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A solid pancreatic mass: Tumour or inflammation?

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KEYWORDS

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Abstract The prognosis for pancreatic cancer is poor, and early diagnosis is essential for surgical management. By comparison with its classic form, the presence of acute or chronic inflammatory signs will hinder its detection and delay its diagnosis. The atypical forms of acute pancreatitis need to be known in order to detect patients who require additional morphological investigations to search for an underlying tumour. In contrast, pseudotumoral forms of inflammation (chronic pancreatitis, cystic dystrophy in heterotopic pancreas, autoimmune pancreatitis) may simulate a cancer, and make up 5–10% of the surgical procedures for suspected cancer. Faced with these pseudotumoral masses, interpretation relies on various differentiating signs and advances in imaging.

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Pancreatic cancer is still a cancer with a poor prognosis. With overall incidence of 7 to 12/100,000, 96,000 new cases were reported in Europe in 2008 [1]. Unlike other cancers where the mortality rate is decreasing (leukaemia, colorectal cancer, breast cancer), projections for 2012 show the rate for pancreatic cancer to be stable, at 5.38 and 8.01/100,000 respectively for women and men, close to its rate of incidence and placing it in 5th position for cancer deaths for both sexes [2]. The 5-year survival rate is low at approximately 5%, if all stages are considered.

At present, surgery is the treatment of choice, as only R0 resection provides hope of improving survival. Imagery performs well in diagnosis and locoregional staging of pancreatic adenocarcinoma in its classic form. However, there are still situations that present both clinicians and radiologists with problems when faced with a solid mass in the pancreas, confronting them with a dilemma: the risk of a false positive diagnosis and thus of unnecessary surgery or, on the other hand, a false negative diagnosis leaving an adenocarcinoma to evolve into a non-resectable stage. This is the case when there are associated acute or chronic inflammatory signs.

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The typical form of adenocarcinoma: the normal situation

Before considering atypical focal solid mass situations, some reminders are needed concerning the main imaging techniques and the radiological signs of pancreatic adenocarcinoma.

Histologically, a pancreatic adenocarcinoma shows hypovascularisation and marked interstitial fibrosis. These two characteristics are the basis for detecting the tumour by imaging, but they are also the source of diagnostic difficulties when the tumour occurs on a pre-existing fibrous background, as in chronic pancreatitis. It is typically seen in imaging as a hypovascular mass with poorly defined contours, which may or may not deform the contours of the pancreas. This hypovascularisation is best detected by CT in the pancreatic phase, 45 seconds after injection of 2 ml/kg iodinated contrast agent at a rate of 3–4 ml/s, which gives the best contrast between the tumour and the pancreas. This acquisition, centred on the pancreas and covering the origin of the celiac trunk and superior mesenteric artery, both marks out the contours of the lesion as well as possible and in particular permits ablation possibilities to be considered. It should be completed by exploration of the whole of the abdominal cavity in the portal phase (70 s) (Fig. 1). These two helices provide the best results in terms of detection and staging, with sensitivity and performance greater than 90% for the diagnosis of classic adenocarcinoma [3]. In MRI, the tumour typically presents as iso-hypointense with T1-weighting and iso-hyperintense with T2-weighting/STIR. After injection, the frequency of the tumour hyposignal is maximal in the arterial phase [4].

The secondary signs associated with the tumour itself are essential for diagnosis and analysis. Dilatation of the pancreatic and/or bile duct upstream of the tumour is a common sign, present in more than 80% of tumours of the head and 50% of tumours of the body of the pancreas (Fig. 2) [5]. The topography of interruption of the duct is a major element



Figure 1. Typical adenocarcinoma of the body of the pancreas. Contrast-enhanced axial CT slice. Hypodense mass of the pancreatic body with posterior extension, vascular sheathing of the celiac trunk and upstream atrophy.

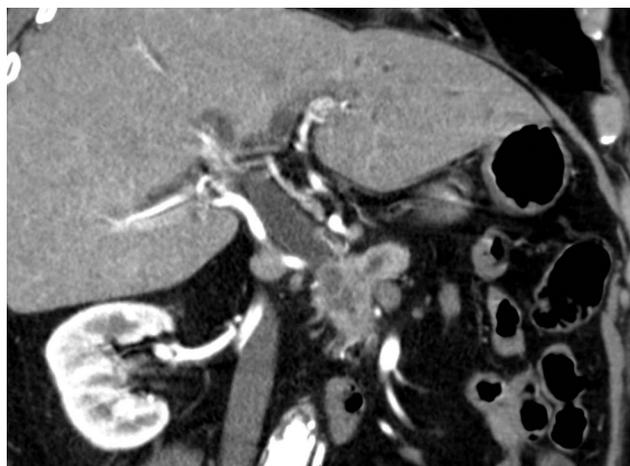


Figure 2. Typical adenocarcinoma of the head of the pancreas. Contrast-enhanced coronal oblique CT reformation. Poorly defined hypodense mass with double biliary and pancreatic dilatation.

and can be the principal secondary sign if the lesion is isodense (11–14% of adenocarcinomas) [6,7]. This isodensity is moreover combined with other factors hindering detection of the tumour: the higher frequency of small tumours (27% for tumours smaller than 20 mm versus 13% for tumours of 21–30 mm) [8] and lower frequency of secondary signs (76% versus 99%). The latter are dominated in this case by stenosis of the pancreatic duct and dilatation of the biliary-pancreatic duct, in contrast to parenchymal atrophy and abnormal contours, which are rarer (21 and 14%).

Upstream parenchymal atrophy, of obstructive origin, is associated with 82% of ductal dilatations due to tumours. In the absence of a visible tumour, its segmental character should result in additional morphological examinations (MRI and endoscopic ultrasonography), to explore the junction between the healthy and atrophic parenchyma (Fig. 3).

The clinician's and radiologist's dilemmas

Surgical resection is currently the only curative treatment for pancreatic adenocarcinoma. However, only 10–15% of



Figure 3. Typical adenocarcinoma of the head of the pancreas. Endoscopic ultrasound. Poorly defined hypoechoic mass.

patients benefit from resection for curing the condition. Given the poor prognosis, delaying surgery at a potentially resectable stage is harmful, but on the other hand, morbidity following pancreatic surgery is still as much as 41% after cephalic duodenopancreatectomy (CDP), mainly due to postoperative fistulae and haemorrhage, with a mortality rate of up to 9% after CDP and 3.5% after left pancreatectomy [9–11].

The frequency of CDP revealing benign lesions and performed for suspected cancer varies between 5 and 11% [12,13]. In a series of 40 CDPs performed because of an initial suspicion of cancer but where the aetiology was found in the end to be benign, surgery was motivated by the discovery of a pancreatic mass in 67.5% of cases, biliary stricture in 40% and false positive cytology in 12.5%. Fifty percent of the patients had jaundice. The main aetiology of these non-carcinomatous lesions was lymphoplasmacytic sclerosing pancreatitis (23.4%) [14].

Adenocarcinoma and acute pancreatitis

The combination of acute pancreatitis and cancer is unusual. Pancreatic cancer represents 1–2% of acute pancreatitis aetiologies and only 3% of cancers manifest as acute pancreatitis [15–17]. The *Association Française de Chirurgie* (French Association of Surgery) series reported frequency of 9.1% for pancreatitis among the 1670 patients operated on for carcinoma [18].

The presence of inflammatory signs can mask the underlying tumour and delay diagnosis (Fig. 4a–d). A mean symptomatic period of 8 months before diagnosis of carcinoma has been reported, with a delay in diagnosis that can reach 12 months [15].

Can certain signs help diagnose secondary acute pancreatitis of tumoral origin? Since the tumour can be masked by inflammation or necrosis, like the upstream atrophy by oedema, secondary signs become of great importance.

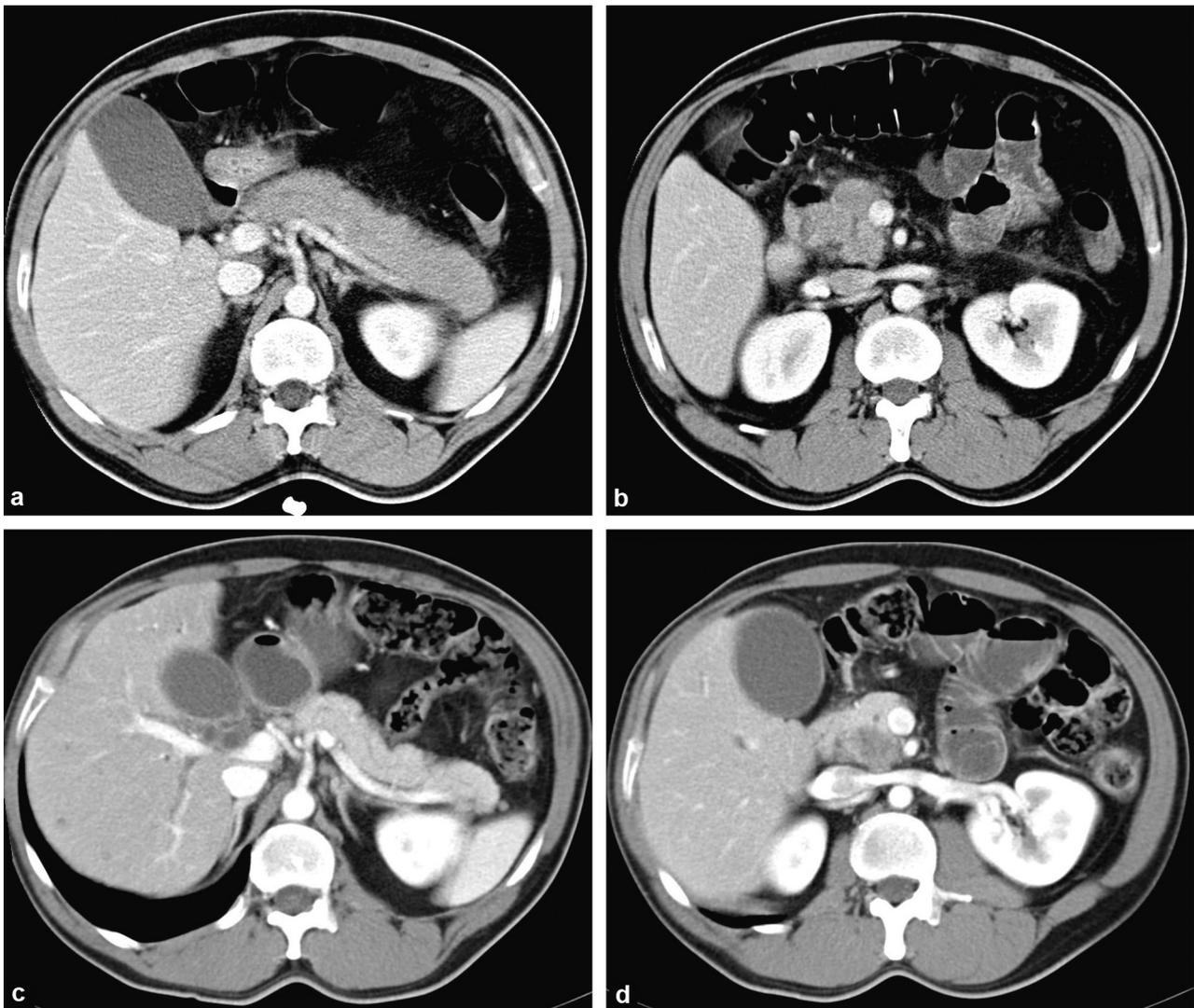


Figure 4. Adenocarcinoma of the head of the pancreas revealed by acute pancreatitis. Contrast-enhanced CT: a, b: initial CT scan showing diffuse pancreatic oedema with no focal lesion; c, d: follow-up CT scan at 3 months. A tumour lesion of the uncinate process of the pancreas can be seen which is characteristic of adenocarcinoma.

Dilatation of the pancreatic duct, a double biliary and pancreatic obstruction or interruption of the pancreatic duct are unusual and should lead to considering an underlying carcinoma [19]. Similarly, a left location or segmental atrophy is a suspect sign (Fig. 5a, b). Upstream pseudocysts can be encountered in both situations, even if they are only seen in 8% of carcinomas, secondary to the acute pancreatitis or due to duct distension and rupture. Their characteristic signs are comparable [20].

Sheathing of the celiac trunk and/or mesenteric artery is seen in 30–60% of CT scans of adenocarcinoma [21]. This sign is sometimes the main pointer in the case of an iso-dense tumour or isthmus location, but cannot be considered as pathognomonic, as it is also described in cases of pancreatitis [22,23]. This is particularly true of autoimmune pancreatitis or IgG4 conditions with extrapancreatic lesions: in sclerosing mesenteritis and retroperitoneal fibrosis, frequencies have been reported of 4% and 5% respectively [24,25]. The location (in contact with the pancreatitis lesions or distant from them) and the stenosing character, or not, of this infiltration are factors to be taken into account.

Finally, 5% of cases of acute pancreatitis where no initial aetiology is found, proved to be caused by a tumour, which is revealed later, thus justifying increased monitoring for patients whose aetiological investigation of acute pancreatitis provides no clear answer [16].

Adenocarcinoma and chronic pancreatitis

Can adenocarcinoma be differentiated from a chronic pancreatitis pseudotumour (CP-pT) when confronted with a mass occurring on a background of chronic pancreatitis? An adenocarcinoma developing on a background of chronic pancreatitis is a rare event, but one with a poor prognosis because of frequently delayed diagnosis. The estimated

relative risk is 13.3% (6.1 to 28.9%) in chronic pancreatitis and may reach 69% in hereditary pancreatitis [26].

The clinical presentation is identical (pain, weight loss, jaundice).

Morphological imaging

Radiologically, the classic signs are also misleading. The double duct obstruction suggestive of adenocarcinoma is present in 36–50% of cases of chronic pancreatitis operated for suspected cancer [13,27]. In a series of 35 cases of pseudotumoral pancreatitis, 25 (71.5%) presented as a focal lesion, and involved the head region in more than 80% of those cases. In the context of chronic pancreatitis, calcifications displaced by the mass are a classic sign suggesting a carcinoma (Fig. 6a–d). However, the presence of intraleisional calcifications, classically described in CP-pT, was only detected in the end in 14–28% of these pseudotumours [28,29].

Pancreatic adenocarcinoma is a tumour with a hypoxic, hypovascular fibrous component, as is the fibrosis of chronic pancreatitis. Confusion may also occur on biopsy specimens if the carcinoma is well differentiated or the fibrous stroma abundant. While a significant reduction in microvascular density has been demonstrated in cancerous and chronic pancreatitis tissue compared with normal pancreatic tissue (respectively by a factor of 4 and 5), the variations between the pathological tissues are similar and insignificant [30]. Similarly, the fibroblastic stromal cells in the fibrous tissue of the tumour have characteristics identical to those of the pancreatic stellate cells present in chronic pancreatitis and the hub of pancreatic fibrosis [31]. A number of additional histopathological and immunohistological parameters are therefore necessary [32]. It is thus easy to understand the difficulties of differentiating, in imaging, between a CP-pT focus and an adenocarcinoma in chronic pancreatitis.

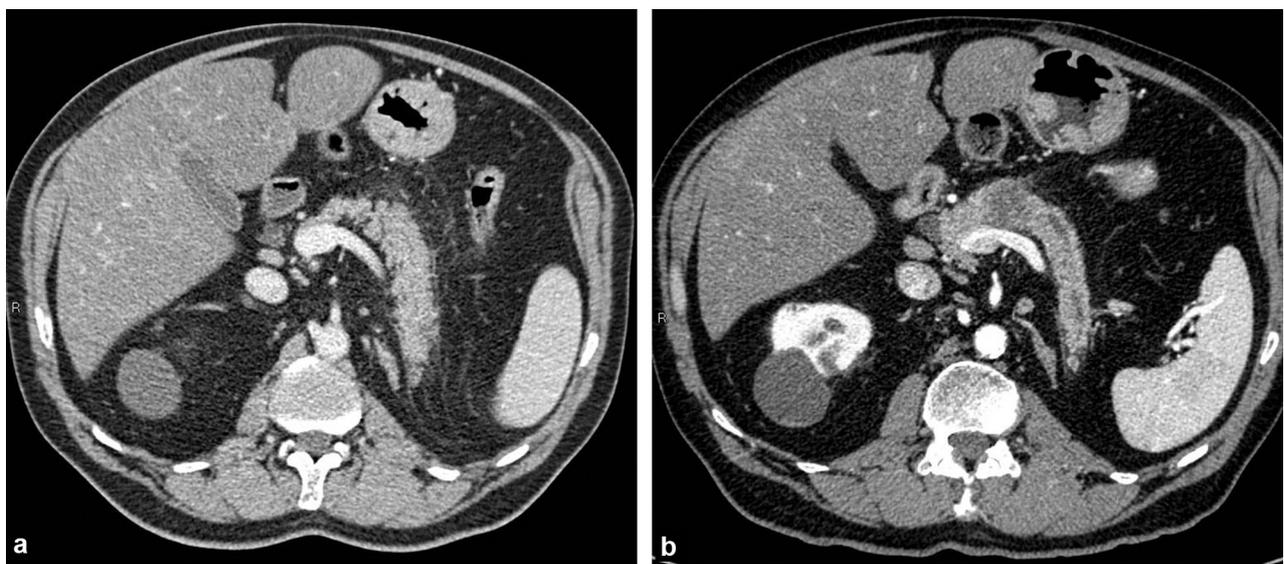


Figure 5. Acute pancreatitis both clinically and according to laboratory values. Contrast-enhanced axial CT slice: a: initial CT scan showing signs of acute pancreatitis with an atypical left location. No atrophy or dilatation of the pancreatic duct; b: follow-up after 9 months: a tumour of the pancreatic body can be observed at the initial limit of inflammation, with upstream dilatation of the pancreatic duct.

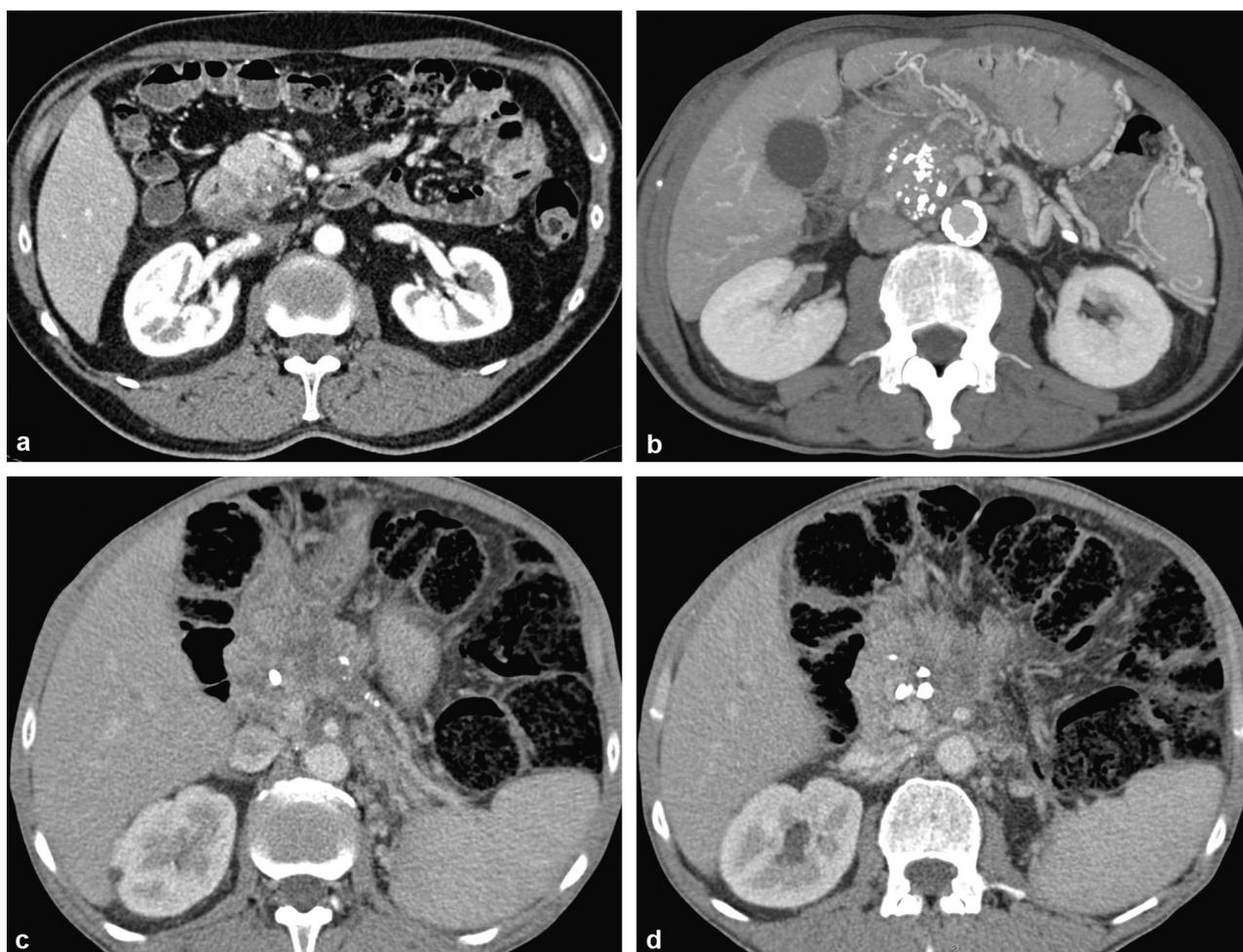


Figure 6. Calcification, chronic pancreatitis and adenocarcinoma: contrast-enhanced CT scans: a: hypodense nodule in the uncinate process of the pancreas with central calcification. This is highly suspect of carcinoma. The biopsies performed and close monitoring led to the conclusion of focal chronic pancreatitis; b: multiple disseminated calcifications in the head on focal chronic pancreatitis; c, d: adenocarcinoma on alcoholic chronic pancreatitis. Hypodense infiltrating mass of the head of the pancreas with posterior celiac infiltration. Chronic pancreatitis macrocalcifications of the head are absent within tumour infiltration.

Functional imaging

Functional imaging developed to search for specific biomarkers when classic morphological criteria are found wanting. Various methods based on tissue enhancement kinetics after injection of a contrast agent have been studied to differentiate lesions.

Ultrasonography

In ultrasound, the morphological criteria are classically based on the echo structure, the limits of the lesion, associated duct abnormalities, the presence of adenopathies and any vascular invasion. With these simple criteria, sensitivity of 73.2% and specificity of 83.3% have been reported with endoscopic ultrasound alone [33]. Its diagnostic performance varies between 63 and 76% [34]. With injection of a contrast agent tissue vascularisation can be explored, due to its purely intravascular distribution, an adenocarcinoma being typically hypovascular with contrast-enhanced ultrasound, in contrast to the presence of parenchymographic enhancement in a CP-pT. Hypovascularisation is thus

a sensitive and specific criterion (91.1% and 93.3%) for the diagnosis of adenocarcinoma [35]. On the other hand, the presence of moderate, continuous lesion enhancement, isovascular with the adjacent parenchyma, provides the diagnosis of CP-pT, with sensitivity of 88.6% and specificity of 97.8%, a positive predictive value of 91.2% and overall performance of 96% [28]. Old, very fibrous forms of CP-pT can however be hypovascular [36]. Improvement in detection with endoscopic ultrasonography of arterial and venous vessels in duplex mode after injection improves diagnostic performance, with sensitivity of 91.5% for adenocarcinoma and specificity of 93.3% for CP-pTs [33]. The addition of the harmonic mode potentiates vascular exploration and the study of pancreatic diffusion by searching for slow flows, while avoiding Doppler artefacts. The heterogeneous hypo- or avascular character of adenocarcinomas is the opposite of the homogeneous isovascular character of CP-pTs [37]. Two studies have shown the importance of this hypovascular criterion (sensitivity 89–96% and specificity 88–64%) for diagnosis of adenocarcinoma [38,39]. Similarly, using a second-generation product, Sonazoid®, marketed in Asia, 95% of carcinomas were hypovascular as against 8% of CP-pTs [40].

While these previous criteria are based on purely visual analysis of enhancement, it is now also possible to study enhancement curves quantitatively. There are as yet not many results. Kersting et al. have shown that, using Sonovue® with transcutaneous ultrasound, the adenocarcinomas had a longer contrast medium transit time and a longer time to peak than CP-pTs, for which the time to peak was similar to or slightly longer than for normal parenchyma. However, maximum intensity and the area under the enhancement curve were not significantly different [41]. Another study using Sonazoid® with endoscopic ultrasonography reported a significant difference in peak intensity between carcinoma and autoimmune pancreatitis, unlike the time to peak [42]. Adding exploration of vascular enhancement kinetics and vascular behaviour seems to increase diagnostic performance compared with the standard B-mode, thus allowing an improvement from 82.6% to approximately 94.7% in the aetiological study of pancreatic masses [43].

CT scan

Unlike the purely vascular distribution of ultrasound contrast agents such as Sonovue®, the distribution of iodinated contrast agents is both vascular and extracellular interstitial. It would thus seem to be potentially useful for exploring and discriminating between cancerous and pancreatitis tissue (the vascular and fibrous aspects). The purely morphological appearance is rarely sufficient for distinguishing between adenocarcinoma and a chronic pancreatitis pseudotumour, especially as the preferred site of CP-pTs in the head is also associated with effects on one or both ducts, which can mimic a carcinoma [28,33]. Comparison of the vascular enhancement dynamics and histological factors has shown a positive correlation between the absolute degree of enhancement in the arterial phase (30 s) and angiogenesis factors (microvascular density and VEGF level) and the opposite with the degree of fibrosis [44]. The presence of fibrosis is responsible for delayed enhancement related to the extravascular-extracellular component. This particularly explains the usefulness of undertaking a delayed phase scan (4 min) for tumour detection if the tumour is isodense [6]. Can enhancement profiles be established, then? Comparison in a triphasic scan after injection of contrast agent differentiated three types of curves: an enhancement peak in the early phase (30–40 s) followed by progressive washout for the normal parenchyma, a peak moved to 60–70 s in the context of chronic pancreatitis followed by progressive washout, and finally progressive enhancement for the adenocarcinoma. Comparison of the curves shows a performance of 82–90% for differentiating chronic pancreatitis from cancer, with sensitivity of 82–94% and specificity of 83–90% [45]. This is consistent with a more recent study where the positive predictive value of a progressive enhancement curve followed by a plateau without secondary washout was 92% for the diagnosis of adenocarcinoma (sensitivity 74.2%, specificity 93.7%). It should however be noted that while the curve profile was observed in 23/25 patients with carcinoma, it was also detected in the upstream atrophic parenchyma [46]. Perfusion techniques also allow angiogenesis parameters to be studied. The perfusion parameters of adenocarcinoma compared

with healthy pancreas (blood flow and volume, permeability area) are significantly decreased [47,48], and reduction in them is more marked for adenocarcinoma than for chronic pancreatitis [49]. Profiles and quantitative studies have been combined by Lu et al., showing a significant difference in the enhancement profile and more pronounced reduction in these three parameters in carcinoma compared with CP-pTs [50].

MRI

With its multiparametric study can MRI help us go further? By combining cholangiographic exploration with injection of gadolinium chelates, sensitivity has been reported of 93% and specificity of 87% for distinguishing between the two conditions. The presence of a hypointense lesion with relatively well-defined contours in the portal phase after gadolinium injection seems to be the most discriminating factor for diagnosis of carcinoma [51]. Studies of enhancement kinetics after injection of gadolinium chelates have given similar results to CT results but are still difficult to use. Gradual enhancement of the lesion was seen in both cases. Only the percentage of enhancement in the delayed phase was significantly different, being more marked in the case of carcinoma [52]. This was also observed in the shape of the intensity/time curve as progressive enhancement until 2–3 min after injection, followed by washout or a plateau. While the presence of a secondary plateau was only seen with carcinomas, there was always an overlap with CP-pTs in the case of secondary washout. For CP-pTs, help was provided by detection of an identical curve in at least one other region of the pancreas [53].

Adapted from endoscopic retrograde cholangiopancreatography, MRI cholangiopancreatography performs well for diagnosing pancreatic cancer, with sensitivity of 84% and specificity of 97% [54]. Using duct morphology criteria, a normal or regularly stenotic duct visualised within the mass is a sign, with good sensitivity at 85% and specificity at 96%, for diagnosis of CP-pT (Fig. 7a, b) [55].

Diffusion imaging is used more and more in oncology. In adenocarcinoma, this diffusion appears to be restricted by virtue of its fibrous character. Exploration with a high *b* value (1,000 s/mm²) appears to be effective for detecting pancreatic adenocarcinoma, with sensitivity of 96.2% and specificity of 98.6% [56]. This restriction will also be seen with CP-pTs. On the other hand, the quantitative data appear to be more disparate [57]. Carcinomas have mean ADC values which are significantly lower than those of the normal pancreas and CP-pTs [58]. However, depending on the differentiation and the fibre content of the tumour, the ADC values calculated overlap between the various conditions [59]. As in all diffusion protocols, the lack, especially, of standardisation makes comparative analysis of literature data difficult, the calculated values varying depending on the sequences and the *b* values used [60]. The ADC of CP-pTs varies between 0.69–1.23, 2.09, 1.04–1.35 10⁻³ mm²/s for the *b* values used of 500, 600 and 1,000 s/mm² respectively [61–63].

MRI perfusion data are similar to CT data: the parameters extracted from pharmacokinetic models of enhancement curves (*K*_{trans}: volume transfer coefficient, the fractions of volume respectively occupied by the vascular and extravascular-extracellular spaces) reflect the respective

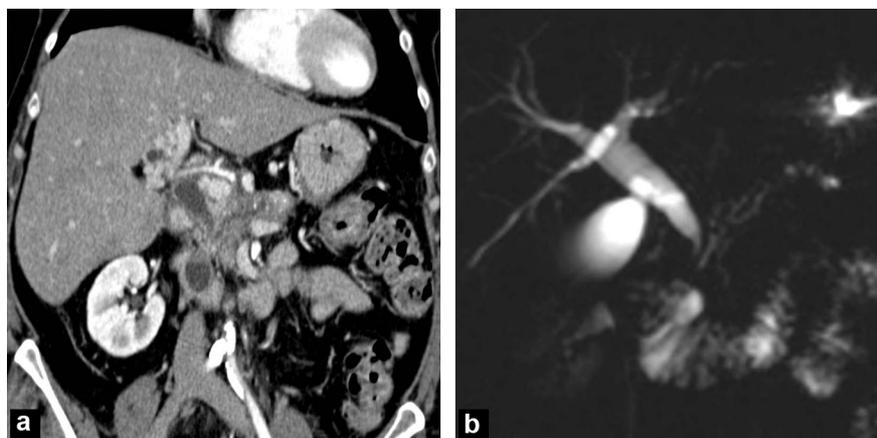


Figure 7. Focus of chronic pancreatitis: penetrating duct sign: a: contrast-enhanced coronal CT reformation. Hypodense area of the pancreatic isthmus. Microcalcifications of the body of the pancreas in chronic calcific pancreatitis. Visualisation of the pancreatic duct with no sign of stenosis; b: corresponding RARE sequence MRCP. Irregular pancreatic duct, but without stenosis, within infiltration of the parenchyma of the isthmus.

components of vascular space (and therefore the density of the microvasculature) and fibrosis. The same difficulties will be encountered in differentiating adenocarcinoma from CP-pT. The signal intensity/time curves have a comparable profile. The difference may be found in the microvascular density (MVD) between the two states, as reflected by the parameters f (distribution fraction) and v_e (fraction of the volume occupied by the extravascular-extracellular space) [64].

While results look promising, regardless of the technique used, it is necessary to standardise acquisition protocols and kinetic models to determine reliable quantitative data for use in everyday practice.

Biopsies and cytology

The identification of masses or pseudotumours in chronic pancreatitis lesions is a source of diagnostic problems, irrespective of the type of imaging used. Cytological samples obtained during endoscopy often provide the definitive evidence swaying the decision. Diagnostic accuracy is high between 80 and 90% for diagnosis of adenocarcinoma. The results are not so good however when there is underlying chronic pancreatic disease, with lower sensitivity (54–74% vs. 89–91%) [65,66]. To improve the quality of sampling, percutaneous biopsy can also be performed with a high success rate and low risk of complications [67].

Carcinoma and groove pancreatitis

The duodenopancreatic groove can be the site of infiltration by a pancreatic carcinoma, but also of pancreatitis lesions in cystic dystrophy in heterotopic pancreas (CDHP). The principle feature of CDHP is the presence of cysts surrounded by inflammation and fibrosis in the wall of the intestine, interspersed with heterotopic pancreas lobules and ducts [68]. Clinical signs are similar in both cases (pain 91%, weight loss 73%, jaundice 13%). In imaging, infiltration of the groove appears hypovascular after injection, and in MRI, T1 and T2-weighted sequences do not discriminate. The principal

sign is the detection of cysts, whether in a CT scan or MR image (Fig. 8a, b and 9a, b), that will hallmark CDHP. Cysts were present in CT scans in 19/20 patients with CDHP, with a mean of 4.2 (two to seven cysts) and ranging in size between 6.8 and 14.7 mm, as against a single cyst detected in one patient in a series of nine adenocarcinomas. One single patient had CDHP without cysts being seen in imaging, but found in a histopathological examination [69,70]. Rare solid forms of CDHP have been reported.

Conversely, where there is infiltration of the groove, some signs should cast a doubt on a diagnosis of CDHP and encourage caution: the presence of biliary dilatation, found cumulatively in 100% of cases of carcinoma compared with 28% of CDHP cases [69–71], involvement of the gastroduodenal artery (sheathing, stenosis or occlusion), the absence of alcohol consumption (present in 86% of CDHP cases), late appearance after 50 years of age. Endoscopic ultrasonography can then provide information by detecting any cysts in the duodenal wall or by allowing cytological samples to be obtained. One case of carcinoma on a background of CDHP has been reported [72].

Adenocarcinoma and autoimmune pancreatitis (AIP)

Autoimmune pancreatitis, a chronic inflammatory process of the pancreas, is rare (1.86 to 6.6% of the causes of chronic pancreatitis). Two histological and clinical conditions have gradually been identified. Type 1 (lymphoplasmacytic sclerosing pancreatitis), more common in Asia, is found in an autoimmune context of IgG4-related systemic diseases, including in 60% of cases of other autoimmune diseases such as cholangitis, autoimmune hepatitis, or Sjögren's syndrome (Fig. 10a–g). It combines a dense lymphoplasmacytic infiltrate, positive with IgG4 immunostaining, fibrosis and venulitis, and is associated with raised serum IgG4 levels [73–75]. Type 2, the most common in Western countries, is characterised by an isolated pancreatic lesion with ductal fibrosis and granulocytic epithelial lesions. Association with an inflammatory condition of the digestive tract is reported

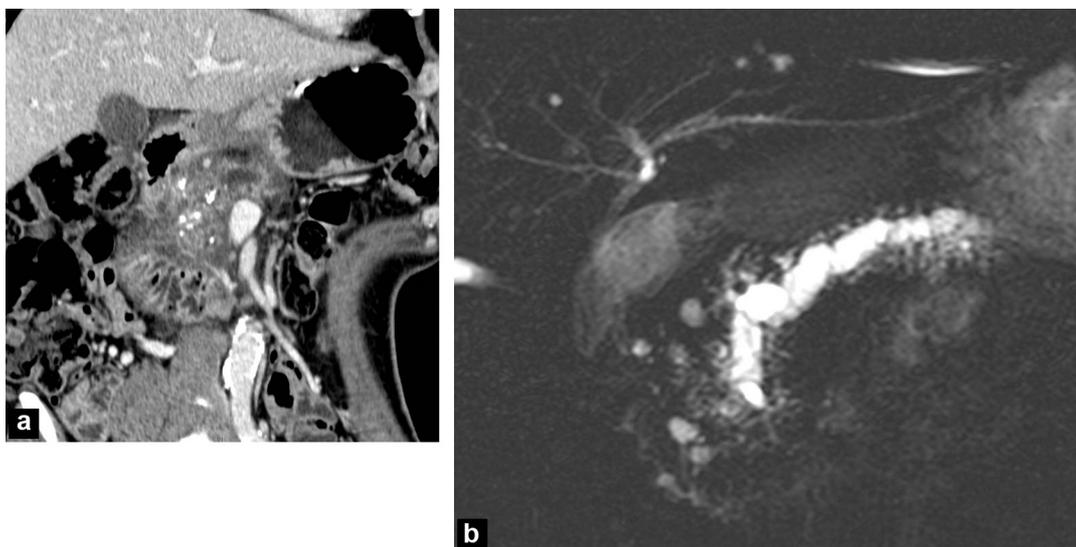


Figure 8. Cystic dystrophy in heterotopic pancreas. Pseudotumour infiltration of the pancreatic groove: a: contrast-enhanced coronal CT reformation. Infiltration of the groove, chronic pancreatitis lesions of the head with calcifications and dilatation of the pancreatic duct; b: corresponding T2-weighted RARE MRCP sequence. Obstructive dilatation of the pancreatic duct due to duct lithiasis in the head of the pancreas. Groove cysts indicating CDHP.

in 20-30% of cases. The IgG4 concentration is normal. A number of clinical, laboratory test, histological and imaging criteria have been put forward for diagnosis of AIP (HISORT criteria, Asian consensus diagnostic criteria) [76–78].

Nearly 10% of presumed carcinomatous masses surgically operated have been composed of pseudotumoral forms of pancreatitis, nearly half of which were thought to be focal forms of autoimmune pancreatitis [79]. These focal forms constitute up to 67% of AIP series, with involvement predominantly of the head [80]. There are many reasons for these resections: ignorance of these atypical forms, absence of preoperative measurement of IgG4, false positives from preoperative cytological samples. The rate of histological false positives for carcinoma or suspected carcinoma is high, reaching 32% for biopsies and 41% for fine needle cytology [81].

Increase in serum IgG4 concentration is an important point in the diagnostic criteria for type 1, but is absent in

type 2, the most common form in the West. A concentration higher than 135 mg/dl seems to have sensitivity of 97% and specificity of 95% for diagnosis of AIP [82], but high concentrations have also been described with carcinoma (10%) [83]. Increased levels of tumour markers (CEA, CA19-9) can be encountered in AIP.

Certain imaging criteria may attract our attention because they are more frequent in AIP: both early and delayed homogeneous enhancement of the lesion, close to that of normal parenchyma, peripheral pseudocapsule, a duct visible in the mass with an hourglass stenosis, absence of upstream atrophy or marked dilatation of the pancreatic duct (< 4 mm), multifocal involvement, absence of contact vascular involvement [74,84].

Given the autoimmune context, the detection of other intra- or extrapancreatic lesions will be of considerable importance. Except in particular contexts (intraductal papillary mucinous tumours of the pancreas), macroscopic

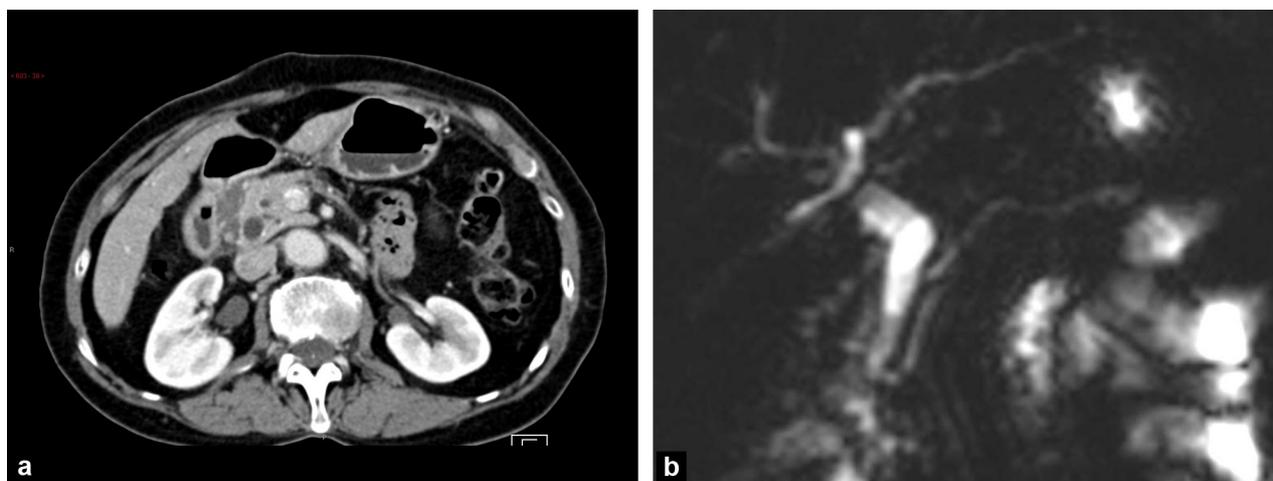


Figure 9. Groove carcinoma. Infiltration of the pancreatic groove: a: contrast-enhanced axial CT slice. Homogeneous infiltration of the groove. Associated dilatation of both ducts; b: corresponding T2-weighted RARE MRCP sequence. No visible cyst.

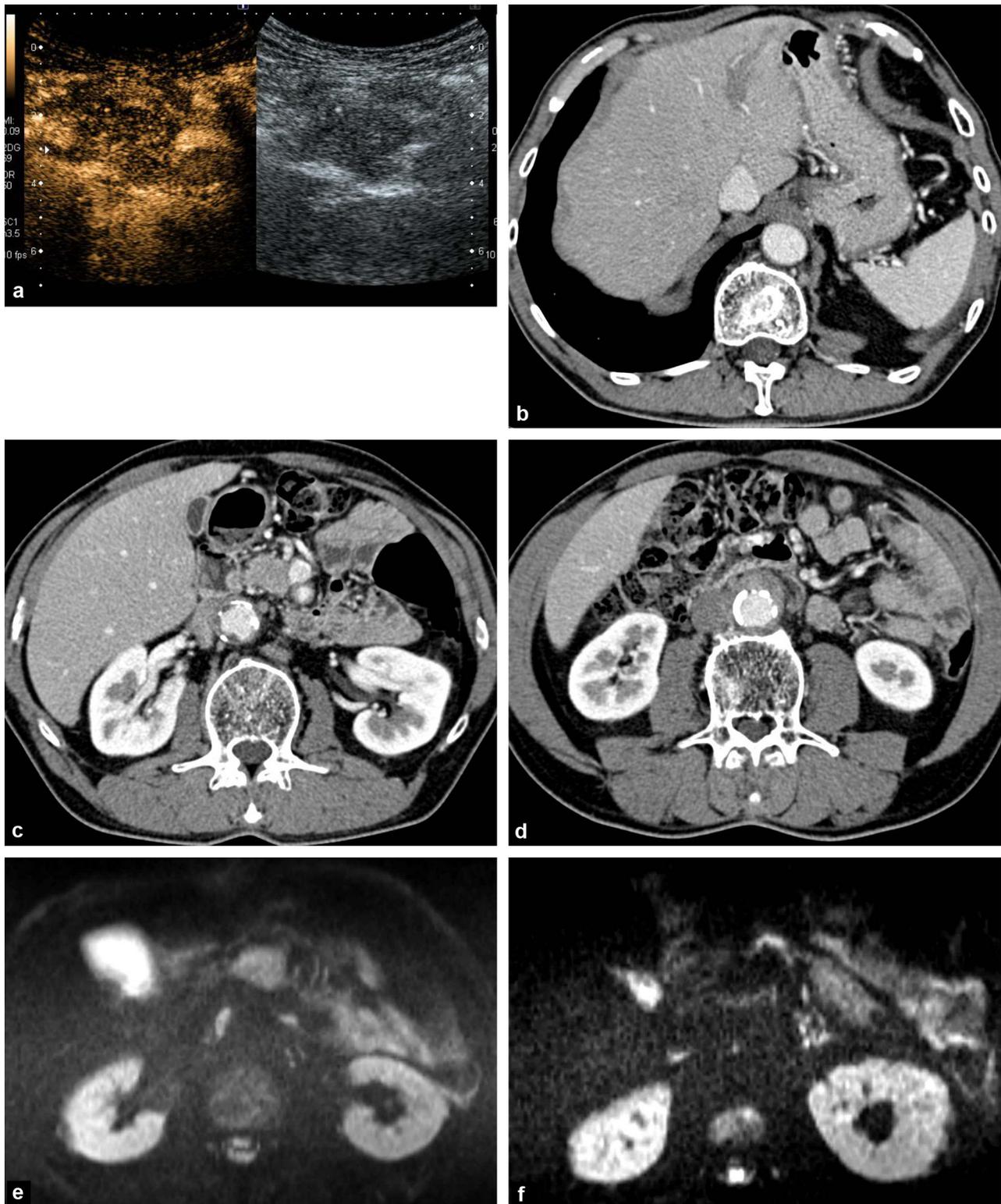


Figure 10. Atypical autoimmune pancreatitis pseudotumour of the head of the pancreas. Discovery, due to abdominal pain, of a hypoechoic nodule of the head: a: contrast-enhanced ultrasound, image at 25 s: well-defined hypoechoic nodule. Early homogeneous enhancement; b–d: axial CT with injection. Peribiliary infiltration of the left hepatic lobe. Isodense nodule of the head of the pancreas. Periarterial sheathing infiltration of the superior mesenteric artery and aorta; e, f: diffusion MRI at b 600. Bifocal pancreatic lesion with head and body hyperintensity; g: axial T1-weighted MRI with injection: periaortitis. In all, multifocal lesions due to an IgG4 pathology confirmed by liver biopsy.

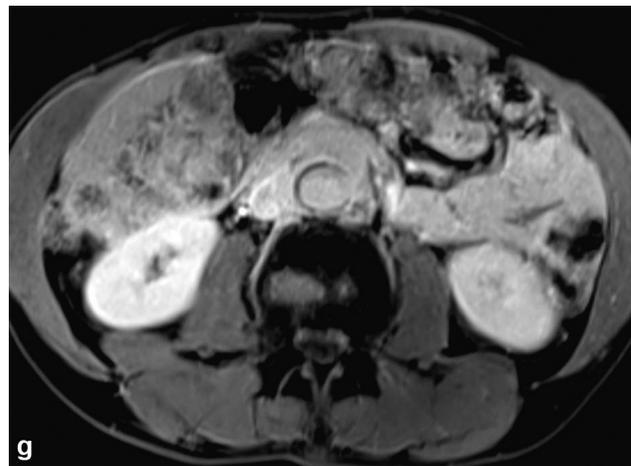


Figure 10. (Continued).

multifocal forms of adenocarcinoma are unusual, even if a microscopic multifocal lesion or identical mutations have been detected in 0–6% of total pancreatectomy specimens [85,86]. Diffusion MRI shows a reduction in the ADC in AIP, with values lower than those of pancreatic carcinoma or the healthy pancreas. However, the optimal discrimination threshold values vary depending on the series and the diffusion sequences (0.88 to $1.075 \times 10^{-3} \text{ mm}^2/\text{s}$) and make them still difficult to use in practice. Detection of hyperintense diffuse or multifocal lesions and longitudinal morphology,

more than measurement of the ADC, are the elements helping with diagnosis, in contrast to the solitary, nodular character of adenocarcinoma [87,88]. FDG-PET is also useful here. While lesional binding is found in virtually 100% of cases of AIP and in 73–82% of cancers, the most interesting differences concern extra-lesional binding: in AIP and cancer, multifocal pancreatic binding is 50% versus 5%, diffuse pancreatic binding 53% versus 3%, salivary binding 35% versus 0% and renal binding 17% versus 0%, respectively (Fig. 11a–c) [89,90].

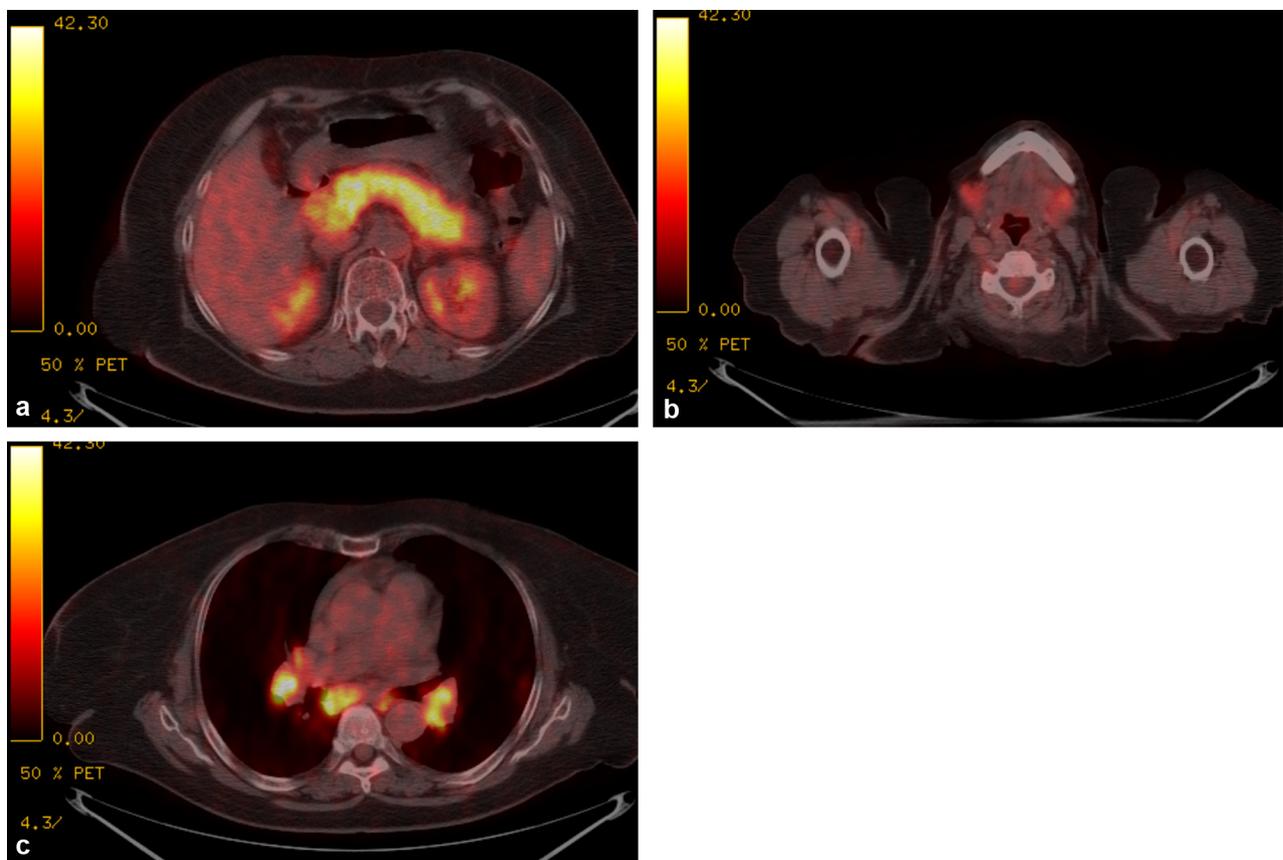


Figure 11. PET appearance of pancreatic and extrapancreatic binding in autoimmune pancreatitis: a: pan-glandular binding; b: salivary binding; c: mediastinal lymph node binding in associated sarcoidosis.

Response to corticosteroid treatment is one of the diagnostic criteria for AIP. A therapeutic test for this can be included in the diagnostic strategy for AIP when the criteria are highly suggestive or compatible but not definitive [91]. In the case of atypical masses which could suggest AIP (a young patient, absence of risk factors, associated with other autoimmune diseases, absence of weight loss or raised CA19-9), a therapeutic test of 15 days of corticosteroids could be included in the diagnostic process [92]. However, according to Levy et al., this should only be envisaged in cases of an atypical mass after at least two biopsies containing no tumour cells have been carried out by experienced specialists [93]. These biopsies are the major determinant for the diagnosis of focal AIP in type 2 lesions. However, they are still difficult to interpret; diagnosis with certainty requires the presence of both pancreatic tissue and ducts, elements that are only present in 26–44% of biopsies [76,94]. It should also be noted that some cases of synchronous carcinoma and AIP have been reported [95].

Conclusion

Imaging techniques are effective in the diagnosis of classic forms of pancreatic adenocarcinoma. Other than in these classic forms, detailed analysis of clinical and imaging signs and symptoms should be undertaken to determine the atypical form, avoid primary diagnostic errors and provide direction for more in-depth investigations. While functional imaging can reveal significant differences between adenocarcinoma and pancreatitis pseudotumours, its utilisation in current practice is still limited for individual use. Eliminating diagnosis of carcinoma must be the primary objective in management of these patients, given its higher frequency in comparison with atypical forms of inflammation and its poor prognosis. Biopsies are an effective means of removing doubts concerning diagnosis.

TAKE-HOME MESSAGES

- Pancreatic adenocarcinoma is still a cancer with a poor prognosis. Currently, only R0 surgical resection can provide hope of better survival.
- Radiological investigations (CT, MRI) are effective for the diagnosis and staging of adenocarcinoma in its classic form.
- Acute pancreatitis associated with cancer is unusual. Any acute pancreatitis where the aetiology has not been found or which has an atypical presentation (left location, duct dilatation or segmental atrophy) must be further investigated (endoscopic ultrasonography, close monitoring).
- In 5 to 11% of cephalic duodenopancreatectomies reported for a solid mass presumed to be a tumour, the cause is benign. The main aetiologies are chronic pancreatitis foci or focal autoimmune pancreatitis. While differences exist, particularly in the analysis of curves of enhancement kinetics after injection, the common fibrous character of these different conditions still makes it difficult to differentiate

between them, no matter what technique is used (ultrasound, CT, perfusion or diffusion MRI).

- A rigorous multimodal approach to the signs and symptoms looking for any discordant feature is essential in order to obtain endoscopic or percutaneous histopathological samples if there is any doubt.
- The absence of cysts or no alcohol consumption should lead to a possible diagnosis of CDHP being questioned where there is infiltration or groove pancreatitis, and result in a subjacent infiltrating tumour being sought.

Clinical case

A 50-year-old male patient referred for jaundice and in whom a lesion of the head of the pancreas was discovered.

CT exploration 70 s (Figs. 12 and 13) and 3 min (Fig. 14) after injection.

Coronal RARE MRCP sequence also performed (Fig. 15).



Figure 12. Axial CT centred on the pancreas 70 s after injection. Pancreatic duct discretely visible.



Figure 13. Axial CT centred on the head of the pancreas 70 s after injection. Irregular hypodense mass in the anterior part of the head.

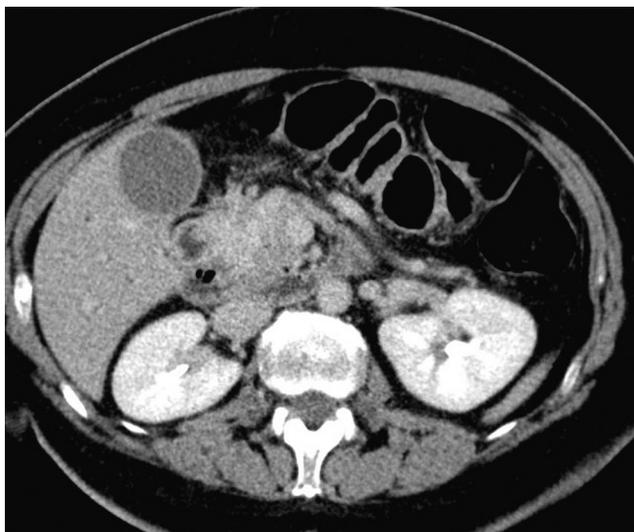


Figure 14. Axial CT centred on the head of the pancreas 3 min (delayed phase) after injection. Progressive enhancement of the mass.

Endoscopic ultrasonography performed with fine needle biopsy. The histopathological results were as follows: inflammatory cells, no tumour cells. IgG4 concentration: 265 (nl 180). A course of 15 days corticosteroid treatment was begun.

Three weeks after the start of corticosteroid treatment a follow-up CT scan was performed to monitor changes (Figs. 16 and 17).

Questions

1. How do you analyse the initial images?
2. Do you agree with the proposed diagnosis of autoimmune pancreatitis?

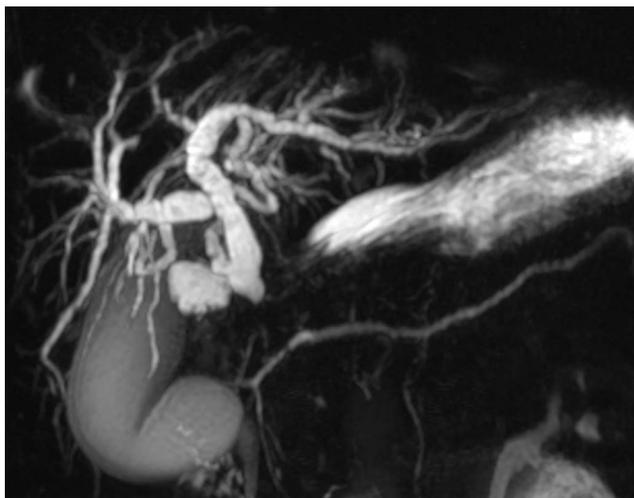


Figure 15. MRCP with coronal incidence and RARE sequence. Bile duct dilatation with stenosis of the intrapancreatic bile duct without affecting the pancreatic duct.



Figure 16. Axial CT centred on the head of the pancreas 70 s after injection performed 3 weeks after the start of corticosteroid treatment. Definite dilatation of the pancreatic duct. Contrast uptake by the biliary stenosis of the lower common bile duct.



Figure 17. Corresponding coronal MPR centred on the head of the pancreas 70 s after injection. Long, tight stenosis of the intrapancreatic bile duct.

Answers

1. The initial CT scans show poorly limited discretely hypodense infiltration of the anterior part of the head of the pancreas, infiltrating the fat in front of the duodenum. No effect on the pancreatic duct can be seen but there is clear dilatation of the bile ducts with an intrapancreatic stenosis. The atypical features for diagnosis of autoimmune pancreatitis are irregular infiltration of the pericephalic fat and, particularly, late enhancement of the lesion suggesting a marked fibrous character. A high IgG4 concentration is possible in 10% of carcinomas.
2. The images at 3 weeks show an increased effect on the bile ducts and above all on the pancreatic duct, which does not fit the diagnosis of AIP and means that this diagnosis should be rapidly reconsidered. New

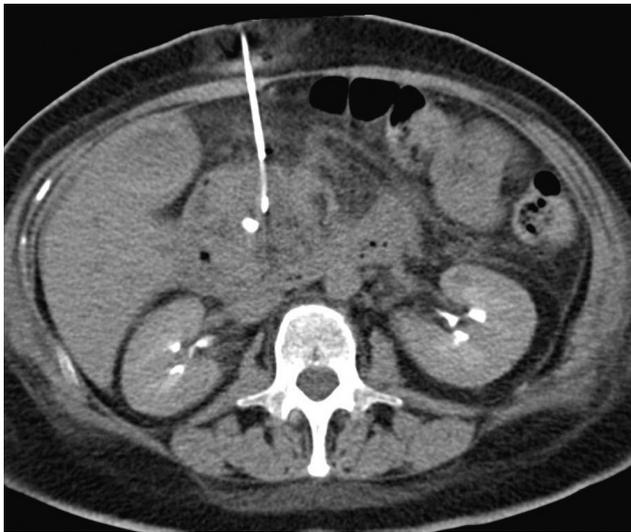


Figure 18. CT scan with injection. Needle biopsy via an anterior approach of the pancreatic mass.

percutaneous biopsies (Fig. 18) led to a diagnosis of pancreatic adenocarcinoma.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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