Pancreatic Tumors

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35.1 Introduction

Pancreatic tumors in infancy and childhood are extremely rare. Even larger institutions can report only few cases over a time period of 20 and more years (Yu et al. 2009). Perez et al. identified 58 patients under the age of 20 years with malignant pancreatic tumors within the United States Surveillance, Epidemiology, and End Results registry (SEER, 1973–2004), accounting for an age-population-adjusted incidence of around 0.018 cases/100,000 in the United States (Perez et al. 2009). In the UK National Registry, 41 pancreatic tumors have been counted in 30 years (Brennan et al. 2004); the Italian TREP project identified 21 patients under the age of 18 years with malignant pancreatic tumors within a 10-year period (Dall'igna et al. 2010).

35.2 Differential Diagnosis

The differential diagnosis for malignant pancreatic tumors includes benign tumors as hemangiomas, cystic lesions like enterogenous cysts, pseudocysts, and abscesses. Also, tumors from adjacent organs like neuroblastoma, Wilms' tumor, and hepatoblastoma, as well as involvement of the pancreas in case of leukemia, lymphoma, or lymphoproliferative disorders, are more common than primary pancreatic tumors (Rebhandl et al. 2001). In case of a primary pancreatic tumor, pancreatoblastomas have to be considered especially under the age of 10 years, a solid-pseudopapillary Neoplasm (SPN) rather in female adolescents. Because of similar morphology, SPN might easily be confused with endocrine tumors. The pathology and clinical behavior of pancreatoblastoma and acinar cell

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Table 35.1 Differential diagnosis of pancreatic tumors in children and adolescents

Group	Entity
Malignant pancreatic tumors	Pancreatoblastoma
	Acinar cell carcinoma
	Ductal adenocarcinoma
Tumors with low malignant potential	Solid-pseudopapillary neoplasm
	Mucinous cystic neoplasm
	Inflammatory myofibroblastic tumor
Endocrine pancreatic tumors	Insulinoma
	Gastrinoma
	Others (VIPoma, glucagonoma, somatostatinoma)
Benign tumors	Hemangioma
	Teratoma (see chapter 39)
Tumor-like lesions	Cyst Local fibrous focus
	Pseudocyst
Congenital hyperinsulinism	
Secondary tumor manifestations	Lymphoma
	Rhabdomyosarcoma
	Primitive neuroectodermal tumor
	Neuroblastoma
	Hepatoblastoma
	Wilms' tumor

carcinoma are very similar, and differentiation between the two can be very difficult (Shorter et al. 2002). Anyway, acinar cell carcinoma as well as ductal adenocarcinoma is extremely rarely seen in children (Luttges et al. 2004; Perez et al. 2009) (Table 35.1).

35.3 Biology, Pathology, and Tumor Characteristics

35.3.1 Pancreatoblastoma

Pancreatoblastoma is the most common pancreatic tumor in children, accounting for approximately 25% of cases (Shorter et al. 2002). A joint analysis of the European Pediatric Rare Tumor Group (EXPeRT) collected 20 cases between 2000 and 2009 (Paper submitted). It mainly occurs in children under the age of 10 years and is rarely reported in neonates (mean age 4.5 years) (Defachelles et al. 2001; Shorter et al. 2002). Pancreatoblastomas have a bimodal age distribution: two-thirds of the cases occur in children and one-third in adults. Pediatric pancreatoblastomas show an incidence peak between second and third years of life (Klimstra et al. 1995). This embryonal tumor has many similarities with hepatoblastoma concerning age group, genetic alterations, and the response to chemotherapy. It shows alterations of the APC/β-catenin pathway and a loss of heterozygosity on chromosome 11p15.5 (Abraham et al. 2001). Pancreatoblastoma can be associated with Wilms' tumor, Beckwith–Wiedemann syndrome, and familiar adenomatous polyposis (Kerr et al. 2002; Antonello et al. 2009).

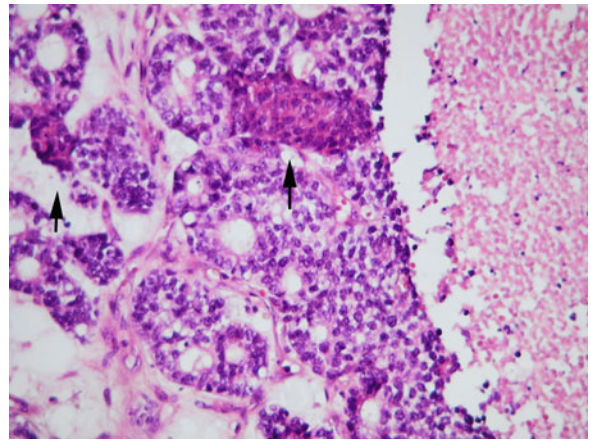

Fig. 35.1 Pancreatoblastoma with acinar-glandular features and with squamoid nests (*arrows*, H & E, ×400)

The tumor is frequently found in the pancreatic head or tail, well defined, and surrounded by a fibrous capsule (Dhebri et al. 2004). It is composed of cells showing predominantly acinar differentiation divided by septa. Neonatal pancreatoblastomas associated with Beckwith–Wiedemann syndrome are cystic (Kerr et al. 2002). Necrotic areas with calcifications are typical. The most important criterion for the histological diagnosis is the presence of squamoid nests (Fig. 35.1). Pancreatoblastomas may exhibit partially endocrine and ductal differentiation or even contain primitive components, somehow recapitulating the embryonic features of pancreas. The proliferative activity is between <1 and 42 mitoses/High power field (HPF). Nuclear polymorphism is low, and tumor cell invasion in perineural space and vessels is rare. The frequency of metastases in regional lymph nodes and liver has been reported to be between 17% and 50% (Dhebri et al. 2004; Perez et al. 2009). In most cases, expression and secretion of AFP can be observed and may serve as

tumor marker to follow the response of therapy (Saif 2007; Antonello et al. 2009).

35.3.2 Solid-Pseudopapillary Neoplasm (SPN)

Solid-pseudopapillary neoplasms (SPN) are rare tumors of the pancreas of low malignant potential mainly occurring in young females (10:1, mean age 22 years) (Papavramidis and Papavramidis 2005). SPNs were also known as "solid and papillary tumor," "solid-cystic tumor," "papillary cystic tumor," "solid and pseudopapillary epithelial neoplasm," "solid and cystic acinar cell neoplasm," and "Frantz tumor" (Kloppel et al. 1996; Papavramidis and Papavramidis 2005; Chung et al. 2006). Not seldom they were misdiagnosed as nonfunctioning islet cell tumors, adenocarcinomas, cystadenocarcinomas, or pseudocysts (Todani et al. 1988; Sclafani et al. 1991; Kloppel et al. 1996; Papavramidis and Papavramidis 2005; Chung et al. 2006). Recently, the tumor has been more recognized and therefore more often diagnosed, accounting for approximately 6% of all exocrine pancreatic tumors in all age groups (Papavramidis and Papavramidis 2005). In children, they account for 8–17% of all cases of pancreatic tumors (Grosfeld et al. 1990; Jaksic et al. 1992). Solid-pseudopapillary neoplasms are enigmatic tumors, with regard to their cell of origin and phenotype. SPNs are composed of unique cells which may exhibit epithelial, mesenchymal, and neuroendocrine features. During fetal development, there is a close relationship between the left genital ridge and the pancreatic anlage. It is speculated, therefore, that SPNs arise from pluripotent precursor cells from this area (Kosmahl et al. 2000). This would explain the female preponderance of >90%. In 95% of the cases, SPNs show an alteration of the APC/β-catenin signaling pathway and LOH on chromosome 5q22.1 (Antonello et al. 2009). In one-third of the SPNs, Fli-1 is over-expressed without exhibiting EWS/Fli-1 translocation, which is observed in pediatric tumors, mostly in Ewing sarcomas. The tumor localization is equally distributed in the pancreas (Rebhandl et al. 2001; Papavramidis and Papavramidis 2005). SPNs are often large tumors with a mean diameter of 6 cm (0.5–34.5 cm). The tumor consistency is soft with friable necrotic grey-hemorrhagic material in the center. Smaller tumors may be completely solid, mimicking endocrine neoplasms. Usually, the tumor is well demarcated and surrounded by a pseudo-capsule, which can be infiltrated by tumor cells (Fig. 35.2). This feature, however, is not a sign of malignancy in SPNs (Fig. 35.3). Histologically, the eponymous pseudopapillary appearance is found around the lacunae. Monomorphous polygonal tumor cells form solid areas or are arranged in pseudo-rosettes. The stromal component is often imperceptible, but it can be myxoid or sclerotic. The proliferation rate is very low (Rebhandl et al. 2001; Kosmahl et al. 2004). SPNs display a characteristic immunohistochemical pattern with expression of nuclear β-catenin, vimentin, CD56, and progesterone receptor (Fig. 35.4).

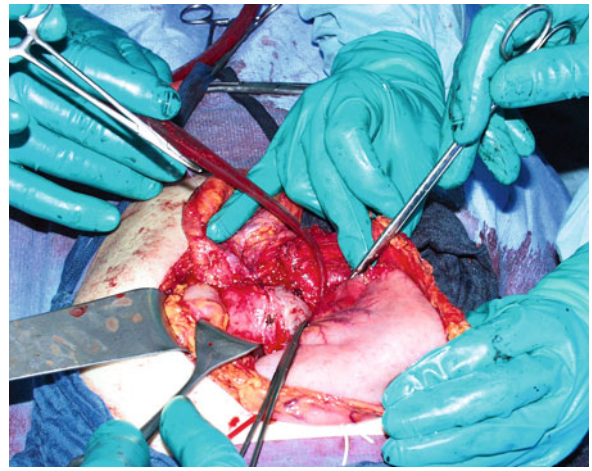

Fig. 35.2 Intraoperative view of a solid-pseudopapillary neoplasm (SPN) in the head of the pancreas in a 14-year-old female

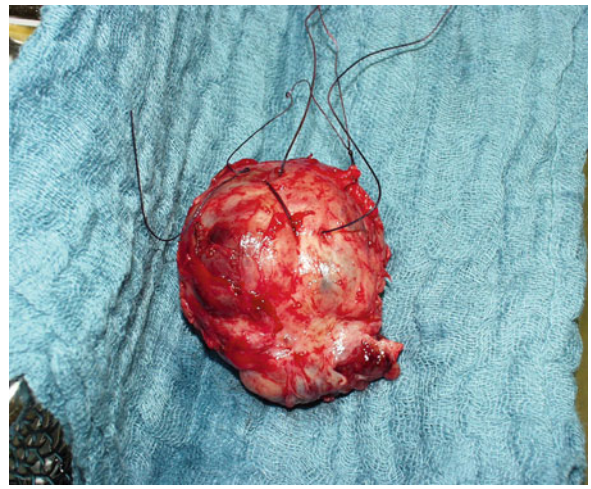

Fig. 35.3 Specimen of the SPN with free margins. Neither the pancreatic nor the choledochal duct has been touched

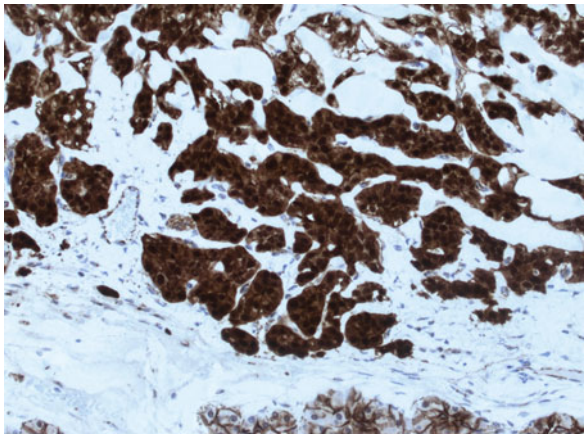

Fig. 35.4 Nuclear β-catenin expression in solid-pseudopapillary neoplasm. At the bottom, normal pancreatic acini with membrane-bound staining (×400)

Most SPNs (>90%) behave in a benign fashion. There are no established morphological criteria of malignancy which can be defined only by presence of metastases, mostly to the peritoneum or liver.

35.3.3 Endocrine Tumors and Congenital Hyperinsulinism

Pancreatic endocrine tumors, also called islet cell tumors, derive from any of the cell types of the islets, and may be benign (adenomas) or malignant (carcinomas), and occur equally often in male and female (Chung et al. 2006). They account for 1–2% of all pancreatic neoplasms at all age groups, but the prevalence is estimated to be much higher around 1/100,000. Insulinomas and gastrinomas arise either sporadically or, as in most pediatric cases, they are associated with multiple endocrine neoplasia (MEN) 1. Up to the fourth decade, gastrinomas develop in about 40% and insulinomas in 10% of all MEN 1 carriers. Additionally, adenomas are observed in the parathyroid gland in 90% and in the pituitary gland in 29% of the cases (Brandi et al. 2001). Other functionally active tumors like glucagonoma, VIPoma, and somatostatinoma are extremely rare. Hybrid tumors with characteristics of insulinoma and gastrinoma have been described (Lodish et al. 2008).

Insulinomas are solid tumors, approximately 1–3 cm in size, and well circumscribed (Bartsch et al. 2000). In contrast to the foci in congenital hyperinsulinism, they can be well distinguished macroscopically from normal pancreatic tissue (Figs. 35.5–35.9). Insulin and proinsulin expression can be shown by immunohistochemistry. In MEN 1, endocrine pancreatic tumors are frequently multifocal. Monohormonal endocrine cell clusters and microadenomas are well-defined precursor lesions of MEN-associated endocrine tumors.

The prognostic stratification of endocrine pancreatic tumors is based on tumor size, proliferation rate, angioinvasion, and infiltration of surrounding tissue (WHO 2000) (Table 35.2). The WHO classification from 2010 provided a more simplified system for risk stratification (WHO 2010) (Table 35.3). Malignancy is proven by metastases which arise in the regional lymph

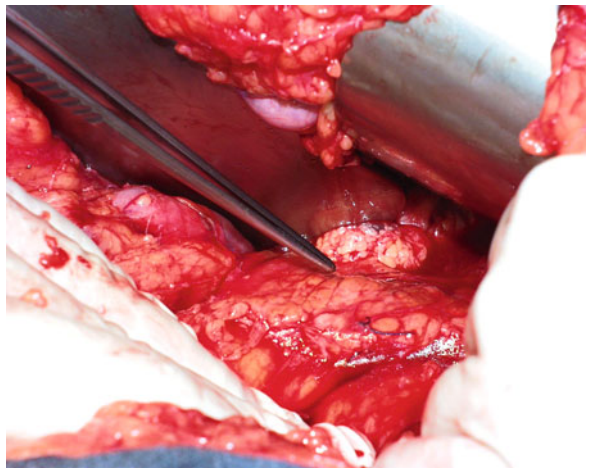

Fig. 35.5 Intraoperative view of an insulinoma (forceps tip) in the middle of the pancreas in a 16-year-old male with the MEN 1 syndrome

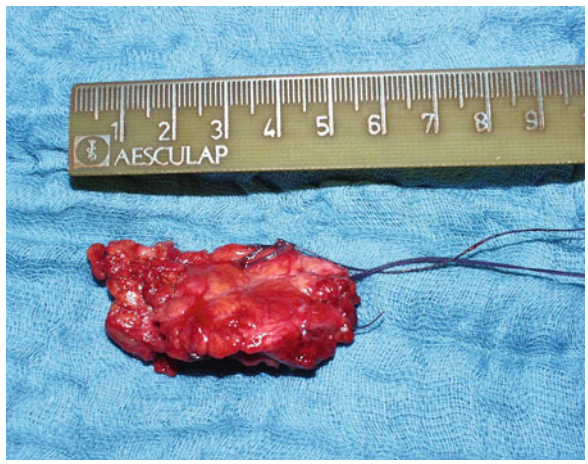

Fig. 35.6 Gross specimen of an insulinoma with free margins

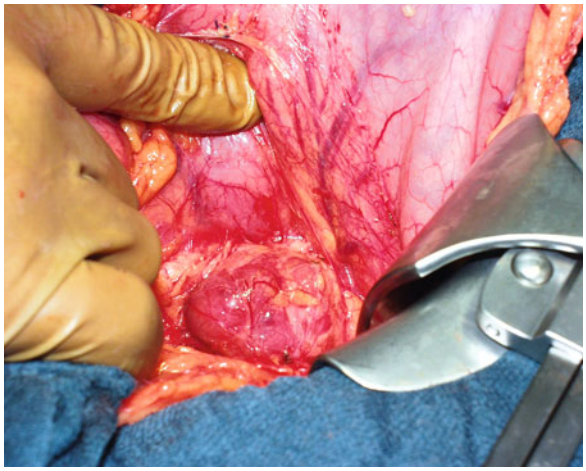

Fig. 35.7 Intraoperative view of an insulinoma in the middle of the pancreas in a 17-year-old female with the MEN 1 syndrome

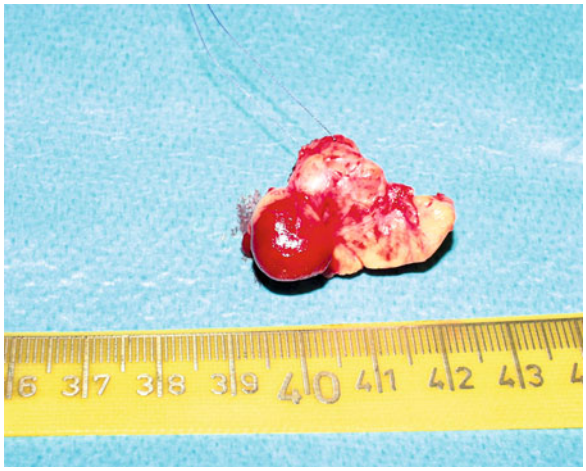

Fig. 35.8 Specimen of an insulinoma of a 14-year-old male with the MEN 1 syndrome

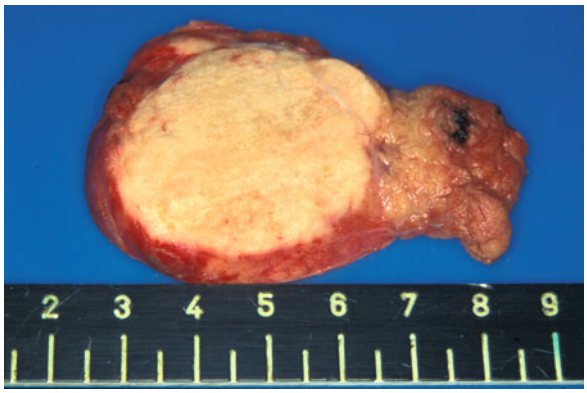

Fig. 35.9 Gross features of pancreatic endocrine neoplasm: well-circumscribed, *white-yellow* nodule without necrosis

Table 35.2 Classification of pancreatic endocrine tumors (Solcia et al. 2000, WHO 2000)

Well-differentiated endocrine tumor
Functioning
Insulin-producing (insulinoma)
Glucagon-producing (glucagonoma)
Somatostatin-producing (somatostatinoma)
Gastrin-producing (gastrinoma)
VIP-producing (VIPoma)
Others
Non-functioning
Microadenoma (<0.5 cm)
Others
Well-differentiated endocrine carcinoma
Functioning
Insulin-producing (insulinoma)
Glucagon-producing (glucagonoma)
Somatostatin-producing (somatostatinoma)
Gastrin-producing (gastrinoma)
VIP-producing (VIPoma)
Serotonin-producing with carcinoid syndrome
ACTH-producing with Cushing syndrome
Non-functioning
Poorly differentiated endocrine carcinoma – small- cell carcinoma
Mixed exocrine–-endocrine carcinoma
VIP, vasoactive intestinal peptide; ACTH, adrenocorticotropic hormone

Table 35.3 Recent classification of neuroendocrine neoplasms of the gastrointestinal tract including pancreas (WHO 2010)

Nomenclature	Features
1. Neuroendocrine Tumour Grade 1 (carcinoid)	Well-differentiated, Ki-67 Index <2%, < 2 mitoses / 10 HPF
2. Neuroendocrine Tumour Grade 2	Well-differentiated, Ki-67 Index <20%, < 20 mitoses / 10 HPF
3. Neuroendocrine Carcinoma	Poorly differentiated, small or large cell, Ki-67 Index >20%, >20 mitoses / 10 HPF
4. Mixed adenoneuroendocrine carcinoma (MANEC)	Epithelial and neuroendocrine components, at least 30% of either
5. Hyperplastic and preneoplastic lesions	

nodes and in the liver. In childhood, >90% of insulinomas are benign (Fig. 35.10).

In contrast, *gastrinomas* in MEN 1 usually include a malignant potential, and more than half of them have metastasized at the time of diagnosis (Brandi

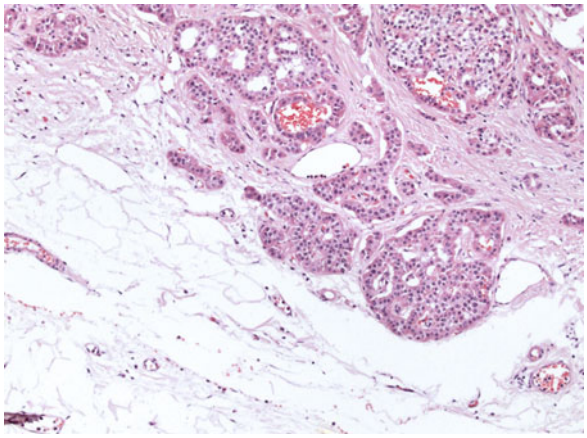

Fig. 35.10 Well-differentiated endocrine tumor composed of monomorphous round/oval cells arranged in nests (HE, ×200)

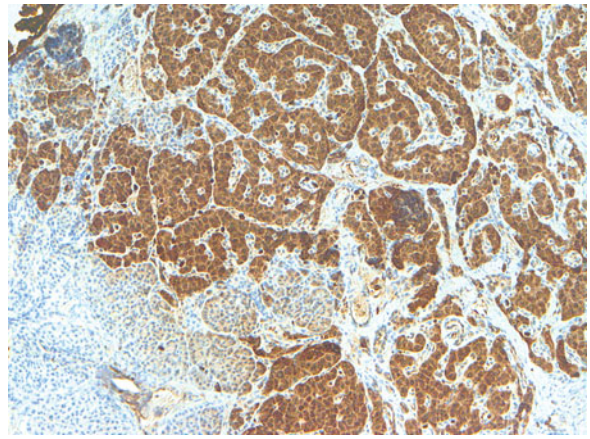

Fig. 35.12 Congenital hyperinsulinism (ancient name: nesidioblastosis) (IHC Proinsulin)

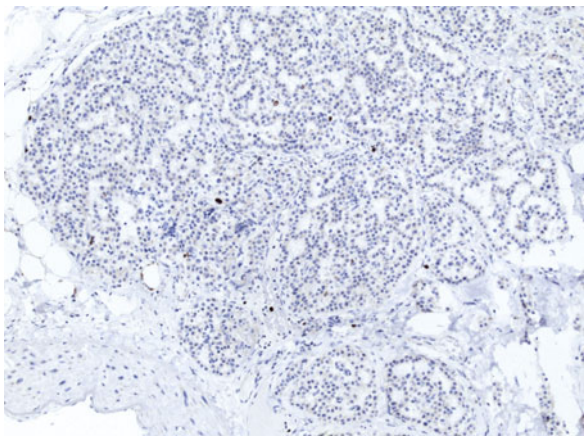

Fig. 35.11 Low proliferation rate in a well-differentiated endocrine tumor (Ki-67 immunostaining, ×200)

et al. 2001). Alike insulinomas, they are solid, well-defined encapsulated tumors (Fig. 35.11). Because of their malignant behavior, small size, multiplicity, and frequent localization in the duodenum, MEN-1-associated gastrinomas represent a diagnostic and therapeutic challenge (Norton et al. 2001).

35.3.3.1 Congenital Hyperinsulinism

Congenital hyperinsulinism – formerly called nesidioblastosis – is defined by morphologic changes in the endocrine pancreas causing hyperinsulinemic hypoglycemia in the absence of an insulinoma. Focal congenital hyperinsulinism is not a neoplastic lesion and represents the most important differential diagnosis of insulinoma. Congenital hyperinsulinism is caused by impaired control of insulin secretion from functionally defective pancreatic beta cells. The defect of the beta cells resides in the glucose recognition system. In most cases of focal congenital hyperinsulinism, there is a general paternal mutation of the K_{ATP} channels on the cellular level and a maternal loss of heterozygosity only in the cells of the focal lesion (deLonlay 2006). Morphologically, there is a diffuse or focal hypertrophy of beta cells (Anlauf et al. 2005) that are macroscopically not recognizable. The histological diagnosis is based on immunohistochemical detection of insulin in the hypertrophic Langerhans' islets (Fig. 35.12).

35.3.4 Acinar Cell Carcinoma (ACC)

Acinar cell carcinomas (ACC) arise from the exocrine acinar cells secreting the pancreatic enzymes. They show similarity to pancreatoblastomas harboring LOH on chromosome 11p in 50% of cases and alterations of the APC/β-catenin signaling pathway in 24% (Abraham et al. 2002). ACCs are large tumors at presentation, averaging 10 cm in diameter. Most ACCs are subdivided by large fibrotic septa and show pushing borders. Frequently, there is a nodular infiltration in the surrounding tissues and vessels. Necrotic areas are typical. Histologically, ACCs are solid but may exhibit a wide range of cell types: acinar, monotonous endocrine-like, trabecular, cystic, or even hepatoid differentiation (Sipos and Kloppel 2005). The mitotic activity is usually high (>50/10 HPF) (Abraham et al. 2002).

Immunohistochemically, pancreatic enzymes such as trypsin, chymotrypsin, and amylase are expressed in ACCs.

35.3.5 Ductal Adenocarcinoma

Ductal adenocarcinoma is the most frequent malignant pancreatic tumor in the adult age group, but is extremely rare in childhood (Grosfeld et al. 1990; Perez et al. 2009). Most cases date to the pre-immunohistochemical era and are usually not well documented. It has been speculated that in ancient reports, some SPNs or pancreatoblastomas had been misinterpreted as pediatric ductal adenocarcinoma (Shorter et al. 2002; Luttges et al. 2004). Nevertheless, according to the SEER registry, ductal adenocarcinomas of the childhood were associated with adverse outcome, exhibiting a 15-year-survival rate of 23% (Perez et al. 2009).

35.3.6 Benign Tumors

35.3.6.1 Inflammatory Myofibroblastic Tumor

Inflammatory myofibroblastic tumors represent a range from truly mesenchymal tumors to reactive-inflammatory lesions. This enigmatic tumor consists of myofibroblasts admixed with inflammatory cells, predominantly with plasma cells and lymphocytes. The proliferation rate is low. It does not show a malignant behavior but is able to grow by infiltration. After incomplete resection, the rate of local recurrence is high (Mizukami et al. 2006).

35.3.6.2 Teratoma

Like in other locations, teratomas in the pancreas show components of all three germinal sheets (Mester 1990). Most of the cases published so far have been dermoid cysts (Kela 2008). Please also refer to Chap. 39 (Germ cell tumors).

35.3.6.3 Mucinous Cystic Neoplasm (MCN)

Mucinous cystic neoplasm is very rare in childhood. In adults, virtually all tumors arise in women located in the pancreatic corpus and tail. By imaging, it is difficult to distinguish from pseudocysts or other cystic tumors (Fukushima and Fukayama 2007). MCNs have no connection to pancreatic ducts. Microscopically, the solitary or multiple cysts are lined by tall, columnar epithelium with mucin secretion. The intra-cystic connective tissue resembles ovarian stroma by conventional histopathology and also by immunohistochemistry, exhibiting expression of estrogen and progesterone receptors as well as α-inhibin. In mucinous cystic neoplasms, the classical sequence from dysplasia and adenoma to carcinoma is well known. This is associated with a loss of tumor suppressor genes Smad4 and p53 and an increasing frequency of K-ras oncogen mutations (Fukushima and Fukayama 2007; Garcea et al. 2008). In children, no malignant transformation has been reported to date.

35.3.6.4 Fibrous Focus

Chronic pancreatitis can result in circumscribed fibrotic indurations in the pancreas which may mimic a tumor. Pancreatitis in childhood can originate from cholelithiasis, choledochal cysts, pancreas divisum, medication, metabolic diseases, hemolytic-uremic syndrome, viral diseases (mumps and coxsackie), and hereditary chronic pancreatitis of childhood with mutations in the PRSS1 gene (Chung et al. 2006; Rebours et al. 2009). Hereditary pancreatitis is frequently associated with an adenocarcinoma of the pancreas later in life.

35.3.6.5 Pancreatic Pseudocysts

Pancreatic pseudocysts are by far the most common cystic lesions in the pediatric pancreas. In most cases, they originate from blunt abdominal trauma, rarely from chronic pancreatitis.

35.4 Diagnosis of Pancreatic Tumors

35.4.1 Clinical Presentation

Pancreatic tumors in children normally present with a palpable mass, abdominal pain, or general symptoms like weight loss, fatigue, and mild gastrointestinal problems (Lack et al. 1983; Klimstra et al. 1995; Shorter et al. 2002). As tumors can arise at any site within the pancreas and origin from the ductal epithelium is rare, jaundice is less often seen in adults (Lack 1989; Shorter et al. 2002). Many cystic tumors are incidentally discovered, some after blunt abdominal trauma (Rebhandl et al. 2001). Most children with a pancreatic malignancy present with advanced tumors. In case of a tumor arising from the head of the pan-

Table 35.4 Diagnostic strategy in pediatric pancreatic tumors

Procedure	Specific questions
Clinical assessment	
Physical examination	Mostly mild and unspecific (gastrointestinal) symptoms, but also signs of obstruction of duodenum, gastric outlet, biliary tract or venous obstruction, palpable mass
Laboratory assessment	
– Hepatic function: Bil (dir. + indir.), AP, γ-GT, GOT, GPT, total protein, albumin	Elevated in case of obstructive jaundice
– Calcium, parathormone, prolactin, chromogranin A, and a hormone profile including insulin, proinsulin, VIP, gastrin, somatostatin, glucagon	In case of suspected endocrine active tumor
– LDH, amylase, lipase	Unspecific marker
– AFP	Pancreatoblastoma
– NSE	Sporadically elevated in SPN
– CA 19.9	Pancreatic ductal adenocarcinoma, sporadically elevated in SPN; not suitable to detect early stages, may be used to monitor for cancer recurrence; also elevated in chronic pancreatitis, benign obstructive jaundice, cystic lesions
– CEA	Assists with evaluating pancreatic cysts as benign or malignant
– CA 125	Pancreatic ductal adenocarcinoma
– Pancreatic oncofetal antigen	Pancreatic ductal adenocarcinoma
– Catecholamines	Exclusion of neuroblastoma, sporadically elevated in SPN
– Blood count	Exclusion of hematologic malignancy
Radiographic assessment	
Abdominal ultrasound and MRI	Tumor size, localization and tumor borders, consistency, presence of cystic and solid components, necrosis, calcification, hemorrhage, dilatation of the pancreatic and bile duct, local and vascular infiltration, ascites, lymphadenopathy, and liver metastases
Abdominal CT and MRI	Site, tumor size, organ of origin, cystic structures or calcification, ascites, obstruction, or invasion of other organs
Chest CT	Lung metastases
CNS MRI	CNS metastases
Bone scan	Skeletal metastases
Histologic assessment	
See above for details	Classification according to WHO
Genetics	
MEN 1	Gastrinoma
KRAS2 gene	Ductal adenocarcinoma
PRSS1 gene	Familial chronic pancreatitis
Other assessments	
Secretin test	In case of suspected gastrinoma
Fasting blood glucose	In case of endocrine active tumor
Screening methods	
Screening tests	Not available, currently ongoing research: e.g., Johns Hopkins Medicine (http://pathology.jhu.edu/pc/BasicScreening.php?area=ba)

creas, the patient might present with mechanical obstruction of the duodenum and gastric outlet, jaundice, and gastrointestinal bleeding. However, these symptoms are rare in childhood, most likely due to the soft consistency of the tumors. Varices, hemorrhage, and ascites, possibly resulting in hepatic failure, may be seen due to venous obstruction (Pappo and Furman 2006). In case of acinar cell carcinoma, painful, subcutaneous nodules and polyarthritis might be seen, which is caused by elevated lipase secretion by the tumor (Klimstra et al. 1992). Functioning endocrine tumors may produce hormones and lead to specific symptoms

related to the active hormone being produced. In case of insulinoma, hypoglycemic symptoms, which might manifest as weakness, fatigue, change in behavior, confusion, seizures, or coma, are seen (Field 1993). Blood glucose levels under 50 mg/dl, hypoglycemia in case of fasting, and immediate disappearance of symptoms with intravenous administration of glucose are typical symptoms. Serum insulin levels are elevated with a higher proportion of proinsulin (Field 1993). Gastrinoma causes the Zollinger–Ellison syndrome with gastric hyperacidity, multiple and recurrent peptic ulcers in uncommon locations, gastroesophageal reflux, and diarrhea (Zollinger 1987). Another functioning islet cell tumor exceedingly rarely seen in children is the VIPoma causing Verner–Morricon syndrome (massive watery diarrhea, hypokalemia, and achlorhydria) (Grosfeld et al. 1990; Chung et al. 2006) (Table 35.4).

35.4.2 Laboratory

In pancreatic tumors in childhood, the routine laboratory tests are of little value. Often there are no abnormal laboratory findings, no evidence of pancreatic insufficiency, cholestasis, impaired liver function, or endocrine syndrome. Even lactate dehydrogenase in the serum is rarely elevated. Anyway, alpha-fetoprotein (AFP) is increased in 68% of cases of pancreatoblastoma and can serve as a tumor marker. In case of solid-pseudopapillary neoplasm, elevated serum levels of neuron-specific enolase (NSE) and CA 19.9 as well as elevation of urinary vanillylmandelic and homovanillic acids have been reported in sporadic cases (Casanova et al. 2003).

If cystic lesions are present, the differential diagnosis between pseudocysts, true cysts (von Hippel–Lindau, cystic fibrosis, and lymphoepithelial cyst), and cystic tumors (SPN, cystic pancreatoblastoma, and cystic teratoma) can be very difficult (Correa-Gallego et al. 2010). Pseudocysts are the most frequent cystic lesions encountered (70%) (Singhal et al. 2006). A cystic tumor can be suspected if there is no history of pancreatitis or blunt abdominal trauma; if the cyst has thick walls, septa, and lobuli; if there is no connection to the pancreatic duct; and if cystic fluid shows low level of amylase (Chung et al. 2006). The detection of elevated tumor markers like CEA and CA 19.9 in the cystic fluid shows low sensitivity and high specificity.

If an endocrine active tumor is suspected, fasting blood glucose and MEN-1-associated parameters calcium, parathormone, prolactin, chromogranin A, and a hormone profile including insulin, proinsulin, VIP, gastrin, somatostatin, and glucagon should be assessed. In suspected gastrinoma, a secretin test is performed.

35.4.3 Imaging

The first-line tool is ultrasonography on suspicion of a pancreatic mass. Tumor size, localization and tumor borders, consistency, presence of cystic and solid components, necrosis, hemorrhage, dilatation of the pancreatic and bile ducts, local and vascular infiltration, lymphadenopathy, and liver metastases can be demonstrated (Montemarano et al. 2000). The value of sonography, however, largely depends on the personal experience of the examiner. Anyway, the examination of the pancreas by ultrasonography is often impaired by air superposition in the bowel, so that CT or MRI may be of assistance regarding localization, extension of the lesion, and presence of metastases. In the case of suspected pancreatoblastoma, CT or MRI is mandatory for precise staging. However, lymph node metastasis or duodenal or vascular infiltration by the tumor may be missed even using up-to-date imaging methods (Montemarano et al. 2000; Chung et al. 2006). A preoperative ERCP or MRCP is indicated if there is a dilatation of the bile or pancreatic duct.

The value of the ^{18}Fluorodeoxyglucose-PET-CT for the diagnosis of a pediatric pancreatic tumor is not known so far. In the adult age group, the ^{18}F-PET-CT was able to distinguish between malignant and benign pancreatic lesions (Herrmann et al. 2008). If endocrine tumors are clinically suspected, PET-CT with new, innovative tracers (^{18}F-L-DOPA, ^{68}Ga-DOTATOC, and ^{11}C-5-Hydroxytryptophane) has been giving promising results (Orlefors et al. 2005; Kauhanen et al. 2007; Tessonnier et al. 2010). If congenital hyperinsulinism is suspected, an ^{18}F-L-DOPA-PET-CT is able to distinguish between diffuse and focal forms and in the latter case to localize the focus exactly (Barthlen et al. 2008).

Skeletal scintigraphy is indicated for pancreatoblastoma to look for bone metastasis. If an endocrine tumor is suspected, a somatostatin receptor scintigraphy (^{111}In-DTPA-DPhe-octreotide) can aid to establish the diagnosis and localize the tumor. Especially for gastrinomas which are often small, multiple, and submucous

Table 35.5 Imaging characteristics of pancreatoblastoma and solid-pseudopapillary neoplasm

Pancreatoblastoma	Solid-pseudopapillary neoplasm
– Child <10 years	– Young female adolescent
– Well-defined, solitary lesion in the pancreas of considerable size	– Usually large, well circumscribed
– Half of the cases occurring in the head of the pancreas	– Equally distributed over the pancreas
– Heterogenous tumor with septa and few calcifications, hemorrhagic and necrotic areas, simultaneous solid and cystic areas	– Heterogenous tumor with simultaneous occurrence of solid, cystic, hemorrhagic, and necrotic areas in the tumor; calcification in the tumor capsule
– Metastasis in regional lymph nodes and liver (up to 50%)	– No metastasis
– Well-vascularized tumor without hemorrhage	– Well-vascularized tumor with hemorrhage
– Rare dilatation of the choledochal duct	– Very rare dilatation of the choledochal duct
– Fibrous capsule	– Thick, fibrous tumor capsule
– Often compressing nearby organs without invading them	– Compression of adjacent structures is more often seen than invasion

in the duodenal wall, the somatostatin receptor scintigraphy became an important diagnostic tool (Norton et al. 2001; Yeung and Pasieka 2009). Functional localization of gastrinomas, measuring gastrin gradients, is performed by hepatic venous sampling after the selective intraarterial injection of secretin (Norton et al. 2004) (Table 35.5).

35.4.4 Biopsy

In most cases of a pancreatic tumor in childhood, it will be impossible to establish a diagnosis from imaging alone. There have been cases of pancreatoblastoma which have been misinterpreted as intraperitoneal cysts prenatally (Sugai et al. 2006). In principle, a tumor biopsy would be advantageous before making a decision for therapy. This biopsy could be done by fine-needle aspiration (Nadler et al. 2002), by laparoscopy (Metzelder et al. 2007), or by open incision. In fine-needle aspiration, however, the amount of tissue obtained is often very small. A definitive diagnosis is difficult to establish, especially concerning the heterogeneity of most pancreatic tumors in childhood. Biopsy by laparoscopy for diagnostic purposes is a well-accepted strategy in pediatric surgery (Metzelder et al. 2007). However, the assessment of resectability of a pancreatic tumor by laparoscopy is by far more difficult than by the open approach. The risk of misinterpretation, therefore, is increased and the chance of a complete healing in the first step is decreased. Additionally, there is the possibility of tumor cell spillage by the CO_2 insufflation. A tight closure of the tumor capsule after the biopsy by laparoscopy is technically demanding. Several cases of local or disseminated peritoneal recurrences of an SPN after laparoscopic biopsy have been reported, even in case of clear margins in initial resection (Fais et al. 2009). Therefore, and with the exception of small, localized tumors in the pancreatic tail which can be resected by laparoscopy, a primary open approach for the definite diagnosis and treatment of pancreatic tumors in childhood and adolescence of unknown biological behavior is strongly recommended.

35.4.5 Staging

The TNM staging system is not used for the very heterogeneous group of pediatric pancreatic and endocrine tumors, and currently no other staging system is in common use (AJCC 2006). Anyway, for endocrine tumors, the WHO classification combines different clinical prognostic factors to differentiate between well-differentiated endocrine tumors with benign or uncertain behavior, well-differentiated endocrine carcinoma, and poorly differentiated endocrine carcinoma (see Table 35.3). In most cases, they are endocrinally active, though with more advanced diagnostical and surgical methods, the percentage of nonfunctioning islet cell tumors has risen in the last 10 years (Anlauf et al. 2005). The active polypeptide can produce clinical symptoms (functioning or hyperfunctioning islet cell tumors) or not (nonfunctioning or clinically silent tumor). Functioning islet cell tumors are further classified into insulinomas, glucagonomas, somatostatinomas, gastrinomas, and vasoactive intestinal polypeptide tumors according to the hormone they produce (see also Table 35.4). In case of production of more than

one hormonally active peptide, clinical symptoms are related to one hormone being predominant. Under all types of functioning islet cell tumors, insulinoma (47%) and gastrinoma (30%) are most often seen (Chung et al. 2006). Microadenomas are tumor nodules with a diameter of less than 0.5 cm, which is the minimum size required for gross detection.

35.5 Treatment of Pancreatic Tumors

Though treatment strategies for pancreatic tumors in children mainly have to be derived from experience in adults, more and more experience is available to understand specific treatment approaches for children and adolescents. The treatment mainly relies on complete resection as most tumors are considered to be not or a little radio- or chemosensitive (Pappo and Furman 2006). An exception seems to be pancreatoblastomas that proved to be sensitive to chemotherapy (Klimstra et al. 1995; Murakami et al. 1996; Chun et al. 1997; Defachelles et al. 2001). Anyway, metastases might occur in several entities, and systemic therapy therefore has to be considered.

35.5.1 Surgical Therapy

With the rare exception of unequivocally proven unresectability and metastasis, all pancreatic tumors must be treated surgically in curative intention. The surgical procedure depends on the malignancy of the tumor and the location. In case of a tumor of the tail or body, a distal pancreatic tail resection with preservation of the spleen can be performed. This can be done conveniently by a laparoscopic approach. The standard surgical procedure for tumors of the head of the pancreas is the Whipple procedure (partial pancreatoduodenectomy), although a less radical resection like pylorus-sparing partial pancreatoduodenectomy (Traverso-Longmire), partial pancreatic resection, or even enucleation might be more adequate in some cases. Patients also seem to profit from tumor debulking in case of unresectability.

35.5.1.1 Surgical Approach

After a transverse laparotomy, the omental bursa is opened, and the situation is evaluated:

- Is an enucleation or a local resection of the tumor possible?
- Is there evidence of peritoneal infiltration or of local or liver metastasis?
- Is there evidence of an infiltration of the duodenum, the choledochal duct, the porta hepatis, the caval vein, or the superior mesenteric vessels?

If the tumor seems to be resectable, it should be removed totally even without knowledge of the histological diagnosis (Perez et al. 2009; Snajdauf et al. 2009). Open biopsy should only be performed in all cases that would necessitate extended surgery (e.g., partial duodenopancreatectomy) for complete resection. The final histopathological diagnosis should be awaited. Frozen sections are valuable for detection of residual tumor cells in the resection margins. However, final diagnosis may not be achieved in all cases because of the necessity of additional immunohistochemical examination in certain tumors (SPN vs. endocrine; pancreatoblastoma/ACC vs. endocrine) Intraoperative tumor cell spillage, however, must be strictly avoided. The tumor capsule must be closed carefully after the biopsy.

35.5.2 Therapy and Prognosis of Specific Entities

35.5.2.1 Pancreatoblastoma

Patients with pancreatoblastoma have good chances for cure if radical resection of all vital tumor tissue is performed (Brennan et al. 2004; Saif 2007; Perez et al. 2009; Yu et al. 2009). In most cases, the tumor is located ventrally in the pancreatic head, surrounded by a capsule and has no connections to the duct system. Therefore, a local resection without mutilating surgery is possible in many cases, achieving tumor-free margins (Dhebri et al. 2004). Radical lymph node dissection is necessary in every case because the prognosis of the patients gets worse if a lymph node metastasis develops after tumor resection (Dhebri et al. 2004). If R0 resection has been achieved and serum AFP level is normal, no further therapy and close clinical follow-up are indicated. Anyway, surgical intervention should be performed only by experienced surgeons who are familiar with the technique of partial duodenopancreatectomy as well. The pylorus-preserving strategy of Traverso-Longmire has to be preferred because the quality of life is significantly better than that after a classical Whipple operation.

Though the mainstay of treatment is complete surgical resection, patients often present with metastases and/or unresectable tumor at the time of diagnosis, and

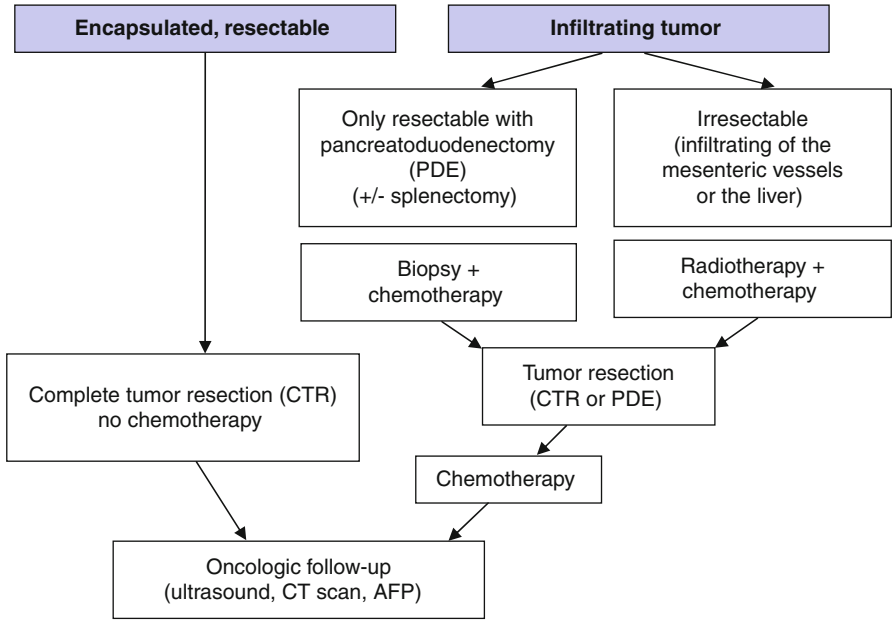

Fig. 35.13 Possible treatment regimen for encapsulated and infiltrating pancreatoblastomas as presented by Vossen et al. (1998)

therefore preoperative chemotherapy treatment might be needed and in fact has lead to marked tumor reduction in several cases (Defachelles et al. 2001). Anyway, the most effective chemotherapy for pancreatoblastoma is not known, and a variety of different regimes have been used so far (Dhebri et al. 2004). The PLADO regime (cisplatin and doxorubicin) as recommended for hepatoblastoma in the SIOPEL study (Ogawa et al. 2000; Perilongo et al. 2000) or a combination of cisplatin, etoposide, ifosfamide, and adriamycin might be considered for treatment (Vossen et al. 1998) (Fig. 35.13). So far, it is not known whether chemotherapy results in improved survival rates and whether adjuvant chemotherapy is successful in resected cases (Shorter et al. 2002). Also, the role of radiotherapy remains unclear though response to irradiation in case of recurrent or incompletely resected pancreatoblastoma has been reported (Griffin et al. 1987; Murakami et al. 1996; Defachelles et al. 2001). Surgical resection of liver metastases should be considered (Grosfeld et al. 1990; Murakami et al. 1996).

35.5.2.2 Prognosis

Approximately one-third of the reported cases of all age groups present with metastases to the liver and abdominal lymph nodes and less common to the lung, brain, and peritoneum (Klimstra et al. 1995; Imamura et al. 1998; Gupta et al. 2000; Montemarano et al. 2000). While in adults pancreatoblastoma is reported to be fatal, especially in case of metastases and unresectability (Dhebri et al. 2004), the tumor seems to behave less aggressively in pediatric patients, showing a better outcome (5-year-survival 50%) (Kohda et al. 2000; Defachelles et al. 2001; Saif 2007). The latest analysis of the EXPeRT group even reported a 5-year event-free survival and overall survival of 58.8% and 79.4%, respectively. Outcome did not correlate with tumor site and size but was influenced by tumor stage and by the feasibility of complete resection. The response rate to chemotherapy was 73% (Bien et. al 2011). Long-term survival after response to radiation and chemotherapy in case of metastatic disease is reported (Griffin et al. 1987; Vannier et al. 1991; Klimstra et al. 1995; Murakami et al. 1996; Vossen et al. 1998; Ogawa et al. 2000; Dhebri et al. 2004). Anyway, recurrence is common (60%) even after complete surgery; therefore, close follow-up is necessary (Shorter et al. 2002).

35.5.2.3 SPN

Specific treatment experience for children does not exist. Because of the low grade of malignancy of SPNs and the existence of a fibrous capsule, an enucleation of the tumor might be sufficient, especially in pediatric cases (Grosfeld et al. 1990; Matsunou and Konishi 1990; Jaksic et al. 1992; Wunsch et al. 1997). But as metastatic and local recurrence does occur in case of incomplete resection or enucleation, complete resection

with save margins should be the aim (Todani et al. 1988; Sclafani et al. 1991; Klimstra et al. 2000; Zhou et al. 2001; Papavramidis et al. 2005). If the tumor is not excised completely, the rate of local recurrence is very high (73%), and the almost 100% survival rate after R0 resection decreases dramatically (Campanile et al. 2011). Papavramidis et al. reported that complete resection of SPN was achieved by local excision in 22%, by pancreatic tail resection in 40%, by a Whipple resection in 22%, and by a Traverso-Longmire partial duodenopancreatectomy in 4% of the cases (Papavramidis et al. 2005). Anyway, radical local approaches or extensive lymphatic dissection are not necessary, and tumor size, recurrence, and limited metastases as well as local invasion (for example, into the portal vein or superior mesenteric artery) should not lead to the conclusion of unresectability (Jeng et al. 1993; Martin et al. 2002). Some of these patients can survive more than 10 years after surgery (Kaufman et al. 1986; Nishihara et al. 1993a; Mao et al. 1995; Papavramidis et al. 2005).

If a central pancreatic resection has to be performed, the drainage of the tail must be accomplished by a Roux-en-Y jejunal loop or a pancreaticogastrostomy (Fisher et al. 2007). If the portal vein, the mesenteric vein, or the venous confluens are infiltrated, a bypass can be constructed using jugular vein graft or a Goretex graft (Goh et al. 2007; Sperti et al. 2008). The spleen should be preserved in childhood in any case to avoid the overwhelming post-splenectomy infection (OPSI) syndrome.

Laparoscopic tumor biopsy is not recommended in suspected SPN because of the risk of tumor cell spillage (Fais et al. 2009). Surgical treatment for metastases should be considered, especially single liver metastases often can be resected (Nishihara et al. 1993b; Ogawa et al. 1993; Panieri et al. 1998; Klimstra et al. 2000; Saiura et al. 2000; Martin et al. 2002). Patients profit from debulking if complete resection is not possible (Todani et al. 1988; Sclafani et al. 1991; Nishihara et al. 1993a; Mao et al. 1995; Wang et al. 1998; Papavramidis et al. 2005). In case of a local recurrence of an SPN, even multiple resections may be of value because the overall prognosis of this slowly growing tumor is excellent (Tipton et al. 2006; Goh et al. 2007; Perez et al. 2009). The role of chemotherapy and radiotherapy in SPT is not known. Rebhandl et al. report successful postoperative treatment of a pediatric patient with metastasized SPN with ifosfamide, cisplatin, and VP16 (Rebhandl et al. 2001). Gemcitabine (Maffuz et al. 2005) and a combination of cisplatin and 5-fluorouracil (Strauss et al. 1993) have been successfully used as preoperative chemotherapy regime in two adult patients with unresectable SPN. Also, radiotherapy might be of value in cases of unresectable tumors (Fried et al. 1985; Matsunou and Konishi 1990; Rebhandl et al. 2001).

As diagnosis might not be established until intraoperative frozen section biopsy, the surgeon and pathologist should be aware of this entity as correct diagnosis might lead to a different surgical approach in case of SPT.

35.5.2.4 Prognosis

Unlike other malignant pancreatic tumors occurring in children, solid-pseudopapillary neoplasms show a slow-growing, low malignant behavior and therefore have an excellent prognosis with surgery alone. Approximately 85% of the patients present with local disease (Mao et al. 1995; Wang et al. 1998; Klimstra et al. 2000), and 95% of these patients can be cured by complete surgical excision (Kaufman et al. 1986; Mao et al. 1995; Papavramidis et al. 2005). In the case of recurrence (6.6%) tumor spread to liver or peritoneum and more rarely to lymph nodes, lung and skin are seen (Rebhandl et al. 2001; Papavramidis et al. 2005). In single cases, repeated surgery for local recurrence and metastasis has proved to be of value (Rebhandl et al. 2001). Metastases occur late (average disease-free survival of 8.5 years) (Gonzalez-Campora et al. 1995; Lam et al. 1999) and are seen more often in older women (Todani et al. 1988; Matsunou and Konishi 1990; Nishihara et al. 1993a; Wang et al. 1998; Zhou et al. 2001). Anyway, until now it is not known if prognosis in children is different from prognosis in adults as specific survival data do not exist.

35.5.2.5 Endocrine Tumors

While 90% of insulinomas are benign, this is the case for only 40% of gastrinomas and 20–30% of glucagonomas (Grosfeld et al. 1990). Large tumors might have metastasized at the time of diagnosis, and metastases may also occur many years after diagnosis (Buetow et al. 1995). Different parameters for prediction of biological behavior and outcome have been found: tumors larger than 2–3 cm, tumor necrosis, well-differentiated tumors, vascular and perineural invasion, high mitotic count, high proliferation, and tumor biology (insulinoma vs. non-insulinoma) have

been strongly correlated with malignant behavior (Donow et al. 1990; La Rosa et al. 1996; Hochwald et al. 2002).

The short-term therapy of insulinoma is to prevent severe hypoglycemia including administration of high-dose glucose i.v. and glucagon and octreotide s.c. In case of gastrinoma, conservative therapy to alleviate symptoms consists of oral PPI. The best long-term survival has been seen in case of complete surgical resection, absence of liver metastases, or aggressive treatment of them, if present (Chu et al. 2002); 90% of insulinomas and most gastrinomas present as solitary mass and therefore can be cured by complete resection alone (Service et al. 1991). Usually, insulinomas are well circumscribed and can be enucleated without touching the pancreatic duct. If an insulinoma is located in the pancreatic tail, a spleen-preserving left resection is indicated. It can be completed, if necessary, by enucleation of additional tumors in the pancreatic corpus or head (Bartsch et al. 2000). If insulinoma cannot be localized, intraoperative ultrasound should be performed.

In case of MEN 1, therapy is complicated by often multiple pancreatic neuroendocrine tumors (Service et al. 1991; Mergo et al. 1997). Therefore, during surgery, the pancreas must be carefully scrutinized with inspection, bimanual palpation, and intraoperative sonography from the uncinate processus to the tip of the tail in order to find and resect all existing tumors. A systematic lymphadenectomy like in pancreatoblastoma, however, is not routinely recommended in insulinoma.

As most of the gastrinomas occur in the so-called gastrinoma triangle around the head of the pancreas, resection for gastrinoma has to involve this area (Machado et al. 2001). As long as additional gastrinomas in the duodenum are excluded, a duodenopancreatectomy is not necessary in most cases (Bartsch et al. 2000; Brandi et al. 2001). A duodenotomy, however, is performed as a routine since duodenal gastrinomas frequently escape preoperative imaging (Norton et al. 2004). MEN-1-associated gastrinomas present multiple, small nodules in the duodenum. Therefore, duodenotomy with transillumination is mandatory (Norton et al. 2004). However, the role of surgery is controversial in MEN-1-associated gastrinoma because complete cure by surgery is extremely rare.

Lymph node metastases are frequent (ca. 70%). An extended lymphadenectomy, therefore, must be performed in all cases of MEN-1-associated gastrinoma. Following these rules, young adults with advanced disease without disseminated distant metastases, who underwent surgical resection, showed comparable 15-year-survival rates (89–100%) to those with limited disease or without an identifiable tumor (Norton et al. 2001). Hypergastrinemia, however, persists in most cases.

Debulking and metastasectomy can diminish the associated endocrine syndrome and might therefore be appropriate (Shorter et al. 2002). Also, antihormonal pharmacologic therapy (for example, cimetidine in the ulcer-producing Zollinger–Ellison syndrome) has to be considered in these cases (Shorter et al. 2002). The role of chemotherapy and radiotherapy, though, is not clear.

35.5.2.6 Prognosis

In childhood, insulinomas usually show a benign biological behavior; therefore, the prognosis is very good. While 90% of insulinomas are benign, this is the case for only 40% of gastrinomas and 20–30% of glucagonomas (Grosfeld et al. 1990). Large tumors might have metastasized at the time of diagnosis, and metastases may also occur many years after diagnosis (Buetow et al. 1995). As the tumor is slow-growing, these patients might show long survival, which is 20–30% in cases of sporadic gastrinoma (Norton et al. 2004).

35.5.2.7 Other Rare Malignant Pancreatic Tumors

The acinar cell carcinoma probably grows less aggressivly in childhood than in adults (Klimstra et al. 1992; Shorter et al. 2002). The prognosis of the rare pediatric ductal adenocarcinoma is as bad as that in the adult age group (Ivy et al. 1990). Of utmost importance is the complete surgical resection. The impact of chemo- and radiotherapy is not clear (Shorter et al. 2002). The inflammatory myofibroblastic tumor (IMT) has a high tendency for local recurrence. A radical surgical resection, therefore, is of vital importance (Mizukami et al. 2006). Successful treatment using steroids has been described in single cases (Dagash et al. 2009).

35.5.2.8 Benign Tumors

The mucinous cystic adenoma is a benign tumor with the potential of malignant transformation and must be totally resected (Grosfeld et al. 1990). For hemangioma, there is an anecdotal report about a spontaneous regres-

sion after the biopsy (England et al. 2006). Teratoma must be totally resected. A circumscribed fibrotic focus associated with pediatric pancreatitis may mimic a neoplastic process (Adsay et al. 2004). This is one more reason why a mutilating resection should not be performed without knowing the final histological diagnosis.

Pancreatic pseudocysts have a high spontaneous healing rate. Initially, therefore, a wait-and-see policy is indicated. If the size does not decrease and symptoms persist, however, a drainage is necessary. This can be achieved by stent insertion directly into the cyst either percutaneously under sonograpic or CT control imaging (Cannon et al. 2009) or endoscopically via ERCP or through the gastric wall (Sharma et al. and Maharshi 2008). If this fails, an open or laparoscopic cystogastrostomy or cystojejunostomy can be performed (Seitz et al. 2006; Yoder et al. 2009). A cystic pancreatic tumor, however, must be excluded before the drainage (Cannon et al. 2009). If the history or the diagnostic findings are equivocal, there is the rule: better resect a cyst than drain a tumor!

35.5.2.9 Focal Congenital Hyperinsulinism

If the existence and location of a focal congenital hyperinsulinism have been confirmed by ^{18}F-DOPA-PET-CT, surgical resection is indicated. Initially, three small biopsies are taken from unaffected areas and examined as frozen sections to exclude diffuse congenital hyperinsulinism. Then, the focal lesion is excised by atypical excision under frozen section monitoring. If the lesion is located in the pancreatic tail, a left resection is indicated which can be done by laparoscopy. Care is taken to preserve as much pancreatic tissue as possible. The excision is finished if all resection margins of the remaining pancreas are clear. If the pancreatic duct is involved, it must be drained by a Roux-en-Y pancreaticojejunostomy (Barthlen et al. 2008).

35.5.2.10 Laparoscopy

There are numerous reports with reasonable patient numbers about laparoscopic pancreatic resections in benign and malignant disease (Palanivelu et al. 2007). In a study including 103 patients, the conversion rate was only 7% (Fernandez-Esparrach et al. 2007). For solid malignant tumors in childhood, however, these favorable results have not been reproducible (Warmann et al. 2003). The development of metastasis on the trocar sites seems to be quite rare. But even highly experienced centers report about high conversion rates in abdominal tumors (up to 42%) because a satisfying overview cannot be achieved (Metzelder et al. 2007). As outlined before, therefore, the laparoscopic approach for pediatric tumors in the pancreatic head and corpus is not recommended, neither for the biopsy (Fais et al. 2009) nor for the resection with curative intention (Spurbeck et al. 2004). An exception are small, delimited tumors in the pancreatic body or tail, which can be removed by pancreatic tail resection (Sokolov et al. 2009). Possible complications of pancreatic surgery are shown in table (Table 35.6). They are rare.

Table 35.6 Possible complications of pancreatic surgery (Adham et al. 2008)

Complications	
Postoperative bleeding	From the remaining pancreas, small vessels to the splenic vein, bleeding from the splenic vein, portal vein, superior mesenteric vein CAVE! Dangerous are arrosion bleedings after leaking of the suture line or septic complications
Thrombosis or ischemia	Of the splenic artery, splenic vein, portal vein, mesenterial vessels, choledochal duct (after close preparation with stricture)
Loss of the spleen	Due to bleeding or thrombosis with risk of overwhelming post-splenectomy infection (OPSI)
Insufficiency	Stump insufficiency of the pancreas after tail resection, insufficiency of the suture line of a pancreatojejunostomy with secretion of digestive juices, abscess, pseudocyst

35.6 Summary and Conclusions

In case of unspecific pain or a palpable mass in the upper abdomen, a pancreatic tumor should be considered, especially in adolescent females. Ultrasound examination in combination with MRT/CT is mandatory. Because imaging alone is not able to assure histological diagnosis, the tumor should be exposed by an open approach, and the possibility of a primary complete resection without extensive surgery should be evaluated. Laparoscopy is indicated in tumors confined to the pancreatic body and tail, which can be resected without touching the tumor itself. If a complete resection does not seem feasible, biopsy should be performed only. Extensive resections of the pancreas and adjacent organs in childhood are justified

only if they are beneficial for the child in knowledge of the histopathology and the staging. The surgical resection of local recurrences and metastases in childhood is always justified, even multiple times. The role of chemo- and radiotherapy currently is hard to define because only single-case reports have been published.

Endocrine tumors are characterized by their hormone profile, imaging, and scintigraphy. Insulinomas must be treated by surgery, whereas the cure rate of gastrinomas by surgery alone is very low, especially in MEN 1 patients.

Children with pancreatic tumors show generally better prognosis than adults, mainly because of a different histologic pattern of the tumors occurring in that age group, but even in the few cases of pediatric pancreatic carcinomas, better results have been observed. Underlying reasons for a different prognosis, e.g., differences in biology and/or genetic makeup over age groups, are still to be investigated.

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