Diseases of the Pancreas

9

Thomas K. Helmberger and Riccardo Manfredi

Learning Objectives

- To understand typical imaging criteria to identify and differentiate solid and cystic pancreatic structural changes and neoplasia.
- To understand the limitations of imaging in complex pancreatic diseases and
- To appreciate the importance of additional clinical information.

Modern cross-sectional imaging with high spatial and contrast resolution allows a perfect delineation of the pancreas in its retroperitoneal home. The organ typically presents itself with a length between 12 and 15 cm and a diameter at the head area of about 2.5 cm, at the body of about 2 cm, and at the tip of the pancreatic tale of about 1.5 cm. Anatomically, the pancreatic head is defined as the area to the right of the left border of the superior mesenteric vein, the body as the area between the left border of the superior mesenteric vein and the left border of the aorta, and the tail as the area between left border of the aorta and the hilum of the spleen. The normal pancreatic duct ranges between 1.5 mm at the tail to 3 mm at the head.

Usually (ca. 60% of cases) the pancreatic main duct (duct of Wirsung), the duct of Santorini, and the common bile duct join together within the pancreatic head, entering the duodenum via the papilla of Vater.

Several conditions that affect the function and integrity of the pancreas, as developmental anomalies, neoplastic and inflammatory diseases will be discussed.

9.1 Developmental Anomalies of the Pancreas

During embryogenesis, the pancreas is formed from a larger, dorsal bud (tail, body, parts of the head) and a small, ventral bud (rest of the head). The ventral bud migrates downwards dorsal from the dorsal bud. During the union of both the buds, the main pancreatic duct within the ventral bud ends via the duct of Santorini in the minor papilla. This duct gets then reduced to an accessory duct, whereas the main pancreatic duct of the dorsal bud merges with the duct of the former ventral bud ending in the major papilla [1, 2]. The disturbed union of the two buds can cause three major anomalies.

Pancreas divisum, a non-union anomaly of the pancreas is found in autopsy studies with a frequency of 1 to 14%, and is characterized by the separate drainage of the main pancreatic duct via the duct of Santorini into the minor papilla, and of the duct of Wirsung into the major papilla. Only 1% of individuals with pancreas divisum will develop unspecific abdominal symptoms (abdominal discomfort, most likely caused by recurrent episodes of mild pancreatitis). Therefore—without real proof—some authors consider pancreas divisum a promoting factor for pancreatic tumors based on recurrent and lately chronic focal pancreatitis [3].

In pancreas annulare, the-non-migration of the ventral bud of the pancreas causes the ventral and dorsal bud forming a ring around the duodenum. This rare anomaly (estimated prevalence 0.01%) can be associated with other birth deformities as congenital duodenal atresia, mesenterium commune, oral facial defects, and Down's syndrome. Clinical signs are determined by stenosis and occlusion of the duodenum.

T. K. Helmberger (✉)
Institute of Radiology, Neuroradiology and Minimal-Invasive Therapy, Muenchen Klinikum Bogenhausen, Academic Teaching Hospital, Technical University Munich, Munich, Germany
e-mail: thomas.helmberger@muenchen-klinik.de

R. Manfredi (✉)
Diagnostic Radiology and General Interventional Radiology at Diagnostic Imaging, Oncological Radiotherapy and Haematology, Fondazione Policlinico Universitario "A. Gemelli"—IRCCS Università Cattolica del Sacro Cuore, Rome, Italy
e-mail: riccardo.manfredi@unicatt.it

To reveal a union/migration anomaly of the pancreas, in most of the cases MRCP will add the crucial information of the distorted duct configuration.

The generally asymptomatic ectopic pancreatic tissue can be found in the stomach, duodenum, and ileum, very rarely in Meckel's diverticulum, gall bladder, bile duct, and spleen, whereas autopsy studies reveal a frequency between 0.6 and 15%. Typically, pancreatic ectopic tissue is detected by endoscopy.

Total agenesis of the pancreatic gland, hypoplasia of the pancreas (partial agenesis), congenital pancreatic cysts (dysontogenetic cysts, hamartosis), multiple congenital cysts associated with von Hippel-Lindau disease (cysts also in the liver and kidneys), and also cystic degenerative transformation of the pancreas in cystic fibrosis are in general rare and are identified by MRI, as well as by sonography and CT, based on the partial or complete missing of the organ or by solitary or multiple cysts [2, 4].

> **Key Point**
> The majority of pancreatic anomalies are asymptomatic. MRI and MRCP are superior in identifying the structural variants and to exclude suspected neoplastic conditions.

9.2 Pancreatic Neoplasms

Pancreatic tumors can be classified according to their cellular origin, enzymatic activity, and their benign or malignant potential. The most recent WHO classification (2010, revised 2012 und 2017) divides pancreatic tumors into primary epithelial and mesenchymal tumors, lymphomas, and secondary tumors; from a clinical-practical point of view tumor like lesions can be added (Table 9.1). In clinical reality, many of the rare and very rare tumors have no specific imaging appearance and can be differentiated only pathologically.

9.2.1 Pancreatic Carcinoma

Exocrine pancreatic carcinoma arising from ductal, acinar, and their stem cells accounts for 85–95% of all malignant pancreatic tumors (15–20% in gastrointestinal malignancies, 3% in all carcinomas), whereas most of the various subtypes of pancreatic carcinoma can be differentiated only by histo- and immunopathology. In general, the tumors are located predominantly in the pancreatic head (60–70%; body: 15% and tail: 5%). A multifocal or diffuse tumor spread is uncommon. The prognosis is poor—slightly better in mucinous, non-cystic CA, and worse in adenosquamous CA—since

Table 9.1 Classification of pancreatic lesions modified according to WHO classification, Pancreas (modified according to [5] and the 2017 update for neuroendocrine tumors [6])

Epithelial tumors	
Benign	Acinar cell cystadenoma **Serous cystadenoma**, not otherwise specified (NOS)
Premalignant lesions	Pancreatic intraepithelial neoplasia, grade 3 (PanIN-3) Intraductal papillary mucinous neoplasm (IPMN) with low- or intermediate-grade dysplasia Intraductal papillary mucinous neoplasm (IPMN) with high-grade dysplasia Intraductal tubulopapillary neoplasm (ITPN) Mucinous cystic neoplasm (MCN) with low- or intermediate-grade dysplasia Mucinous cystic neoplasm (MCN) with high-grade dysplasia
Malignant lesions	**Ductal adenocarcinoma** Adenosquamous carcinoma Mucinous adenocarcinoma (colloid, non-cystic) Hepatoid carcinoma Medullary carcinoma, NOS Signet ring cell carcinoma Undifferentiated carcinoma Undifferentiated carcinoma with osteoclast-like cells Acinar cell carcinoma Acinar cell cystadenocarcinoma **Intraductal papillary mucinous carcinoma (IPMN)** with an associated invasive carcinoma Mixed acinar-ductal carcinoma Mixed acinar-neuroendocrine carcinoma Mixed acinar-neuroendocrine-ductal carcinoma Mixed ductal-neuroendocrine carcinoma **Mucinous cystic neoplasm** (MCN) with an associated invasive carcinoma **Pancreatoblastoma** **Serous cystadenocarcinoma**, NOS **Solid-pseudopapillary neoplasm**
Neuroendocrine neoplasms	Nonfunctioning (nonsyndromic) neuroendocrine tumors (PanNEN G1/G2/G3) Pancreatic neuroendocrine microadenoma Non-functioning pancreatic neuroendocrine tumor Functioning (syndromic) neuroendocrine tumors (PanNEN G1/G2/G3) Insulinoma Glucagonoma Somatostatinoma Gastrinoma VIPoma Serotonin-producing tumors with and without carcinoid syndrome ACTH-producing tumor with Cushing syndrome Pancreatic neuroendocrine carcinoma (PanNEC G3, poorly differentiated neuroendocrine neoplasm) Mixed neuroendocrine non-neuroendocrine neoplasms (MiNEN) Mixed ductal neuroendocrine carcinoma Mixed acinar neuroendocrine carcinoma

Table 9.1 (continued)

Epithelial tumors	
Mesenchymal tumors	Lymphangioma, NOS Lipoma, NOS Solitary fibrous tumor Ewing sarcoma Desmoplastic small round cell tumor Perivascular epithelioid cell neoplasm
Lymphomas	Diffuse large B-cell lymphoma (DLBCL), NOS
Secondary tumors	Metastases
Tumor-like lesions	Acute pancreatitis Chronic pancreatitis Groove pancreatitis Autoimmune pancreatitis Cystic lesions Pancreas divisum Pancreas annulare

most tumors are detected late in an advanced stage of spread. An early metastatic spread along perivascular, ductal, lymphatic, and perineural pathways is promoted by the absence of a true capsule around the organ.

For detection, staging and follow-up after treatment endoscopic ultrasound, contrast-enhanced CT, MRI, and FDG-PET may be applied, whereas endoscopic ultrasound presents the highest accuracy in detecting small pancreatic head and periampullary tumors, and FDG-PET in detecting distant metastatic spread. Nevertheless, CECT and MRI provide a sufficient and comprehensive display of the primary tumor and its sequalae with an accuracy of about 90% and even more [7–9].

The imaging appearance of common pancreatic adenocarcinoma is determined by its typically dense, fibrous, low vascularized stroma resulting in low soft-tissue density in CT and low signal on T1-weighted and T2-weighted in MRI, and no or only minor contrast enhancement (Fig. 9.1) what makes the tumors best delineable to the normal glandular parenchyma on CE-imaging.

The pancreatic duct maybe involved depending on the primary tumor localization within the pancreas ranging from no duct involvement at all in peripheral tumors, over segmental obstruction due to intraductal tumor invasion (duct penetrating sign), to obstruction of both pancreatic and common bile duct (double duct sign) in pancreatic head tumors.

The relation between tumor and ducts is non-invasively seen best on MRCP.

Assessing potential invasive local growth, metastatic spread to local and regional lymph nodes, to the liver, and vascular invasion, completes staging of pancreatic malignancies (Fig. 9.1).

Not well-defined tumor margins and blurred surroundings are still a challenge for every imaging modality since microscopic local invasive peritumoral spread and an inflammatory desmoplastic reaction can often not be differentiated causing over- or underestimation of the T-stage of the tumor [10].

At the time of diagnosis of the primary, about two thirds of the patients will present distant metastases (lymph node metastases 40%, hematogenous metastases to the liver 40%, peritoneal metastases 35%) which will be detected with accuracies above 90% by CE-MRI and FDG-PET-CT [11, 12]. Non-resectability in pancreatic cancer is determined by vascular encasement of the superior mesenteric artery, the celiac trunk, hepatic or splenic artery, and peripancreatic veins which is very likely if a vessel circumference is encased more than 50% (typical signs: decreased vessel caliber, dilated peripancreatic veins, teardrop shape of superior mesenteric vein present).

9.2.2 Other Tumors of Ductal Origin

This heterogeneous group of tumors embrace cystic neoplasms, tumors neuroendocrine components, and a variety of very rare tumors as pancreatoblastoma and solid-pseudopapillary neoplasm.

> **Key Point**
> Pancreatic adenocarcinoma is the most common malignancy of the pancreas. CT and MRI are the established imaging tools for diagnosing the primary, staging the extent of the disease and to establish operability.
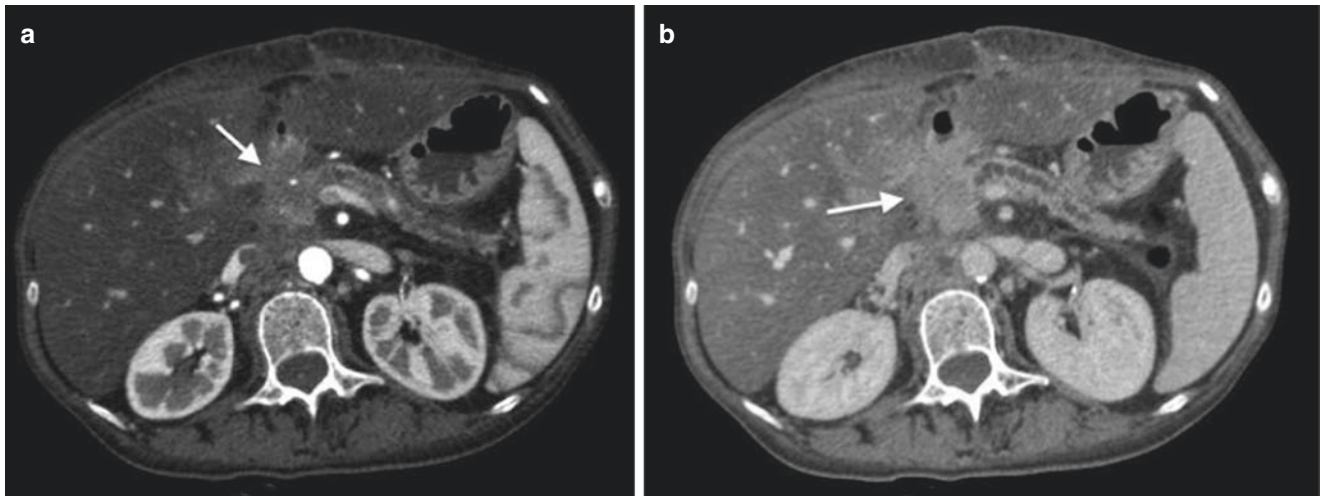
Fig. 9.1 (**a**, **b**) Adenocarcinoma of the head of the pancreas locally invasive. (**a**) Axial contrast-enhanced Computed Tomography (CT) during the pancreatic phase shows a hypovascular focal pancreatic lesion of the head, responsible of infiltration of the main pancreatic duct with obstructive chronic pancreatitis and infiltration of the peripancreatic fat (arrow). (**b**) Axial contrast-enhanced Computed Tomography (CT) during the portal venous phase shows infiltration of the posterior peripancreatic fat

9.3 Cystic Neoplasm

In modern high-resolution imaging, pancreatic cysts are a common finding by MRI (~20%) and CT (~3%). Due to the slightly increased risk of malignancy in incidental cysts, mainly in the younger than 65 of years, incidentally found pancreatic cysts have to be assessed carefully without exaggerating unnecessary therapeutical consequences [13, 14].

9.3.1 Serous Cystadenoma

Serous cystic neoplasms are accounting for about 50% of all cystic tumors including serous cystadenomas, serous oligocystic adenomas, cystic lesions in von Hippel-Lindau syndrome, and rarely serous cystadenocarcinomas [15, 16].

The most common subtype is the benign serous cystadenoma (microcystic type), typically in elderly women (60–80 years of age). In most cases, the lesion is located in the pancreatic head, composed of multiple tiny cysts, separated by thin septae. Spotty calcifications and a central stellate nidus might be present (Fig. 9.2).

About 10% of all serous cystic tumors present as an oligocystic variant with only a few cysts of 2 to 20 mm diameter and a higher prevalence in men (30–40 years).

The rare cystadenocarcinomas are usually large at clinical presentation already with local invasive growth and metastases to lymph nodes and liver.

The diagnosis of serous cystic lesions of the pancreas by imaging is ruled by the proportion of small cysts and septae without contrast enhancement what may create an almost solid impression in CT, whereas the cystic components still can be best appreciated by MRI. Even if the tumors can grow rather large the mismatch of tumor size, missing both ductal involvement and secondary signs of malignancy will direct to the right diagnosis.

For the differentiation of oligocystic adenomas from mucinous cystic tumors, IPMN or walled-off cysts tumor localization, an "empty" clinical history, and normal ducts in MRCP can be helpful [17, 18].

9.3.2 Mucinous Cystic Neoplasm (MCN)

Mucin-producing cystic tumors, typically in middle-aged women (f:m = 19:1), are characterized by a missing connection to the pancreatic ducts and the histological presence of an ovarian-like stroma. In comparison to SCN, MCN are less frequent (10% of all cystic pancreatic lesions), in general asymptomatic, detected as solitary, large lesions arising in the body and tail of the pancreas (95%), and composed of only few cysts with pronounced septae. Since the cysts may contain mucinous, hemorrhagic, necrotic, jelly-like content they may present intermediate and higher densities and signal intensities on CT and MRI whereas T2-weighted MRI displays the true cystic structure of the tumor the best. Nodular enhancement of
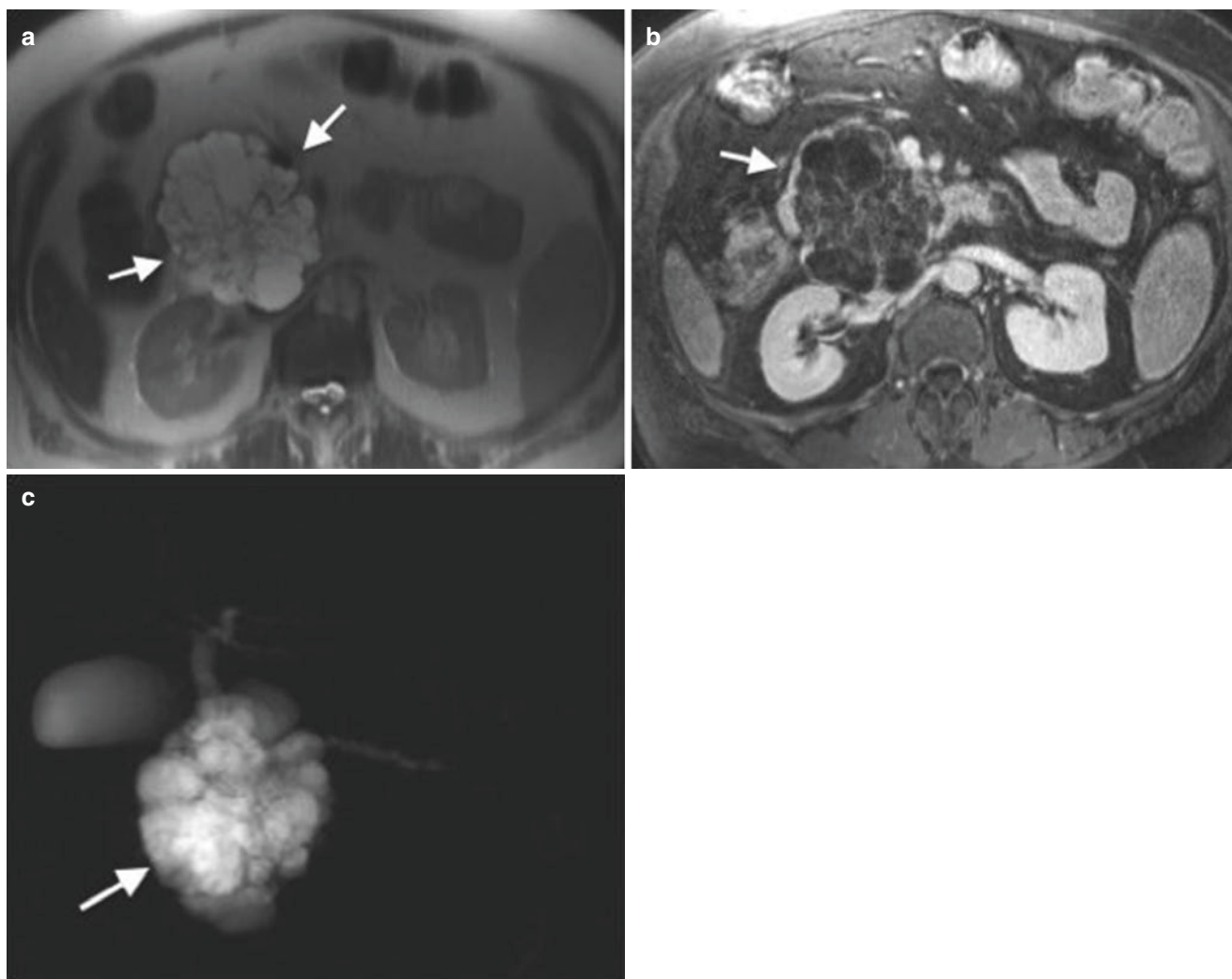
Fig. 9.2 (**a–c**) Serous cystadenoma. A) Axial T2-weighted Turbo Spin Echo image (TR/TE 4500/102) shows a multicystic microcystic neoplasm of the head of the pancreas (arrows). (**b**) On axial fat-saturated volumetric T1-weighted Gradient Echo image (TR/TE 4.86/1.87 ms) during the portal venous phase of the dynamic study following Gd-chelates administration serous cystadenoma shows enhancement of the internal septa and lack of a peripheral wall. (**c**) On the coronal MRCP image, single shot RARE (TR/TE ∞/110 ms), serous cystadenoma is responsible of compression of the main pancreatic duct with upstream dilatation

the septae is indicating potential malignancy which occurs in up to 30% of MCN [17–19].

9.3.3 Intraductal Papillary Mucinous Neoplasm (IPMN)

Due to increased detection rates by high-resolution imaging IPMN is considered the most common cystic neoplasm of the pancreas, seen more often in men than in women.

IPMNs may affect the main duct (28%), side branches (46%), or both duct components (26%) based on a mucin-producing neoplasm arising from the ductal epithelium. The side branch type can be found as a solitary or multifocal duct dilatation all over the pancreas and may also form a system of cystic dilated ducts that may mimic a microcystic appearance as in SCN. Segmental or general dilatation is typical for the main duct type creating a chronic pancreatitis like appearance. In such cases, patients' history is the crucial differential diagnostic information.

Since main duct type IPMN and MCN have a low malignant potential a thorough follow-up regimen should be recommend in non-surgical cases (Table 9.2).

> **Key Point**
> MRI is the superior imaging method allowing the detailed characterization of cystic lesions and neoplasia of the pancreas.

Table 9.2 Guideline recommendations for stratifying treatment and surveillance in pancreatic cystic lesions [20–25]

Guideline	High-risk stigmata indicating surgery in fit patients					Surveillance (in patients without worrisome features)	
	Symptoms	Size	Mural nodule	MPD	Cytology	Follow-up	Surveillance
WGO 2019 [25]	Jaundice, pancreatitis	≥3 cm growth rate ≥3 mm/year	Any	≥10 mm	+ high CA19.9	6–12 months for 1 year, then every 2 years, after 5 years, annually, if resources allow. Consider closer intervals for cysts >2 cm or if changes occur	As long as fit for surgery
Eu 2018 [24]	Jaundice, pancreatitis new diabetes mell.	≥4 cm growth rate ≥5 mm/year	>5 mm	≥10 mm	+ high CA19.9	EUS/MRI and CA 19-9 after 6 months then EUS/MRI and CA 19-9 yearly	Lifelong as long as fit for surgery
ACG 2018 [21]	Jaundice, pancreatitis new diabetes mell.	≥3 cm growth rate ≥3 mm/year	Any	≥5 mm	+ high CA19.9	Similar to ICG	Lifelong as long as fit for surgery. Not in older than 75 years
ICG 2017 [26]	Jaundice	Size alone is not appropriate	>5 mm	≥10 mm	+	<1 cm—CT/MRI in 2-3 years 1-2 cm—CT/MRI yearly × 2 then lengthen as appropriate *2–3 cm—EUS in 3–6 months then lengthen as appropriate *>3 cm—MRI/EUS every 3–6 months up to 1 year	Lifelong as long as fit for surgery
ACR 2017 [20]	Jaundice	Size-dependent growth rate of 50-100% in cysts ≤15 mm, of 20% in cysts >15 mm	Any	>7 mm	+	Similar to ICG	If stable up to 10 years or patient older than 80 years
AGA 2015 [22]	Na	Na	Any	Dilated	+	MRI after 1 year then MRI every 2 years	If stable up to 5 years

9.4 Other Neoplasm

9.4.1 Neuroendocrine Tumors

The WHO (2010, last modification 2017, unchanged in 2019) classified these tumors mainly according to their grading (well—moderately—poor differentiated) and their hormonal activity (PanNEN: pancreatic neuroendocrine neoplasm), as well as the Ki67 proliferative index.

In general, these tumors are rare and account for about 5–7% of all pancreatic tumors with the most common subtypes being insulinoma, glucagonoma, and nonhormonal active tumors. If a specific hormone release is not the leading clinical sign, also imaging features of various PanNEN are often rather similar what makes immuno-histochemical staining a crucial issue (Fig. 9.3) [27, 28].

9.4.1.1 Insulinoma
The presentation of insulinomas—the most common PanNEN (60%)—is determined by hyperinsulinism (Whipple triad: starvation attack, hypoglycemia after fasting, and relief by i.v. dextrose). The majority of tumors are solitary (95%), small (<2 cm), hypervascularized with a peripherally pronounced enhancement, and localized in the pancreatic body and tail [29].

9.4.1.2 Gastrinoma
Gastrinoma is the second most common PanNEN (20–30%) clinically associated with the Zollinger—Ellison syndrome (peptic ulcer disease, diarrhea) due to the massively elevated gastrin blood levels. At detection, the tumors usually present with a moderate size (mean 3 cm, ranging from 0.1–20 cm) and in half of the cases with multiple nodules. The vast majority of gastrinomas will arise within the gastrinoma triangle determined by the confluence of the cystic and common bile duct, the junction of the second and third portions of the duodenum, and the junction of the neck and body of the pancreas. On imaging, gastrinomas are revealed as mainly solid tumors with intermediate densities and signal intensities on both CT and MRI with moderate to strong contrast enhancement. Even if about 60% of the tumors are malignant, extensive metastatic spread is rare [30].

9.4.2 Other Rare Pancreatic Neoplasm

Beside the above displayed neoplasms, there is still a wide variety of pancreatic tumors which—in general—can be differentiated only by specific immunohistologic staining. This rare tumors comprise a number of variably differentiated neuroendocrine tumors inclusively mixed neuroendocrine non-
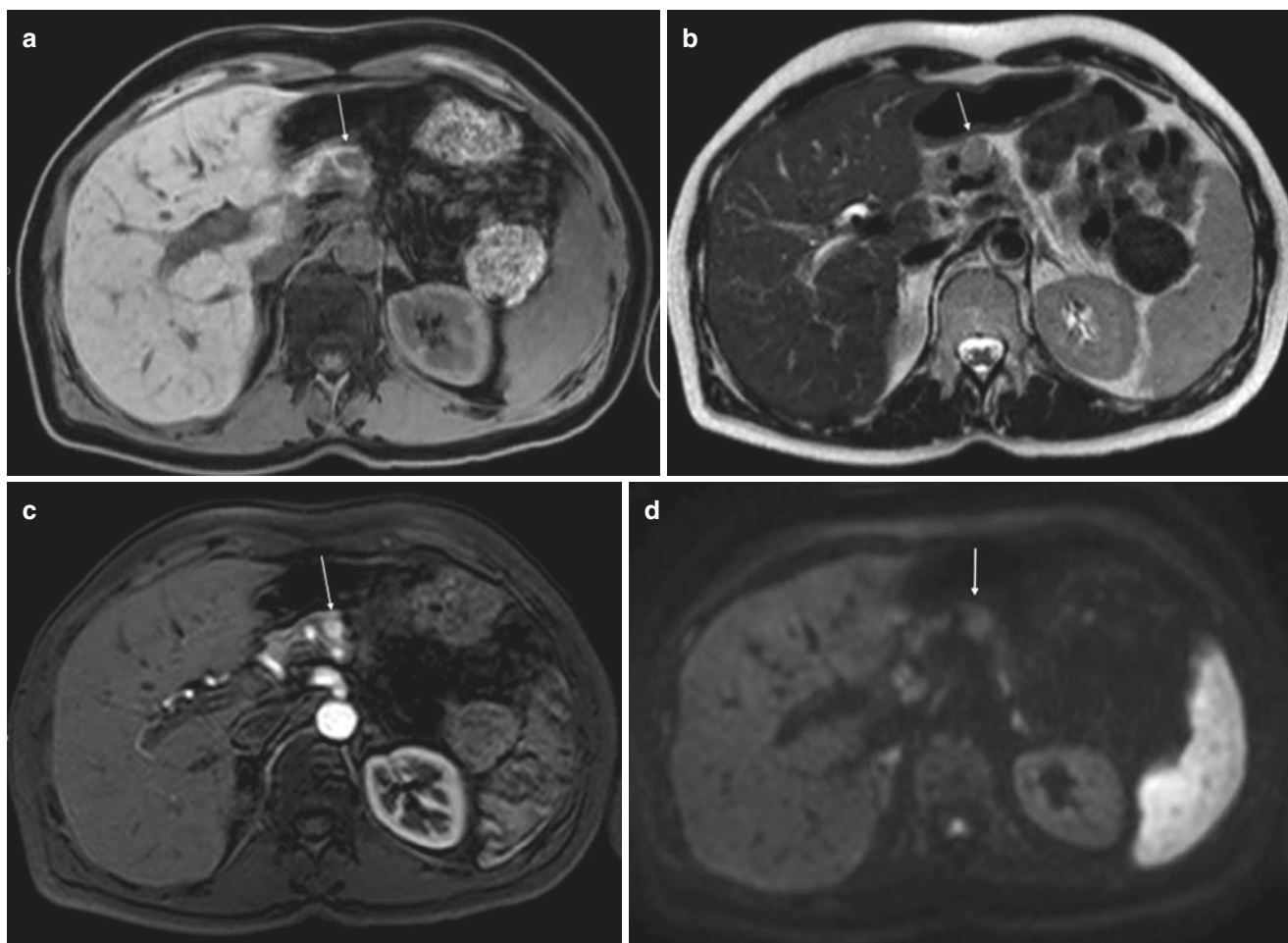
Fig. 9.3 (**a**–**d**) Small neuroendocrine neoplasm. (**a**) Axial T1-weighted Gradient Echo image (TR/TE 180/4.66 ms) with fat saturation shows a neuroendocrine neoplasm that appears hypointense compared to adjacent pancreatic parenchyma (arrow). (**b**) Axial T2-weighted Turbo Spin Echo image (TR/TE 4500/102) shows a small neuroendocrine neoplasm that appears hyperintense compared to adjacent parenchyma (arrow). (**c**) On the axial fat-saturated volumetric T1-weighted Gradient Echo image (TR/TE 4.86/1.87 ms) during the pancreatic phase of the dynamic study following Gd-chelates administration, the neuroendocrine neoplasms appear hyperintense compared to adjacent pancreatic parenchyma (arrow). (**d**) On axial diffusion-weighted image ($b = 1000$), the neuroendocrine neoplasms show restricted diffusion (arrow)

neuroendocrine tumors, mostly without functional activity, rare malignant pancreatoblastoma in children (a large, encapsulated tumor in the pancreatic head often associated with elevated alpha-fetoprotein levels and metastases to liver and lymph nodes), acinar cell carcinoma (relatively large tumors in elderly men with an imaging appearance similar to pancreatic adenocarcinomas and potential excessive release of serum lipase followed by focal panniculitis and polyarthritis as diagnostic hint), and solid pseudopapillary tumor (of mainly young women (frequently incidental tumor in women 20–30 years of age; m:f = 1:10; large, heterogenous tumor of uncertain dignity) and occasionally children) [31].

Mesenchymal tumors (sarcoma, cystic dermoid, lymphangioma, leiomyosarcoma, hemangiopericytoma, hemangioma, malignant fibrous histiocytoma, lymphoepithelial cysts, primary lymphoma) and secondary tumors (secondary lymphoma, metastases) of the pancreas are very rare and

may be identified due to specific imaging features as peripheral nodular enhancement on dynamic imaging or high signal intensity in T1- and T2-weighted imaging as, for example, hemangioma or lipoma; otherwise, clinical context and histopathological proof will determine the diagnosis.

Key Point

PanNEN comprises a complex group of neoplasia which can be identified usually by imaging—beside very small tumors. Nevertheless, without clinical information and immune-histopathological correlation a precise diagnosis is not possible. In malignant transformation, the mismatch between tumor size and missing secondary signs of malignant spread as common in pancreatic cancer can be helpful.

9.5   Inflammatory Diseases of the Pancreas

9.5.1   Acute and Chronic Pancreatitis

Especially in the Western world the incidence of inflammatory diseases of the pancreas is increasing. The most common causes are biliary stone disease and alcohol abuse; nevertheless, a heterogenous variety of other causes as metabolic syndrome (hyperlipidemia types I, IV, V; hypercalcemia), drugs, infections, trauma (e.g., post surgery), and very rare conditions as alpha-1-antitrypsin deficiency, or mutations of protease serine (PRSS) and serine protease inhibitor Kazal type (SPINK1) has been identified as promoting factor. Depending on the type and severity of the inflammatory process no, mild or extensive morphological and functional deterioration is seen.

In general, the task of imaging is to monitor substantial structural changes and complications in acute pancreatitis, as parenchymal integrity vs. necrosis, peripancreatic inflammation, subtle and substantial fluid collections, formation of pseudo cysts and walled-off cysts, vascular and ductal affections (Fig. 9.4), and to assist in the clinical outcome prognosis together with the clinical assessment [32–36].

In chronic pancreatitis differentiation of long-term parenchymal and ductal changes from similar changes caused by neoplasms—e.g., focal or complete duct dilation, focal parenchymal lesions, and cystic degeneration—is mandatory to rule out complications and potential pancreatic cancer (Fig. 9.5). Perfusion MRI, DWI, and FDG-PET can be helpful in such cases. Nevertheless, the common clinical presenta-
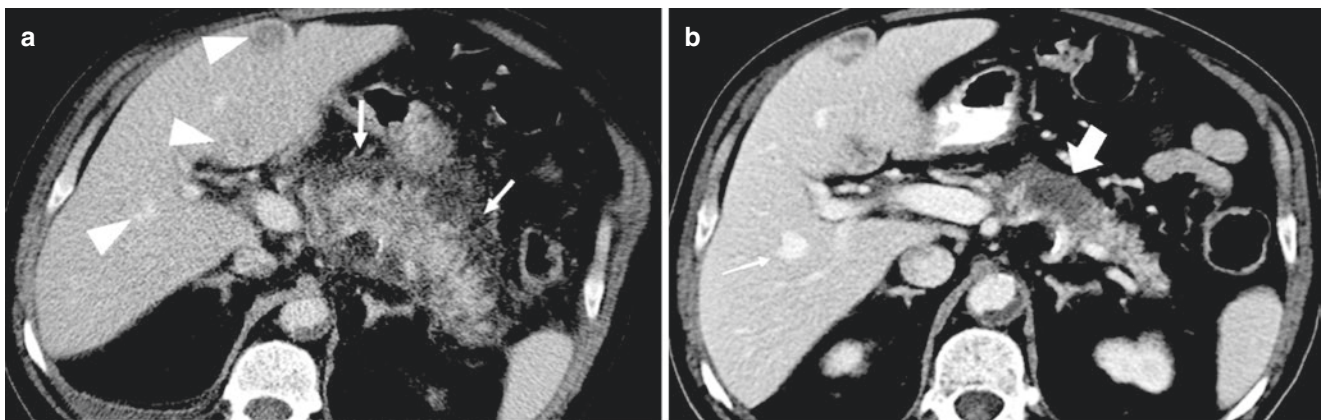

Fig. 9.4 Acute severe pancreatitis. At the patient's admission, contrast-enhanced CT during the venous phase (**a**) displayed a fuzzy contour of the pancreatic gland together with peripancreatic exudation (arrow). Note the hypo- and hyperdense hepatic lesions (arrow heads). A control scan 10 days later (**b**) revealed an almost normal gland with resorption of the peripancreatic fluid. However, there was an area with a lack of enhancement representing focal necrosis (large arrow). In the liver, one lesion turned out to be a hemangioma (arrow) while the other two lesions were small abscesses
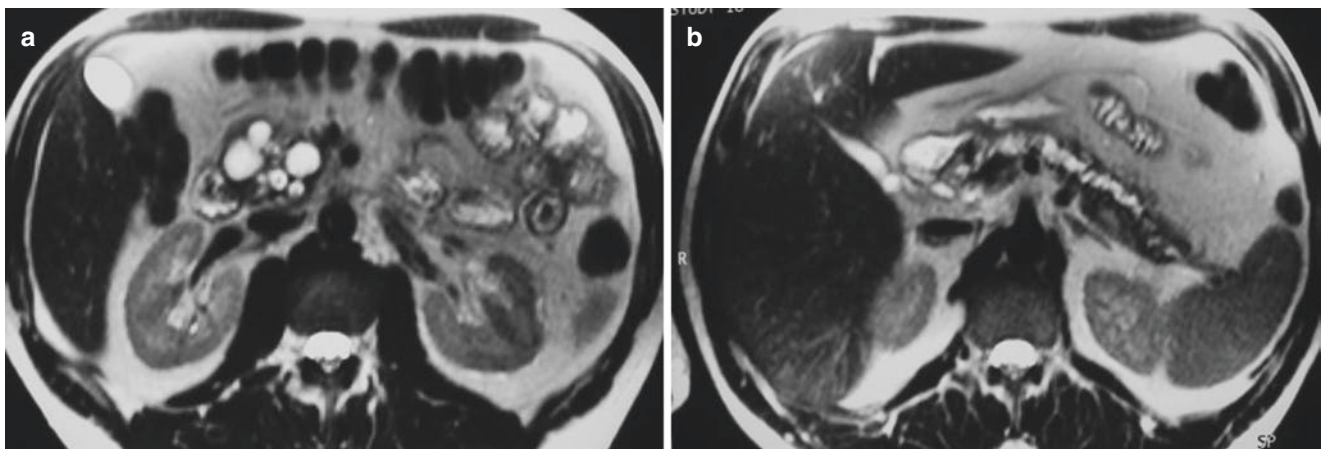

Fig. 9.5 Chronic pancreatitis. Cystic degeneration of the pancreatic head (**a**) together with irregular dilatation of the pancreatic main duct (**b**) in MRI (fastSE T2). Note the similar imaging appearance to other cystic lesions of the pancreas

tion with chronic abdominal pain in chronic pancreatitis does not correlate very well with imaging findings [35, 37–42].

9.5.2   Autoimmune Pancreatitis

In comparison to gall stone or alcohol-associated pancreatitis, autoimmune pancreatitis (AIP) is a rare disease in which the pathophysiological understanding has evolved significantly over the last years. The most common form, type 1 AIP is associated with IgG4-related diseases. Type 2 AIP is a different, even rarer entity and may be associated to chronic inflammatory bowel disease [43–45].

Both diseases have a similar clinical presentation with unspecific upper abdominal pain, obstructive jaundice, furthermore weight loss, and endo- and/or exocrine pancreatic insufficiency. Clinically, there is an overlap with pancreatic carcinoma, which cannot be solved by imaging alone since AIP may provide diffuse ("sausage" like) or focal ("mass forming") enlargement of the gland together with segmental or focal duct strictures or dilatation. In consequence, the task of imaging and further parameters as serology and histology is the differentiation of both entities to guide each to the appropriate therapy and to avoid the small number, but unnecessary pancreatectomies (Fig. 9.6).

The International Association of Pancreatology defined diagnostic consensus criteria (Table 9.3) which provide a high accuracy in identifying an AIP. Both types of AIP usually present an excellent response to steroid therapy, however, in Type 1 AIP 60% of patients will have relapse. Over the last years the body of knowledge in AIP was growing significantly, identifying also AIP not otherwise specified (NOS) not meeting the criteria for Type 1 or 2 AIP, and AIP in the context of IgG4-related disease (IgG4-RD) characterized by immune-mediated fibroinflammatory multi-organ involvement [46, 47].

Key Point
Acute and chronic pancreatitis are common diseases, whereas the diagnosis is ruled by the clinical history and/or presentation. Imaging adds the crucial information on the severity and complications of the disease. In AIP imaging findings contribute to the cardinal criteria, however, imaging alone is not suitable to establish the diagnosis in AIP.

Take-Home Message
Pancreatic lesions encompass a wide variety of anatomical variants as well as benign and malignant neoplastic, and inflammatory diseases. The specific anatomical position of the gland and patient-specific conditions allows often only limited insight by ultrasound and endoscopy. Therefore, cross-sectional imaging by CT and MRI is of ample importance in assessing the pancreas and related disorders, allowing for a very high accuracy in depicting structural alterations of the parenchymal and ductal components of the gland. In the majority of clinical-diagnostic situations, there is no significant difference between the two imaging modalities with respect to diagnostic efficacy. However, MRI will reveal its superiority particularly in conditions where the assessment of ductal and intra- and peripancreatic cystic structures as well as subtle parenchymal changes is pivotal.
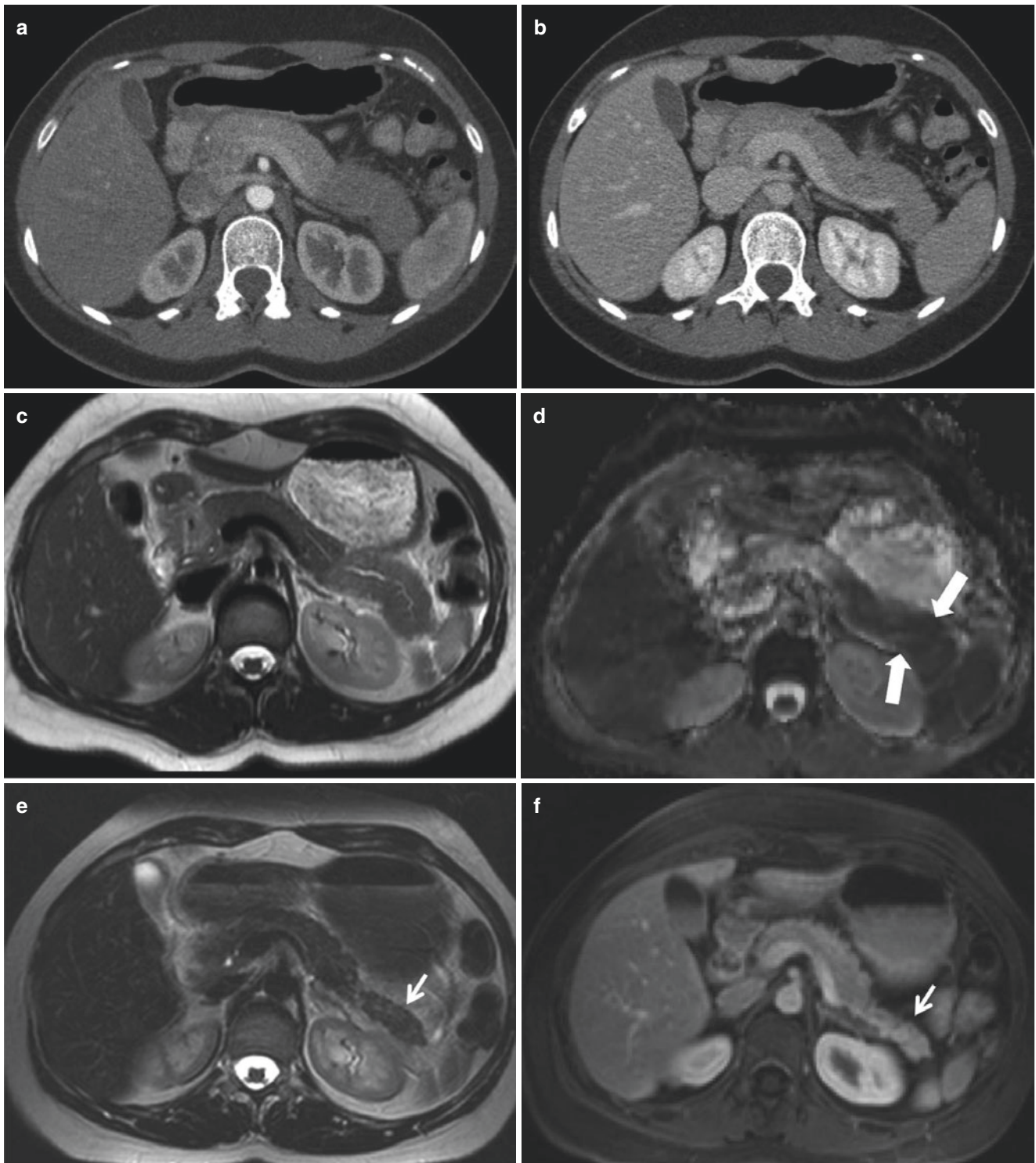
Fig. 9.6 AIP type 1. Well-demarcated focal enlargement of the pancreatic tail on CT (**a**, **b**). Note the slightly reduced perfusion in the early parenchymal phase (**a**). Low signal intensity on T2-weighted MRI (**c**) and diffusion restriction on DWI ADC Map (**d**) reveals the lymphoplasmatic infiltration with fibrotic components in contrast to edema in "usual" pancreatitis. After 6 weeks therapy with steroids, note the significant atrophy of the pancreatic tail on T2-weighted (**e**) and CE T1-weighted MRI (**f**)

Table 9.3 Revised consensus criteria in type 1 and type 2 AIP ([48–50] modified acc. to Shimosegawa et al. [51], and O'Reilly et al. [52]; L level, ERP endoscopic retrograde pancreatography, IgG4-RD IgG4-related disease, IBD inflammatory bowel disease, GEL granulocytic epithelial lesions)

	Type 1 AIP		Type 2 AIP	
Synonym	Lymphoplasmacellular sclerosing pancreatitis (LPSP)		Idiopathic ductal-centric pancreatitis (IDCP)	
Incidence	0.9/100.000			
Geographic frequency seiche	EU/USA 50%, Asia 95%		EU/USA 50%	
Age (years)	50–70		30–50	
Sex	M (75%) ≫ F		M = F	
Consensus Criteria of the International Association of Pancreatology [51]				
Cardinal criteria	Level 1	Level 2	Level 1	Level 2
Imaging: Parenchyma (P)	Typical: diffuse enlargement ("sausage sign"), delayed (interstitial) enhancement (sometimes capsule-like, nodular enhancement)	Indeterminate:: focal enlargement with delayed enhancement	Typical: diffuse enlargement ("sausage sign"), delayed (interstitial) enhancement (sometimes capsule-like, nodular enhancement)	Indeterminate:: focal enlargement with delayed enhancement atypical: hypodense in CT, duct dilatations, atrophy
Imaging: Pancreatic duct (D), validated for ERP; analogue interpretation in MRCP	Long (>1/3 of duct length) or multiple strictures (skip lesions) without proximal (upstream) dilatation, duct penetrating sign	Segmental/focal strictures with proximal (upstream) dilatation (<5 mm)	Long (>1/3 of duct length) or multiple strictures (skip lesions) without proximal (upstream) dilatation, duct penetrating sign	Segmental/focal strictures with proximal (upstream) dilatation (<5 mm)
Serology (S)	IgG4 >2 × upper limit	IgG4 1–2 × upper limit	–	–
Other organ involvement (OOI)	IgG4-related disease (RD) (50%)		No association with IgG4-RD	
	≥3 histological findings in other organs: – Lymphoplasmatic cellular infiltrates and fibrosis without granulocytes – Storiform fibrosis – Obliterating phlebitis – IgG4-positive cells (>10/HPF) ≥1 radiological finding: – Segmental/multiple bile duct strictures – Retroperitoneal fibrosis IgG4-RD (ca. 60%) – Chronic-sclerosing sialadenitis (14–39%) – IgG4-assoc cholangitis (IAC) (12–47%) – IgG4-assoc tubulointerstitial nephritis and renal parenchymal lesions (35%) – Enlarged hilar pulmonary LN (8–13%) – Retroperitoneal fibrosis – Chronic thyroiditis – Prostatitis – Chronic inflammatory bowel disease (0.1–6%)	Bile duct involvement plus both – Lymphoplasmatic cellular infiltrates without granulocytes – IgG4-positive cells (>10/HPF) Or ≥1 criterion (imaging or clinical exam) – symmetric enlarged salivary glands – renal involvement	– Histological and/or clinical diagnosis of inflammatory bowel disease (16%) – Involvement of proximal bile duct possible – Involvement of thyroid possible	

Table 9.3 (continued)

	Type 1 AIP		Type 2 AIP	
Histology (H), TruCut-biopsy or resection, EUS-FNB not suitable	Periductal lymphoplasmacellular infiltrations, inflammatory, cell-rich stroma			
	3 of 4 criteria – Storiform fibrosis – Obliterative phlebitis – Prominent lymphatic follicles – IgG4-positive plasma cell – No neoplastic cells detected and no signs of malignancy in imaging – No neoplastic cells detected by EUS-FNA	2 of 4 criteria – Storiform fibrosis – Obliterative phlebitis – Prominent lymphatic follicles – IgG4-positive plasma cells – No neoplastic cells detected and no signs of malignancy in imaging	– GEL with or without granulocytic acinar infiltration – No or few (10 <10 HPF) IgG4-positive plasma cells – No neoplastic cells detected and no signs of malignancy in imaging	– Granulocytic and lymphoplasmatic acinar infiltrate – No or few (>10 HPF) IgG4-positive plasma cells – No neoplastic cells detected and no signs of malignancy in imaging
Response to steroids (Rt)	Rapid (≤2 weeks) response to therapy with significant improvement in imaging			
Relapse post steroids	20–60%		<10%	
Diagnosis based on criteria	Type 1 AIP		Type 2 AIP	
Definitive	Histo L1 + imaging L1/2 Imaging L1 + other criteria L1/2 Imaging L2 + ≥ 2 criteria L1 Steroid Response + Bildgebung L2 + 3 Kriterien L1 oder 4 Kriterien L2		Imaging L1/2 + Histo L1 or IBD + Histo L2 + response to steroids	
Probable	Imaging L2 + other criteria L2		Imaging L1/2 + Histo L2 + IBD + response to steroids	

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