 2000;17:472–4.
28. Numanoglu A, Davies J, Millar AJW, Rode H. Congenital solitary intestinal fibromatosis. Eur J Pediatr Surg. 2002;12:337–40.
29. Choo KL, Borzi PA, Mortimore RJ. Neonatal intestinal obstruction from solitary intestinal fibromatosis. Pediatr Surg Int. 2001;17:467–9.
30. Abbas AE, Deschamps C, Cassivi SD, et al. Chest wall desmoid tumors: results of surgical intervention. Ann Thorac Surg. 2004;78:1219–23.
31. Buitendijk S, van de Ven CP, Dumans TG, et al. Pediatric aggressive fibromatosis. Cancer. 2005;104:1090–9.
32. Knudsen AL, Bulow S. Desmoid tumour in familial adenomatous polyposis. Fam Cancer. 2001;1:111–9.
33. Bar-Maor JA, Shabshin U. Mesenteric fibromatosis. J Pediatr Surg. 1993;28:1618–9.
34. Shih SL, Sheu JC, Chen BF, Ma YC. Malignant hemangioendothelioma presenting as omental masses in a child. J Pediatr Surg. 1995;30:118–9.
35. Ferrari A, Casanova M, Bisogno G, et al. Malignant vascular tumors in children and adolescents: a report from the Italian and German Soft Tissue Sarcoma Cooperative Group. Med Pediatr Oncol. 2002;39:109–14.
36. den Hoed ID, Granzen B, Aronson DC, et al. Metastasized angiosarcoma of the spleen in a 2-year old girl. Pediatr Hematol Oncol. 2005;5:387–90.
37. Mueller BU. HIV-associated malignancies in children. AIDS Patient Care STDS. 1999;13:527–33.
38. Manji KP, Amir H, Maduhu IZ. Aggressive Kaposi's sarcoma in a 6-month African infant: case report and a review of the literature. Trop Med Int Health. 2000;5:85–7.
39. Hengge UR, Ruzicka TH, Tyring SK, et al. Update on Kaposi's sarcoma and other HHV8 associated diseases. Part 2. Lancet Infect Dis. 2002;2:344–52.
40. Krown SE. Therapy of AIDS-associated Kaposi's sarcoma: targeting pathogenetic mechanisms. Hematol Oncol Clin North Am. 2003;17(3):763–83 (review).
41. Ferrari A, Casanova M, Bisogno G, et al. Hemangiopericytoma in pediatric ages. A report from the Italian and German Soft Tissue Sarcoma Cooperative Group. Cancer. 2001;92:2692–8.
42. Curless RG, Toledano SR, Ragheb J, Cleveland WW, Falcone S. Hematogenous brain metastases in children. Pediatr Neurol. 2002;26:219–21.
43. van den Heuvel-Eibrink MM, Graf N, Pein F, et al. Intracranial relapse in Wilms tumor patients. Pediatr Blood Cancer. 2004;43:737–41.
44. MacRae R, Grimard L, Hsu E, et al. Brain metastases in Wilms tumor: a case report and literature review. J Pediatr Hematol Oncol. 2002;24:149–53.
45. Kebudi R, Ayan I, Görgün O, et al. Brain metastasis in pediatric extracranial solid tumors: survey and literature review. J Neurooncol. 2005;71:43–8.
46. Srotjan P, Benedik MD, Krageli B, et al. Combined radiation and chemotherapy for advanced undifferentiated nasopharyngeal carcinoma in children. Med Pediatr Oncol. 1997;28:366–9.
47. Levine DA, Rao BN, Bowman L, et al. Primary malignancy of the salivary gland in children. J Pediatr Surg. 1994;29:44–7.
48. Taylor RE, Galtamaneni HR, Spooner D. Salivary gland carcinomas in children: a review of 15 cases. Med Pediatr Oncol. 1993;21:429–32.
49. Rutigliano D, Wong R, Meyers P, LaQuaglia M. Mucoepidermoid carcinoma as a secondary malignancy in pediatric sarcoma. Stockholm: Presented at BAPS Annual Conference; 2006.
50. Morland B, Cox G, Randall C, et al. Synovial sarcoma of the larynx in a child: case report and histological appearances. Med Pediatr Oncol. 1994;23:64–8.
51. Lazar CC, Liard A, Lechevallier J, Bachy B, Michot C. Secondary localization of an intra-thoracic benign mesenchymoma in the fossa poplitea: a rare pediatric case. Eur J Pediatr Surg. 2006;16:49–51.
52. Rothstein DH, Voss SD, Isakoff M, Puder M. Thymoma in a child: case report and review in the literature. Pediatr Surg Int. 2005;21:548–51.
53. Dhall G, Ginsburg HB, Bodenstein L, et al. Thymoma in children. Report of two cases and a review of literature. J Pediatr Hematol Oncol. 2004;26:681–5.
54. Gaissert HA. Primary tracheal tumors. Chest Surg Clin N Am. 2003;13:247–56.

55. Curtis JM, Lacey D, Smyth R, Cart H. Endobronchial tumours in childhood. Eur J Radiol. 1998;29:11–20.
56. Al-Qahtani AR, Di Lorenzo M, Yazbeck S. Endobronchial tumors in children: institutional experience and literature review. J Pediatr Surg. 2003;38:733–6.
57. Moraes TJ, Langer JC, Forte V, Shayan K, Sweezey N. Pediatric pulmonary carcinoid. Pediatr Pulmonol. 2003;35:318–22.
58. Craig ST, Hamzah M, Walker WS. Video assisted thoracoscopic pneumonectomy for bronchial carcinoid tumor in a 14-year-old girl. J Pediatr Surg. 1995;30:322–4.
59. Welsh JH, Maxson T, Jaksic T, Shahab I, Hicks J. Tracheobronchial mucoepidermoid carcinoma in childhood and adolescence: case report an review of the literature. Int J Pediatr Otorhinolaryngol. 1998;45:265–73.
60. Chan EYY, MacCormick JA, Rubin S, Nizalik E. Mucoepidermoid carcinoma of the trachea in a 4-year old boy. J Otolaryngol. 2005;34:235–8.
61. Moore BA, Rutter MJ, Cotton R, Werkhaven J. Maffucci's syndrome and cartilaginous neoplasms of the trachea. Otolaryngol Head Neck Surg. 2003;128:583–6.
62. Kelsey AM, McNally K, Birch J, et al. Case of extrapulmonary, pleuropulmonary blastoma in a child. Pathological and cytogenetic findings. Med Pediatr Oncol. 1997;29:61–4.
63. MacSweeney F, Papagiannopoulos K, Goldstra P, et al. An assessment of the expanded classification of congenital adenomatoid malformations and their relationship to malignant transformation. Am J Surg Pathol. 2003;27:1139–46.
64. Hill DA. USCAP Specialty Conference, case 1-type I pleuropulmonary blastoma. Pediatr Dev Pathol. 2005;8:77–84.
65. Bal N, Kayaselcuk F, Polat A, et al. Familial cystic nephroma in two siblings with pleuropulmonary blastoma. Pathol Oncol Res. 2005;11:53–6.
66. Delahunt B, Thomson KJ, Ferguson AF, et al. Familial cystic nephroma and pleuropulmonary blastoma. Cancer. 1993;71:1338–42.
67. Knudson AG. Commentary: on a new genetic syndrome. Med Pediatr Oncol. 2000;35:428.
68. Ishida Y, Kato K, Kigasawa H, et al. Synchronous occurrence of pleuropulmonary blastoma and cystic nephroma: possible genetic link in cystic lesions of the lung and kidney. Med Pediatr Oncol. 2000;35:85–7.
69. DiTullio MT, Indolfi P, Casale F, et al. Pleuropulmonary blastoma: survival after intraocular recurrence. Med Pediatr Oncol. 1999;33:588–90.
70. d'Agostino S, Banoldi E, Dante S, et al. Embryonal rhabdomyosarcoma of lung arising in cystic adenomatoid malformation. Case report and review of the literature. J Pediatr Surg. 1997;32:1381–3.
71. Hancock BS, Di Lorenzo M, Youssef S, et al. Childhood primary pulmonary neoplasms. J Pediatr Surg. 1993;28:1133–6.
72. Cada M, Gertle JT, Traubici J, Ngan BY, Capra ML. Approach to diagnosis and treatment of pediatric primary tumors of the diaphragm. J Pediatr Surg. 2006;41:1722–6.
73. van Leeuwen EF, Klokman WJ, van't Veer MB, et al. Embryonal rhabdomyosarcoma of lung arising in cystic adenomatoid malformation. Case report and review of the literature. J Clin Oncol. 2000;18:487–97.
74. Powers A, Cox C, Reintgen DS. Breast cancer screening in childhood cancer survivors. Med Pediatr Oncol. 2000;34:210–2.
75. Corpron CA, Black CT, Singletary SE, et al. Breast cancer in adolescent females. J Pediatr Surg. 1995;30:322–4.
76. Rogers DA, Lobe TE, Rao BN, et al. Breast malignancy in children. J Pediatr Surg. 1994;29:48–51.
77. Arca MJ, Caniano DA. Breast disorders in the adolescent patient. Adolesc Med. 2004;125:473–85.
78. Binokay F, Soyupak SK, Inal M, Celiktas M, et al. Primary and metastatic rhabdomyosarcoma in the breast: report of two pediatric cases. Eur J Radiol. 2003;48:282–4.
79. Gonzalez-Crussi F, Sotelo-Avila C, deMello DE. Primary peritoneal, omental, and mesenteric tumors in childhood. Semin Diagn Pathol. 1986;3:122–37.
80. Moriwaki Y, Kobayashi S, Harada H, et al. Cystic mesothelioma of the peritoneum. J Gastroenterol. 1996;31:868–74.
81. Niggli FK, Gray TJ, Raafat F, Stevens MC. Spectrum of peritoneal mesothelioma in childhood: clinical and histopathologic features, including DNA cytometry. Pediatr Hematol Oncol. 1994;11:399–408.
82. Andrion A, Bosia S, Paoletti L, Feyles E, Lanfranco C, et al. Malignant peritoneal mesothelioma in a 17-year old boy with evidence of previous exposure to chrysotile and tremolite asbestos. Hum Pathol. 1994;25:617–22.
83. Kelsey A. Mesothelioma in childhood. Pediatr Hematol Oncol. 1994;11:461–2.
84. Takekawa Y, Ugajin W, Koide H, Nishio S, et al. Pathologic, cytologic and immunohistochemical findings of an intra-abdominal desmoplastic small round cell tumor in a 15-year old male. Pathol Int. 2000;50:417–20.
85. Furman J, Murphy WM, Wajsman Z, Berry AD. Urogenital involvement by desmoplastic small round cell tumor. J Urol. 1997;158:1506–9.
86. Roganovich J, Bisogno G, Cecchetto G, D'Amore ESG, Carli M. Paratesticular desmoplastic small round cell tumor: case report and review of the literature. J Surg Oncol. 1999;71:269–72.
87. Slomovitz BM, Girotra M, Aledo A, et al. Desmoplastic small round cell tumor with primary ovarian involvement: case report and review. Gynecol Oncol. 2000;79:124–8.
88. Crombleholme TM, Harris BH, Jacir NN, Latchaw LA, Kretschmar CS, et al. The desmoplastic round cell tumor: a new solid tumor of childhood. J Pediatr Surg. 1993;28:1023–5.
89. Kretschmar CS, Colbach C, Bham I, et al. Desmoplastic small cell tumor. A report of three cases and review of the literature. J Pediatr Hematol Oncol. 1996;18:293–9.
90. O'Donnell KA, Caty MG, Allen JE, Fisher JE. Lipoblastoma: better termed infantile lipoma? Pediatr Surg Int. 2000;16:458–61.
91. McVay M, Keller JE, Wagner CW, et al. Surgical management of lipoblastoma. J Pediatr Surg. 2006;41:1067–71.
92. Arda IS, Senocak ME, Göü S, Büyükpamukçu N. A case of benign intrascrotal lipoblastoma clinically mimicking testicular torsion: a review of the literature. J Pediatr Surg. 1993;28:259–61.
93. Hicks J, Dilley A, Patel D, et al. Lipoblastoma and lipoblastomatosis in infancy and childhood: histopathologic, ultrastructural and cytogenetic features. Ultrastruct Pathol. 2001;25:321–33.
94. Wright NB, Skinner R, Lee RE, Craft AW. Myxoid liposarcoma of the porta hepatis in childhood. Pediatr Radiol. 1993;23:620–1.
95. Bouche-Pillon MA, Behar C, Munzer M, Gaillard D, Lefebvre F, et al. Liposarcoma in children. À propos of 3 cases and a review of the literature. Chir Pediatr. 1989;30:181–4.
96. Soares FA, Landell GA, Peres LC, Oliveira MA, Vicente YA, Tone LG. Liposarcoma of hepatic hilum in childhood. Med Pediatr Oncol. 1989;17:239–49.
97. Ladd AP, Grosfeld JL. Gastrointestinal tumors in children and adolescents. Semin Pediatr Surg. 2006;15:37–47.
98. Büyükpamukçu M, Berbero lu S, Büyükpamukçu N, Sarialio lu F, Kale G, et al. Nonlymphoid gastrointestinal malignancies in Turkish children. Med Pediatr Oncol. 1996;26:28–35.
99. Gangopadhyay AN, Mohanty PK, Gopal C, et al. Adenocarcinoma of the oesophagus in an 8-year-old boy. J Pediatr Surg. 1997;32:1259–60.
100. Gould Chadwick E, Connor EJ, Guerra Hanson C, Joshi VV, Abu-Farsakh H, et al. Tumors of smooth-muscle origin in HIV-infected children. J Am Med Assoc. 1990;263:3182–4.
101. Balsam D, Segal S. Two smooth muscle tumors in the airway of an HIV-infected child. Pediatr Radiol. 1992;22:552–3.
102. Blatt J, Olshan A, Gula MJ, Dickman PS, Zaranek B. Second malignancies in very-long-term survivors of childhood cancer. Am J Med. 1992;93:57–60.

103. Tamate S, Lee N, Sou H, Nagata N, Takeuchi S, Nakahira M, Kobayashi Y. Leiomyoblastoma causing acute gastric outlet obstruction in an infant. J Pediatr Surg. 1994;29:1386–7.
104. Cypriano MS, Jenkins JJ, Pappo AS, Rao BN, Daw NC. Pediatric gastrointestinal stromal tumors and leiomyosarcoma. Cancer. 2004;101:39–50.
105. Goedert JJ. The epidemiology of the acquired immunodeficiency syndrome. Semin Oncol. 2000;27:390–401.
106. Lack EE. Leiomyosarcomas in childhood: a clinical and pathologic study of 10 cases. Pediatr Pathol. 1986;6:191–7.
107. Miser JS, Pizzo PA. Soft tissue sarcomas in childhood. Pediatr Clin North Am. 1985;32:779–800.
108. Posen JA, Bar-Mao JA. Leiomyosarcoma of the colon in an infant. A case report and review of the literature. Cancer. 1983;52:1458–61.
109. Lau WY, Chan CW. Intestinal leiomyosarcoma in childhood. Eur J Pediatr. 1985;144:263–5.
110. Durham MM, Gow KW, Shehata BM, et al. Gastrointestinal stromal tumors arising from the stomach: a report of three children. J Pediatr Surg. 2004;39:1495–9.
111. Wiechman LS, Tirabassi MV, Tashjian D, et al. GIST: a rare tumor with a novel therapy. Vancouver: Presentation SIOP; 2005.
112. Price VE, Zielenska M, Chilton-McNeill S, et al. Clinical and molecular characteristics of pediatric gastrointestinal stromal tumors (GISTs). Pediatr Blood Cancer. 2005;45:20–4.
113. Prakash S, Sairan I, Socci N, et al. Gastrointestinal stromal tumors in children and young adults: a clinicopathologic, molecular and genomic study of 15 cases and review of the literature. J Pediatr Hematol Oncol. 2005;27:179–87.
114. Miettinen M, Lasota J, Sobin LH. Gastrointestinal stromal tumors of the stomach in children and young adults: a clinicopathologic, immunohistochemical and molecular genetic study of 44 cases with long-term follow-up and review of the literature. Am J Surg Pathol. 2005;29:1373–81.
115. Towu E, Stanton M. Gastrointestinal stromal tumour presenting with severe bleeding: a review of molecular biology. Pediatr Surg Int. 2006;22:462–4.
116. Argos MD, Ruiz A, Sanchez F, Garcia C, Gaztambide J. Gastric leiomyoblastoma associated with extraadrenal paraganglioma and pulmonary chondroma: a new case of Carney's triad. J Pediatr Surg. 1993;28:1545–9.
117. Nmadu PT, Mabogunje OA, Lawrie JH. Gastric teratoma: a case report. Ann Trop Paediatr. 1993;13:291–2.
118. Blecker U. Heliobacter pylori disease in childhood. Clin Pediatr. 1996;35:175–83.
119. Brumback RA, Gerber JE, Hicks DG, Strauchen JA. Adenocarcinoma of the stomach following irradiation and chemotherapy for lymphoma in young patients. Cancer. 1984;54:994–8.
120. McGill TW, Downey EC, Westbrook J, Wade D, de la Garza J. Gastric carcinoma in children. J Pediatr Surg. 1993;28:1620–1.
121. Murphy S, Shaw K, Blanchard H. Report of three gastric tumors in children. J Pediatr Surg. 1994;29:1202–4.
122. Katz S, Berenheim J, Kaufman Z, et al. Pernicious anaemia and adenocarcinoma of the stomach in an adolescent. Clinical presentation and histopathology. J Pediatr Surg. 1997;32:1384–5.
123. Lowichik A, Jackson WD, Coffin CM. Gastrointestinal polyposis in childhood: clinicopathologic and genetic features. Pediatr Dev Pathol. 2003;6:371–91.
124. Mestre JR. The changing pattern of juvenile polyps. Am J Gastroenterol. 1986;81:312–4.
125. Hyer W. Polyposis syndromes, pediatric implications. Gastrointest Endosc Clin N Am. 2001;11:659–82.
126. Desi DC, Neale KF, Talbot IC, Hodgson SV, Phillips RK. Juvenile polyposis. Br J Surg. 1995;82:14–7.
127. Cameron GS, Lau GYP. Juvenile polyposis coli: a case treated with ileoendorectal pull-through. J Pediatr Surg. 1979;14:536–7.
128. Doxey BW, Kuwada SK, Burt RW. Inherited polyposis syndromes: molecular mechanisms, clinicopathology, and genetic testing. Clin Gastroenterol Hepatol. 2005;3:633–41.
129. Tovar JA, Eizaguirre I, Albert A, Jimenez J. Peutz-Jeghers syndrome in children: report of two cases and review of the literature. J Pediatr Surg. 1983;18:1–6.
130. Cordts AE, Chabot JR. Jejunal carcinoma in a child. J Pediatr Surg. 1983;18:180–1.
131. Jansen M, de Leng WWJ, Bass AF, et al. Mucosal prolapse in the pathogenesis of Peutz-Jeghers polyposis. Gut. 2006;55:10–5.
132. Forbes D, Rubin S, Trevenen C, Gall G, Scott B. Familial polyposis coli in childhood. Clin Invest Med. 1987;10:5–9.
133. Fonkalsrud EW. Long-term results after colectomy and ileoanal pull-through procedure in children. Arch Surg. 1996;131:881–6.
134. Davis C, Alexander F, Lavery I, Fazio VW. Results of mucosal proctectomy versus extrarectal dissection for ulcerative colitis and familial polyposis in children and young adults. J Pediatr Surg. 1994;29:305–9.
135. Hughes LJ, Michels VV. Risk of hepatoblastoma in familial adenomatous polyposis. Am J Med Genet. 1992;43:1023–5.
136. Naylor EW, Lebenthal E. Early detection of adenomatous polyposis coli in Gardner's syndrome. Pediatrics. 1979;63:222–7.
137. Vasudevan SA, Patel JC, Wesson DE, et al. Severe dysplasia in children with familial adenomatous polyposis: rare or simply overlooked? J Pediatr Surg. 2006;41:658–61.
138. LaQuaglia MP, Heller G, Filippa DA, Karasakalides A, Vlamis V, et al. Prognostic factors and outcome in patients 21 years and under with colorectal carcinoma. J Pediatr Surg. 1992;27:1085–90.
139. Brown RA, Rode H, Millar AJW, Sinclair-Smith C, Cywes S. Colorectal carcinoma in children. J Pediatr Surg. 1992;27:919–21.
140. Taguchi T, Suita S, Hirata Y, Ishii E, Ueda K. Carcinoma of the colon in children: a case report and review of 41 Japanese cases. J Pediatr Gastroenterol Nutr. 1991;12:394–9.
141. Harzmann R, Kopper B, Carl P. Cancer induction by urinary drainage or diversion through intestinal segments? Urologe A. 1986;25:198–203.
142. Carachi R. Polyposis coli: an experimental animal model. J Pediatr Surg. 1983;18:51–7.
143. Rubin SZ, Mancer JF, Stephens CA. Carcinoid in a rectal duplication: a unique pediatric surgical problem. Can J Surg. 1981;24:351–2.
144. Parkes SE, Muir KR, Sheyyab al M, Cameron AH, Pincott JR, et al. Carcinoid tumors of the appendix in children 1957–1986: incidence, treatment and outcome. Br J Surg. 1993;80:502–4.
145. Tireli GA, Sander S, Dervisoglu S, Demirali O, Unal M. Embryonal rhabdomyosarcoma of the common bile duct mimicking choledochal cyst. J Hepatobiliary Pancreat Surg. 2005;12:263–5.
146. Lack EE, Perez-Atayde AR, Schuster SR. Botryoid rhabdomyosarcoma of the biliary tract. Am J Surg Pathol. 1981;5:643–52.
147. Ruymann FB, Raney BR, Crist WM, Lawrence W. Rhabdomyosarcoma of the biliary tree in childhood. A report from the Intergroup Rhabdomyosarcoma Study. Cancer. 1985;56:575–81.
148. Sanz N, de Mingo L, Florez F, Rollan V. Rhabdomyosarcoma of the biliary tree. Pediatr Surg Int. 1997;12:200–1.
149. Spunt SL, Lobe TE, Pasppo AS, et al. Aggressive surgery is unwarranted for biliary tract rhabdomyosarcoma. J Pediatr Surg. 2000;35:309–15.
150. Roebuck DJ, Yang WT, Lam WWM, Stanley P. Hepatobiliary rhabdomyosarcoma in children: diagnostic radiology. Pediatr Radiol. 1998;28:101–8.
151. Komi N, Tamura T, Miyoshi Y, Kunitomo K, Udaka H, Takehara H. Nationwide survey of cases of choledochal cyst. Analysis of coexistent anomalies, complications and surgical treatment in 645 cases. Surg Gastroenterol. 1984;3:69–73.
152. Benjamin IS. Biliary cystic disease: the risk of cancer. J Hepatobiliary Pancreat Surg. 2003;10:335–9.
153. Tokiwa K, Iwai N. Early mucosal changes of the gallbladder in patients with anomalous arrangement of the pancreaticobiliary duct. Gastroenterology. 1996;110:1614–8.
154. Ando H, Ito T, Nagaya M, Watanabe Y, Seo T, Kaneko K. Pancreaticobiliary maljunction without choledochal cysts in infants and children: clinical features and surgical therapy. J Pediatr Surg. 1995;30:1658–62.

155. Vossen S, Goretzki PE, Goebel U, Willnow U. Therapeutic management of rare malignant pancreatic tumors in children. World J Surg. 1998;22:879–82.
156. Shorter NA, Glick RD, Klimstra DS, et al. Malignant pancreatic tumors in childhood and adolescence: the Memorial Sloan-Kettering experience 1967 to present. J Pediatr Surg. 2002;37:887–92.
157. Eisenhuber E, Schoefl R, Wiesbauer P, Bankier AA. Primary pancreatic lymphoma presenting as acute pancreatitis in a child. Med Pediatr Oncol. 2001;37:53–4.
158. Dhebri AR, Connor S, Campbell F, et al. Diagnosis, treatment and outcome of pancreatoblastoma. Pancreatology. 2004;4:441–51.
159. Sugai M, Kimura N, Umehara M, et al. A case of pancreatoblastoma prenatally diagnosed as intraperitoneal cyst. Pediatr Surg Int. 2006;22:845–7.
160. Pelizzo G, Conoscenti G, Kalache KD, et al. Antenatal manifestation of congenital pancreatoblastoma in a fetus with Beckwith-Wiedeman syndrome. Prenat Diagn. 2003;23:292–4.
161. Muguerza R, Rodriguez A, Formigo E, et al. Pancreatoblastoma associated with incomplete Beckwith-Wiedeman syndrome: case report and review of the literature. J Pediatr Surg. 2005;40:1341–4.
162. Barenboim-Stapleton L, Yang X, Tsokos M, et al. Pediatric pancreatoblastoma: histopathologic and cytogenetic characterization of tumor and derived cell line. Cancer Genet Cytogenet. 2005;157:109–17.
163. Montemarano H, Lonergan G, Bulas DI, Selby DM. Pancreatoblastoma: imaging findings in 10 patients and review of the literature. Radiology. 2000;214:476–82.
164. Kloeppel G, Kosmahl M, Jaenig U, Luettges J. Pancreatoblastoma: one of the rarest among the rare pancreatic neoplasms. Pancreatology. 2004;4:452–3.
165. Papavramidis T, Papavramidis S. Solid pseudopapillary tumors of the pancreas: review of 718 patients reported in the English literature. J Am Coll Surg. 2005;200:965–72.
166. Zhou H, Cheng W, Lam KY, et al. Solid-cystic papillary tumor of the pancreas in children. Pediatr Surg Int. 2001;17:614–20.
167. Kosmahl M, Seada LS, Jaenig U, et al. Solid-pseudopapillary tumor of the pancreas: its origin revisited. Virchows Arch. 2000;436:473–80.
168. Rebhandl W, Felberbauer FX, Puig S, et al. Solidpseudopapillary tumor of the pancreas (Frantz tumor) in children: report of four cases and a review of the literature. J Surg Oncol. 2001;76:289–96.
169. Andronikou S, Moon A, Ussher R. Peritoneal metastatic disease in a child after excision of a solid pseudopapillary tumour of the pancreas: a unique case. Pediatr Radiol. 2003;33:269–71.
170. Nadler EP, Novikov A, Landzberg BR, et al. The use of endoscopic ultrasound in the diagnosis of solid pseudo-papillary tumors of the pancreas in children. J Pediatr Surg. 2002;37:1370–3.
171. Luettges J, Stigge C, Pacena M, Kloeppel G. Rare ductal adenocarcinoma of the pancreas in patients younger than age 40 years. Cancer. 2004;1000:173–83.
172. Dotzenrath C, Goretzki PE, Cupisti K, et al. Malignant endocrine tumors in patients with MEN 1 disease. Surgery. 2001;129:91–5.
173. Verhoef S, van Diemen-Steenvoorde R, Akkersdijk WL, et al. Malignant pancreatic tumour within the spectrum of tuberous sclerosis complex in childhood. Eur J Pediatr. 1999;158:284–7.
174. Francalanci P, Diomedi-Camassei F, Purificato C, et al. Malignant pancreatic endocrine tumor in a child with tuberous sclerosis. Am J Surg Pathol. 2003;27:1386–9.
175. Aronson DC, Medary I, Finlay JL, et al. Renal cell carcinoma in childhood and adolescents. A retrospective survey for prognostic factor in 22 cases. J Pediatr Surg. 1996;31:183–6.
176. Cook A, Lorenzo AJ, Pippi Salle J, et al. Pediatric renal cell carcinoma: single institution 25-year case series and initial experience with partial nephrectomy. J Urol. 2006;175:1456–60.
177. Robertson FM, Cendron M, Klauber GT, et al. Renal cell carcinoma in association with tuberous sclerosis in children. J Pediatr Surg. 1996;31:729–30.
178. Hoenig DM, McRae S, Chen SC, et al. Transitional cell carcinoma of the bladder in the pediatric patient. J Urol. 1996;156:203–5.
179. Soergel TM, Cain MP, Misseri R, et al. Transitional cell carcinoma of the bladder following augmentation cystoplasty for the neuropathic bladder. J Urol. 2004;172:1649–52.
180. Streif W, Gabner I, Janetschek G, et al. Partial nephrectomy in a cystic partially differentiated nephroblastoma. Med Pediatr Oncol. 1997;28:416–9.
181. Blakely ML, Shamberger RC, Norkoo P, et al. Outcome of children with cystic partially differentiated nephroblastoma treated with or without chemotherapy. J Pediatr Surg. 2003;38:897–900.
182. Vujanic GM, Webb D, Kelsey A. B cell non-Hodgkin's lymphoma as a primary renal tumour. Med Pediatr Oncol. 1995;25:423–6.
183. Li CK, Yeung CK, Chow J, et al. Postatic non-Hodgkin's lymphoma causing acute urinary retention in childhood. Med Pediatr Oncol. 1995;25:420–2.
184. Levy DA, Kay R, Elder JS. Neonatal testis tumours. A review of the prepubertal testis tumour registry. J Urol. 1994;151:715–7.
185. Agarwal PK, Palmer JS. Testicular and paratesticular neoplasms in prepubertal males. J Urol. 2006;176:875–91.
186. Ellison DA, Corredor-Buchmann J, Parham DM, Jackson RJ. Malignant triton tumor presenting as a rectal mass in an 11-month-old. Pediatr Dev Pathol. 2005;8:235–9.
187. Hajivassiliou CA, Carachi R, Simpson E, et al. Ectomesenchymoma—one or two tumors? Case report and review of literature. J Pediatr Surg. 1997;32:1351–5.
188. Chow LTC, Kumta SM. Primary osteochondrorhabdomyosarcoma (malignant mesenchymoma) of the fibula: a rare tumor in an unusual site—case report and a review of the literature. APMIS. 2004;112:617–23.
189. Mrad K, Sassi S, Smida M, et al. Osteosarcoma with rhabdomyosarcomatous component or so-called malignant mesenchymoma of bone. Pathologica. 2004;96:475–8.
190. Oppenheimer O, Athanasian E, Meyers P, et al. Malignant ectomesenchymoma in the wrist of a child: case report and review of the literature. Int J Surg Pathol. 2005;13:113–6.
191. Ceballos PI, Ruiz-Maldonado R, Mihm MC. Melanoma in children. N Engl J Med. 1995;332:656–62.
192. Huynh PM, Grant-Kelsd JM, Grin CM. Childhood melanoma: update and treatment. Int J Dermatol. 2005;44:715–23.
193. Oliveria SA, Saraiya M, Geller AC, Heneghan MK, Jorgenson C. Sun exposure and risk of melanoma. Arch Dis Child. 2006;91:131–8.
194. Mones JM, Ackerman AB. Melanomas in prepubescent children. Review comprehensively, critique historically, criteria diagnostically, and course biologically. Am J Dermatopathol. 2003;25:223–38.
195. Pensler JM, Hijjawi J, Paller AS. Melanoma in prepubertal children. Int Surg. 1993;78:247–9.
196. Daryanani D, Plukker JT, Nap RE, et al. Adolescent melanoma: risk factors and long-term survival. Eur J Surg Oncol. 2006;32:218–23.
197. Zaal LH, Mooi WJ, Sillevis Smit JH, van der Horst CMAM. Classification of congenital melanocytic naevi and malignant transformation: a review of the literature. Br J Plast Surg. 2004;57:707–19.
198. Balch CM, Cascinelli N. Sentinel-node biopsy in melanoma. N Engl J Med. 2006;355:1370–1.
199. Beahrs OH, Henson DE, Hutter RVP, et al., editors. American Joint Committee on cancer: manual for staging of cancer. 3rd ed. Philadelphia: J. B. Lippincott; 1988.