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Clinical and CT imaging features of pancreatic acinar cell carcinoma

Aspetti clinici e TC del carcinoma a cellule acinari del pancreas

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Abstract
Purpose. This study was undertaken to analyse the clinical characteristics and computed tomography (CT) imaging features of patients with pancreatic acinar cell carcinoma and to clarify characteristic imaging features.
Materials and methods. Clinical and CT imaging records of ten patients with pancreatic acinar cell carcinoma (three women and seven men; mean age, 58 years) examined using multidetector CT scanners were retrospectively studied. CT features emphasised included lesion location, size, shape, margin, solid or cystic component, density and enhancement. Imaging results were correlated with intraoperative surgical and pathological results.
Results. Lesions were distributed throughout the pancreatic head (n=3), body (n=3), tail (n=2) and both body and tail (n=2). The average diameter was 6.1 cm, varying from 2.3 cm to 15.8 cm. The tumours were round or oval (n=7) or lobular (n=3). Seven tumours appeared as enhanced solid pancreatic masses, with the large masses having hypodense areas; three had >75 % cystic component; seven (70%), including four solid and three cystic masses, had well-circumscribed or partially well-defined thin, enhanced encapsulation. After contrast injection, the masses presented heterogeneous enhancement.
Conclusions. Acinar cell carcinoma should always be considered when a large pancreatic mass with typical imaging is found in solid masses with variably sized central cystic areas or cystic masses.

Keywords CT · Acinar cell carcinoma · Pancreas · Cystic mass · Mural nodules

Obiettivo. *Lo scopo di questo studio è stato quello di analizzare le caratteristiche cliniche e di imaging TC dei pazienti con carcinoma a cellule acinari del pancreas e di chiarire le caratteristiche imaging del carcinoma a cellule acinari.*
Materiali e metodi. *Sono stati retrospettivamente esaminate gli aspetti clinici e di imaging TC di 10 pazienti con diagnosi di carcinoma a cellule acinari del pancreas (tre femmine e sette maschi, età media 58 anni) sottoposti ad esame TC multidetettore. Le caratteristiche TC analizzate hanno incluso sede, dimensione, forma, margini, componente solida o cistica, densità ed enhancement delle lesioni. Gli aspetti dell' imaging sono stati quindi correlati con i risultati intraoperatori chirurgici e patologici.*
Risultati. *La sede delle lesioni è risultata ubiquitaria a livello di testa (n=3), corpo (n=3), coda (n=2), e sia di corpo che coda (n=2) del pancreas. Il diametro medio della lesione è risultato pari a 6,1 cm, compreso tra 2,3 cm e 15,8 m. I tumori sono risultati di forma rotonda o ovale (n=7) o lobulare (n=3). Sette tumori sono risultate lesioni solide del pancreas, con aree ipodense contestuali; tre presentavano componenti cistica superiore al 75%; sette tumori (70%), di cui quattro solidi e tre con componente cistica, presentavano pareti sottili ben circoscritte o pazialmente sottile, vascolarizzata. Dopo iniezione di mezzo di contrasto, l'enhancement risultava eterogeneo.*
Conclusioni. *La diagnosi di carcinoma a cellule acinari dovrebbe essere presa in considerazione nel caso di lesioni pancreatiche solide di grandi dimensioni con caratteristiche imaging tipiche e presenza di aree centrali cistiche di dimensioni variabili.*

Parole chiave *TC · Carcinoma a cellule acinari · Pancreas · Massa cistica · Noduli murali*

Introduction

Acinar cell carcinoma (ACC) is a rare neoplasm of the pancreas originating from acinar elements of the exocrine pancreas, accounting for approximately 1 % of nonendocrine tumours [1, 2]. Given its rarity, the clinical and imaging appearance, treatment and outcome of this disease have not been fully investigated; case reports, multicentre studies, small-scale studies and relatively limited literature reviews represent the available literature on this disease [3–7]. However, previously published papers mostly focus on clinicopathological features, and radiological characteristics have not yet been fully clarified. In addition, imaging manifestations of ACC show a solid mass with a varying proportion of cystic components and a thin, enhanced capsule [8–11]. Interestingly, there is a high incidence of cystic ACC lesions in the hospital with which the authors are affiliated. Thus, imaging features and clinical characteristics of ten patients with ACC, including both solid and cystic masses verified by surgery and pathology, are delineated and discussed to help radiologists become more proficient with recognising ACC and thus providing more accurate diagnosis.

Materials and methods

Clinical data

The protocol for this study was approved by the Institutional Review Board of our institution, and informed consent for this retrospective study was acquired from the patients. The records of ten patients diagnosed with pancreatic ACC (seven men and three women; age range 38–71 years) from January 2004 to June 2011 were reviewed. The available clinical manifestations, as well as surgical and pathological reports were reviewed. After their operations, patients were assessed clinically and with ultrasonography (US), as well as with multidetector computed tomography (MDCT) on follow-up, which ranged from 2 to 58 (mean, 30) months.

CT examination

CT examinations were performed for all ten patients using a LightSpeed VCT 64 (GE Medical Systems, Milwaukee, WI, USA). All patients were administered 500–800 ml of water 30 min prior to CT scan and an additional 250–300 ml immediately prior to the study to achieve adequate gastric and duodenal distension. A total of 80–130 ml of nonionic iodinated contrast material (Omnipaque 300 mg I/ml, GE Healthcare) was injected intravenously at a rate of 2.5–3.5 ml/s with a power injector (Ulrich Medical, Germany) through an 18-gauge intravenous catheter inserted into the antecubital vein. The volume of contrast material delivered was 1.5–2 ml/kg body weight. A 15 ml flush of normal saline solution was administered immediately after the contrast material injection. Three patients underwent dual-phase CT scans during the unenhanced, pancreatic and hepatic venous phases, whereas the other seven underwent triple-phase CT during the same phases. Delay times of arterial, pancreatic and hepatic venous phases were 20–25, 35–45 and 65–75 s, respectively, from the beginning of intravenous infusion. The major scanning parameters were as follows: 100–120 kV, 250 mA, 1.0–1.5 pitch, 0.625- to 4-mm collimation, with slice thickness and intervals of 2.5–5 mm. Coronal and sagittal multiplanar images were also reconstructed from the axial CT data set.

Imaging analysis

Two readers independently reviewed MDCT images on a Picture Archiving and Communication System (PACS) workstation. Both readers were fellowship-trained abdominal radiologists with >10 years of experience in reading pancreatic CT images. Final decisions were made by consensus. Imaging features comprised:

- location (head, neck, body, tail);
- size;
- shape;
- margin and enhanced capsule;
- fraction composed of solid versus cystic material (greater or less than 50 % solid);
- internal attenuation characteristics on enhanced arterial and pancreatic phase images compared with surrounding pancreatic tissue (hypoattenuation, isoattenuation or hyperattenuation);
- enhancement pattern (peripheral, complete, mural nodule);
- calcification (present or absent);
- biliary and pancreatic ductal dilatation.

Local invasion, vascular encasement, and metastasis were also recorded by each reader. If the radiological and pathological evaluations differed, the pathologic evaluation was considered final.

Pathological technique

All the pathology specimens were reviewed retrospectively by two pathologists. All specimens were fixed in 10% neutral-buffered formaldehyde solution and embedded in paraffin wax. Haematoxylin and eosin (H&E) staining was performed, and macroscopic appearances of each resected segment were analysed with photomacrographs; analysis comprised location, size, shape and edge.

Results

Clinical analysis

Patients comprised seven men and three women with a mean age of 58 (range, 38–71) years. Patients' clinical characteristics are summarised in Table 1. Their complaints included abdominal pain or vague abdominal discomfort (7/10). In three patients (3/10), masses were found incidentally at routine physical examination, one of whom showed an abdominal mass at the beginning of the physical examination. Serum carbohydrate antigen (CA) 19-9 was increased in four patients, with levels four to six times the normal level, whereas alpha-fetoprotein (AFP) was increased mildly in one patient. Other markers [cancer embryonic antigen (CEA) and cancer antigen (CA)-125] were within normal limits in all patients.

All lesions were surgically resected: six patients underwent a pancreaticoduodenectomy, four a distal pancreatectomy with a concurrent splenectomy, and one partial hepatectomy because of metastases. Median survival time was 35 (5–70) months; two patients died from disease recurrence during follow-up.

Image analysis

Table 2 summarises CT features with respect to lesion location, size, shape, margin and encapsulation, composition, calcification and enhancement pattern. Abdominal CT scans localised tumours in the pancreatic head (n=3), body (n=3), tail (n=2) and body and tail (n=2). Tumour diameters ranged between 2.3 cm and 15.8 cm, with an average of 6.1 cm. Seven masses (56%) were round or oval; three (33%) were lobular. Seven (70%) were solid masses, with >75% solid component; five (50%) had relatively distinct borders, uniformly or partially well-defined with thin and enhanced capsules (Fig. 1). Among the seven solid masses, central cystic components were identified in four larger tumours (diameter >4.5 cm) (Fig. 2). Cystic components with or without small solid mural nodules were observed in three tumours (Figs. 3 and 4). Cystic components remained unenhanced during multiphasic scans, whereas mural nodules were enhanced (Figs. 3 and 4). Six tumours exhibited solid masses with heterogeneous hypodensity (n=6) (Fig. 2) and homogeneous hyperdensity (n=1) in the arterial and portal phases (Fig. 5a, b). All six solid tumours and the small solid or mural nodules in the three cystic lesions appeared with a progressively filled-in enhanced pattern during dual-phase scans; however, enhancement in tumours was less than that of adjacent normal pancreatic parenchyma.

Amorphous intratumoural calcifications were identified in one case (Fig. 6a). The pancreatic duct was dilated in one lesion (Fig. 5c). Infiltrative growth was observed in four

Table 1 Clinical features of patients with pancreatic acinar cell carcinoma (ACC)

Tabella 1 *Caratteristiche cliniche dei pazienti con diagnosi di carcinoma a cellule acinari del pancreas (ACC)*

Clinical features	ACC (n=10), n
Sex	
Male	7
Female	3
Median age (years)	58 (38–71)
Clinical manifestations	
Abdominal pain or discomfort	6
Palpable mass	1
No symptoms	3
Obstructive jaundice	2
CA 19-9 (≥35 u/l)	4
AFP (≥8.04 u/l)	1

CA 19-9, cancer antigen 19-9; *AFP*, alpha-fetoprotein

Table 2 Computed tomography imaging manifestations of acinar cell carcinomas (ACC)

Tabella 2 *Caratteristiche imaging alla TC del carcinoma a cellule acinari del pancreas (ACC)*

Imaging manifestations	ACC (n=10), n
Location of tumour	
Head	3
Body and tail	2
Body	3
Tail	2
Mean tumour size	6.1±4.1 cm (2.3–15.8)
Shape	
Round or oval	7
Lobular	3
Encapsulation	7 (4 solid; 3 cystic)
Well circumscribed	5
Partially encapsulated	2
Enhancing capsule	4
Intratumoural calcification	1
Tumour composition	
Cystic lesions(<50% solid)	3
With mural nodule	2
Without mural nodule	1
Solid masses (>50% solid)	7
With central cystic or necrosis	5
Without central cystic or necrosis	2
Enhancement of solid masses	
Hyperdensity	1
Heterogeneous hypodensity	6
Local invasion	3
Vascular encasement	2
Bile duct dilatation	1
Pancreatic duct dilation	1
Lymph node metastases	3
Distant metastases	1

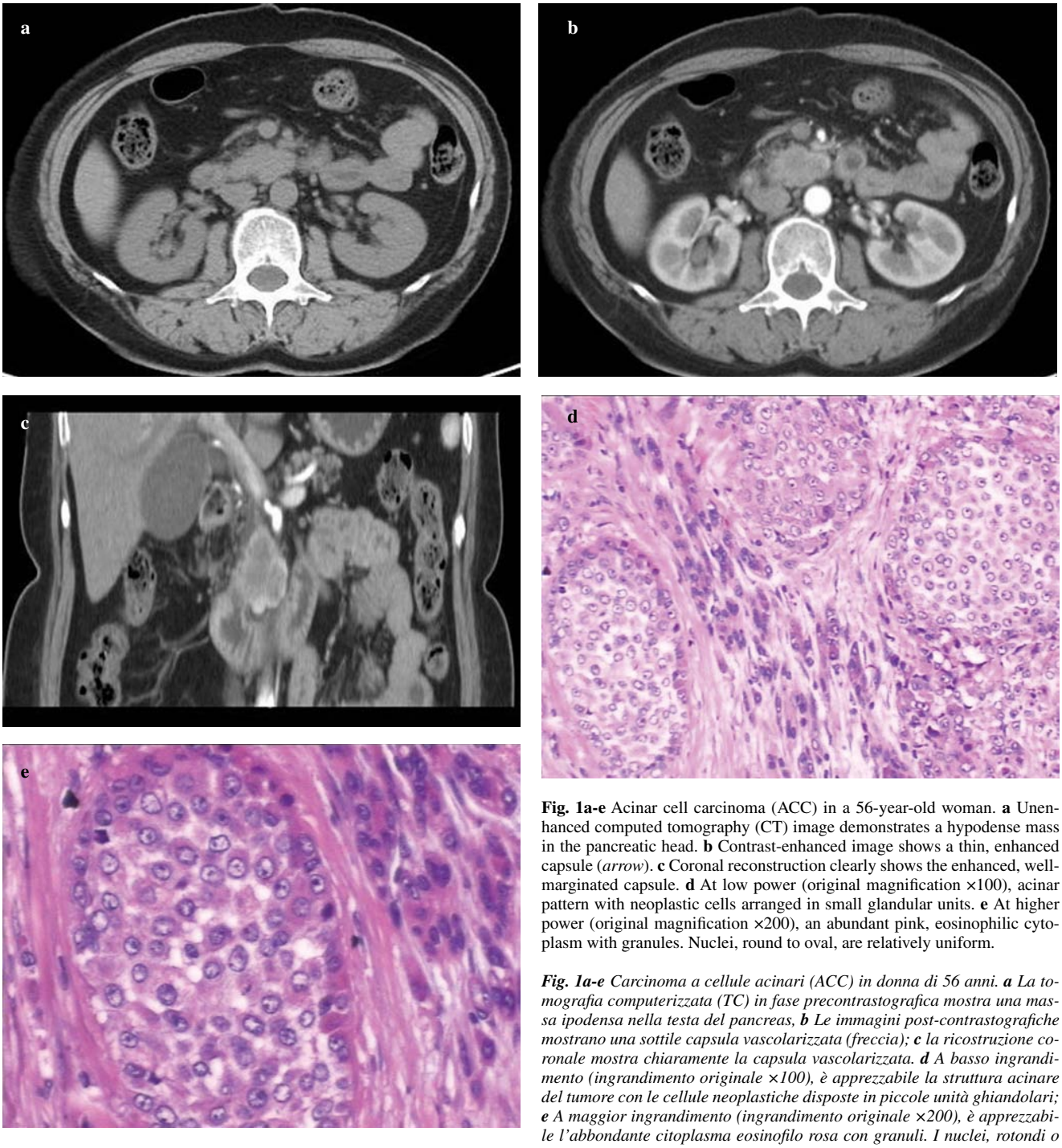


Fig. 1a-e Acinar cell carcinoma (ACC) in a 56-year-old woman. **a** Unenhanced computed tomography (CT) image demonstrates a hypodense mass in the pancreatic head. **b** Contrast-enhanced image shows a thin, enhanced capsule (*arrow*). **c** Coronal reconstruction clearly shows the enhanced, well-marginated capsule. **d** At low power (original magnification ×100), acinar pattern with neoplastic cells arranged in small glandular units. **e** At higher power (original magnification ×200), an abundant pink, eosinophilic cytoplasm with granules. Nuclei, round to oval, are relatively uniform.

Fig. 1a-e *Carcinoma a cellule acinari (ACC) in donna di 56 anni.* ***a*** *La tomografia computerizzata (TC) in fase precontrastografica mostra una massa ipodensa nella testa del pancreas,* ***b*** *Le immagini post-contrastografiche mostrano una sottile capsula vascolarizzata (freccia);* ***c*** *la ricostruzione coronale mostra chiaramente la capsula vascolarizzata.* ***d*** *A basso ingrandimento (ingrandimento originale ×100), è apprezzabile la struttura acinare del tumore con le cellule neoplastiche disposte in piccole unità ghiandolari;* ***e*** *A maggior ingrandimento (ingrandimento originale ×200), è apprezzabile l'abbondante citoplasma eosinofilo rosa con granuli. I nuclei, rotondi o ovali, sono relativamente uniformi.*

masses, which invaded the spleen or an adrenal gland (Fig. 7). Two infiltrative masses encased the surrounding artery or vein (Fig. 7). The bile duct, including the intrahepatic bile duct, ductus choledochus and pancreatic duct, were dilated in one lesion, located in the uncinate of the pancreatic head. The pancreatic duct was dilated, with beading and a diameter of 16 mm. The pancreatic parenchyma was atrophied in the body and tail (Fig. 5c). Three patients had surrounding lymph node metastases (Fig. 5b). Liver metastases were found in one patient (Fig. 2c).

Pathological analysis

Macroscopically, seven tumours were typically solid, with cystic variants being found in three cases. The distinguishing feature of ACC includes circumscription and central

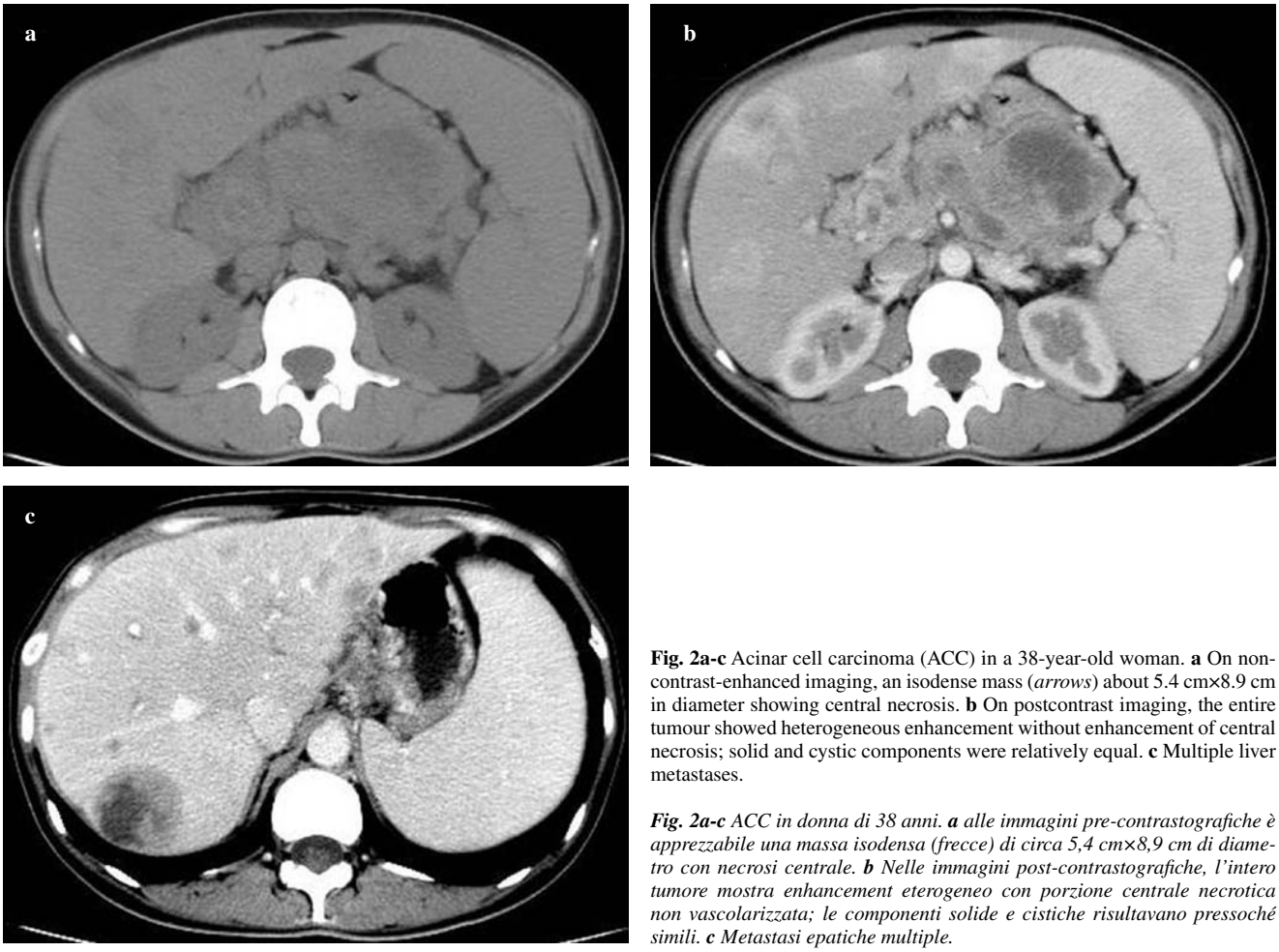


Fig. 2a-c Acinar cell carcinoma (ACC) in a 38-year-old woman. **a** On non-contrast-enhanced imaging, an isodense mass (*arrows*) about 5.4 cm×8.9 cm in diameter showing central necrosis. **b** On postcontrast imaging, the entire tumour showed heterogeneous enhancement without enhancement of central necrosis; solid and cystic components were relatively equal. **c** Multiple liver metastases.

Fig. 2a-c *ACC in donna di 38 anni.* ***a*** *alle immagini pre-contrastografiche è apprezzabile una massa isodensa (frecce) di circa 5,4 cm×8,9 cm di diametro con necrosi centrale.* ***b*** *Nelle immagini post-contrastografiche, l'intero tumore mostra enhancement eterogeneo con porzione centrale necrotica non vascolarizzata; le componenti solide e cistiche risultavano pressoché simili.* ***c*** *Metastasi epatiche multiple.*

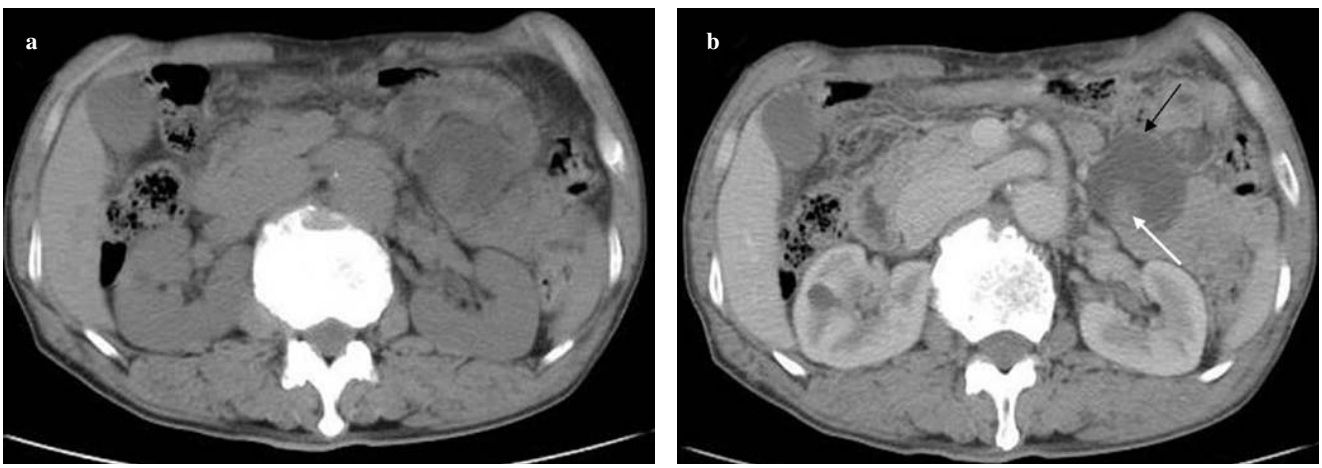


Fig. 3a,b Acinar cell carcinoma (ACC) in a 71-year-old man. **a** Unenhanced computed tomography (CT) revealed a mass about 4.5 cm×4.1 cm in diameter in the pancreatic tail; cystic components with small, solid wall nodules. **b** On enhanced CT, no enhancement was observed in the cystic necrotic area, whereas the thin cystic wall (*black arrow*) and wall nodules (*white arrow*) were enhanced.

Fig. 3a,b *ACC in uomo di 71 anni.* ***a*** *La TC in fase precontrastografica mostra una massa di circa 4,5 cm×4,1 cm di diametro nella coda del pancreas con componenti cistiche con piccoli noduli solidi parietali.* ***b*** *All'esame TC in fase precontrastografica non si evidenzia enhancement a carico della zona necrotica cistica, mentre la sottile parete cistica (freccia nera) e i noduli parietali (freccia bianca) appaiono vascolarizzati.*

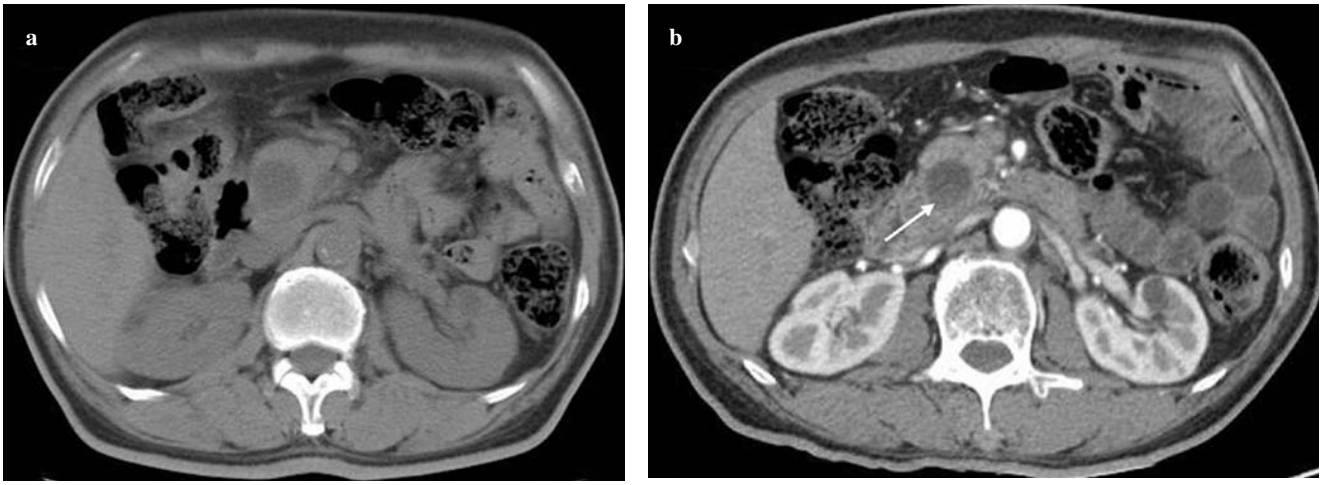


Fig. 4a,b A 66-year-old man with acinar cell carcinoma (ACC) in the pancreatic head. **a** Unenhanced computed tomography (CT). **b** Enhanced CT showing cystic and well-circumscribed tumour, with mildly enhanced mural nodule (*white arrow*) without peripheral enhancement.

Fig. 4a,b *Donna di 66 anni con ACC della testa del pancreas.* ***a*** *TC in fase precontrastografica;* ***b*** *la TC in fase postcontrastografica mostra il tumore cistico e ben circoscritto, con nodulo murale leggermente vascolarizzato (freccia bianca) senza enhancement periferico.*

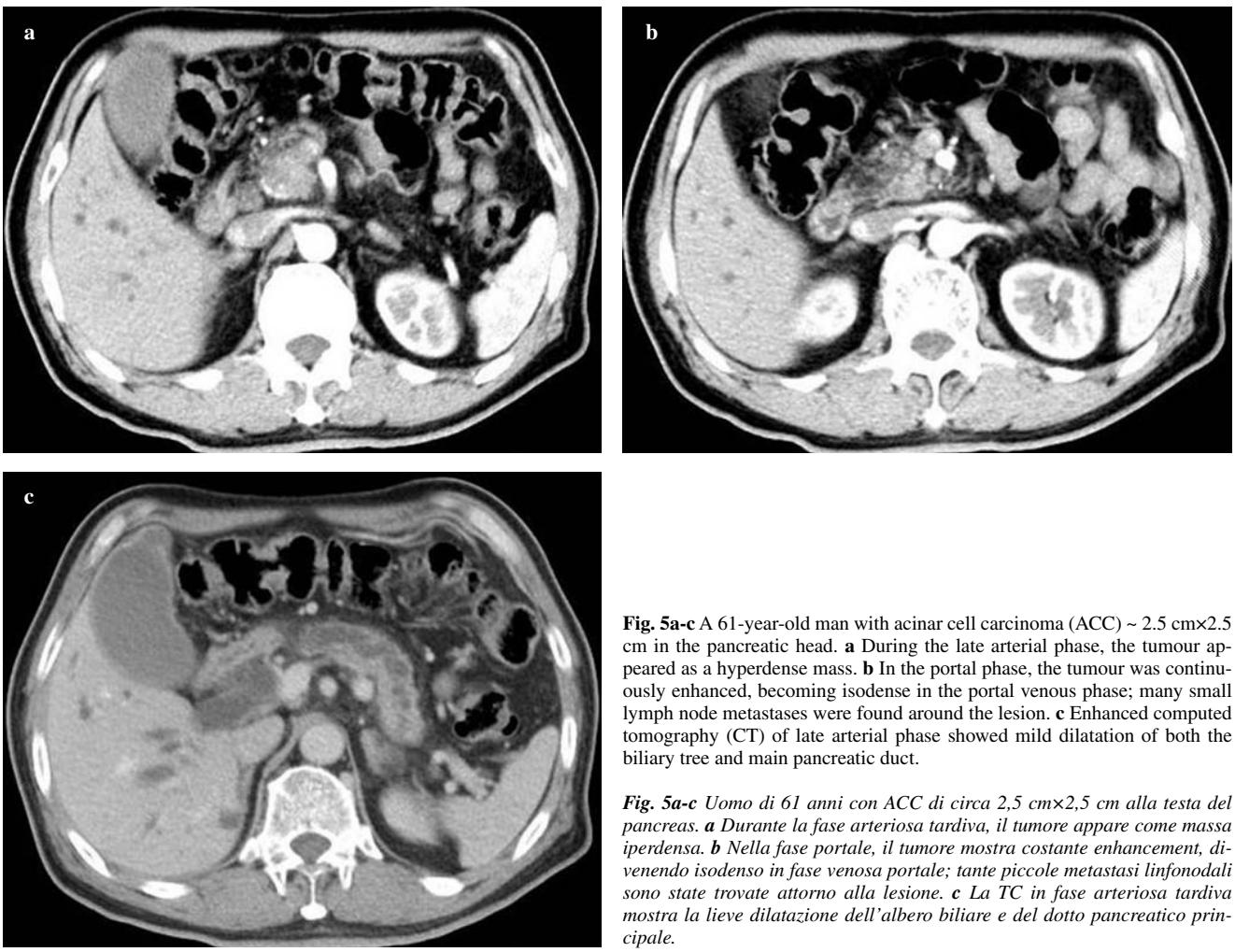
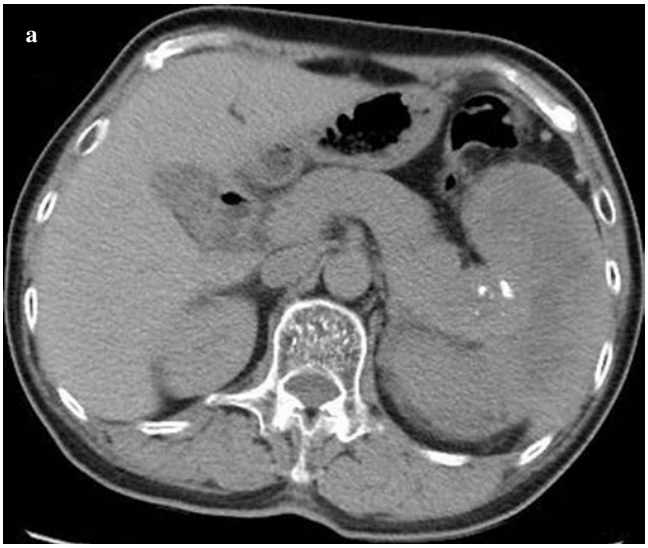


Fig. 5a-c A 61-year-old man with acinar cell carcinoma (ACC) ~ 2.5 cm×2.5 cm in the pancreatic head. **a** During the late arterial phase, the tumour appeared as a hyperdense mass. **b** In the portal phase, the tumour was continuously enhanced, becoming isodense in the portal venous phase; many small lymph node metastases were found around the lesion. **c** Enhanced computed tomography (CT) of late arterial phase showed mild dilatation of both the biliary tree and main pancreatic duct.

Fig. 5a-c *Uomo di 61 anni con ACC di circa 2,5 cm×2,5 cm alla testa del pancreas.* ***a*** *Durante la fase arteriosa tardiva, il tumore appare come massa iperdensa.* ***b*** *Nella fase portale, il tumore mostra costante enhancement, divenendo isodenso in fase venosa portale; tante piccole metastasi linfonodali sono state trovate attorno alla lesione.* ***c*** *La TC in fase arteriosa tardiva mostra la lieve dilatazione dell'albero biliare e del dotto pancreatico principale.*



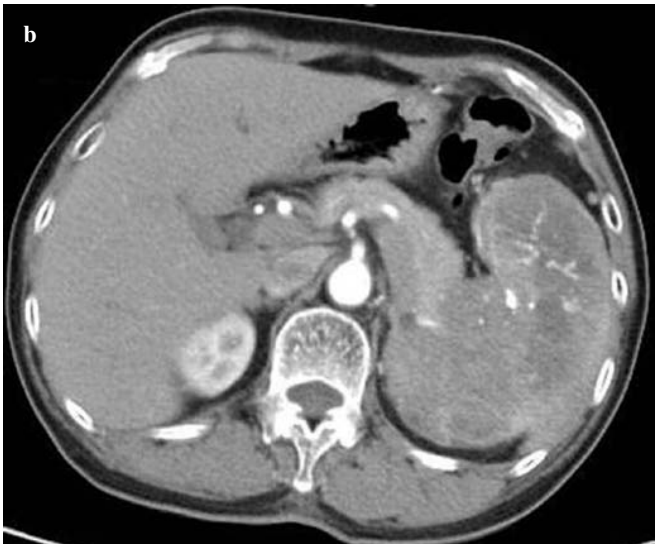


Fig. 6a,b A-62-year-old man with acinar cell carcinoma (ACC) in the pancreatic tail. **a** Unenhanced computed tomography (CT) revealed coarse calcification in the centre of the lesion. **b** Enhanced CT showed a hypodense mass in the pancreatic tail. The lesion invaded the spleen, and its origin was difficult to distinguish.

Fig. 6a,b *Uomo di 62 anni con ACC alla coda del pancreas.* ***a*** *La TC in fase precontrastografica mostra grossolane calcificazioni al centro della lesione.* ***b*** *La TC in fase postcontrastografica mostra una massa ipodensa alla coda del pancreas. La lesione invade la milza e la sua origine risulta difficile da riconoscere.*

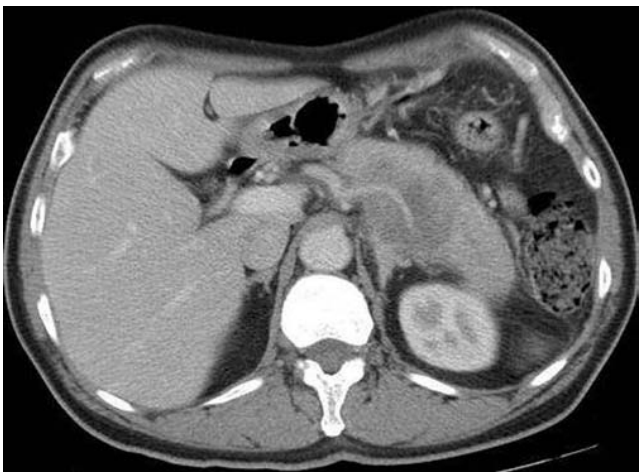


Fig. 7 Acinar cell carcinoma (ACC) in the pancreatic body and tail in a 57-year-old man. The tumour infiltrated the left adrenal gland, and the splenic artery was encased.

Fig. 7 *ACC di corpo e coda del pancreas in un uomo di 57 anni. Il tumore invade il surrene di sinistra ed infiltra l'arteria splenica.*

necrosis. Histopathologically, a pure ACC has two predominant patterns of growth: an acinar pattern, consisting of cells growing in well-formed acini; and a solid pattern, characterised by sheets and cords of cells in a fibrovascular stroma. The microscopic appearance of ACC is distinctive: acinar structures are the hallmark of this neoplasm; thick, fibrous bands separate tumour cells into lobules; the tumour is encapsulated and highly cellular with stroma under light microscope (Fig.1 d,e).

Discussion

Pancreatic ductal adenocarcinoma (DAC) is the most common pancreatic neoplasm, comprising >90 % of all pancreatic neoplasms. ACC accounts for 1% of pancreatic exocrine malignant tumours [12]. Given its rarity, its imaging features have not been fully investigated. It is defined as a carcinoma that exhibits pancreatic enzyme production by neoplastic exocrine cells, and its clinical presentation is usually related to either the local effects of the tumour or to metastases [8]. ACC has nonspecific clinical symptoms, with 55% of patients presenting abdominal pain, weight loss, nausea and vomiting, and some patients with a palpable abdominal mass [13]. ACC is often misdiagnosed as DAC. However, patients with ACC have better prognosis and better long-term survival than those with DAC [1, 14]. The clinical presentation is generally nonspecific, but in 16 % of cases, systemic manifestations related to the liberation of lipase, such as panniculitis and polyarthralgia, may occur [15, 16]. No patient in our study had the corresponding systemic symptoms.

A recent study provided evidence of male predominance in ACC patients and a mean age of 59.6 years, which is consistent with our results, which found seven of the ten

patients were men, with an average age of 58 years.

Few studies have described the radiological findings of ACC [8–10]. The lesion usually appears well marginated, with a thin, enhanced capsule that can be identified in approximately 60% of patients. Most tumours in our review were uniformly or partially well defined, especially after contrast enhancement. Seven tumours (70%) either had well-circumscribed, thin enhanced capsules (n=5) or were partially encapsulated (n=2) on CT imaging. These features can be used to differentiate ACC from DAC, with margins of the latter usually being infiltrative.

In our study, radiological manifestations of ACC were clearly clarified as a large, solid mass with a varying proportion of cystic components, which represented necrosis and haemorrhage. The central hypodense area might be composed of hypovascular neoplastic tissue and/or a necrotic portion [8–10]. The solid portion, when large, contains cystic areas because of necrosis [9, 17]. Mean diameter of tumours with cystic areas were 10.1 cm [9]. To our knowledge, the cystic feature of solid pancreatic tumours may result from necrosis, haemorrhage and tumour-cell degeneration [18]. The study reported here analysed ACC imaging features and clinical characteristics from solid masses without cystic degeneration to mainly cystic components. In a previous study of ours, cystic degeneration occurred in small tumours (up to 2.5 cm in diameter), which is inconsistent with results of this study. Central necrosis only occurred in tumours of larger sizes, with an average diameter of 5.1 cm. Three lesions in our study had >75% cystic component, as shown by hypodensity on unenhanced CT scans, and heterogeneous cystic wall and small solid components or mural nodule enhanced on dual-phase imaging (Figs. 3 and 4). Their diameters were classified into 2.6 cm, 4.1 cm and 5.3 cm, with an average diameter of 4.1 cm.

In our series, the ten ACC lesions did not tend to localise in a specific area; cystic ACC occurs in every part of the pancreas: three cystic masses were located in the head, body and tail, respectively.

ACC is usually a large tumour. Holen et al. [19] studied 37 cases over a 20-year period and showed that eight patients had tumours >10 cm in size. In contrast, the average diameter of DAC is 2–3 cm [20].

Considering the intraductal epithelial origin of DAC, pancreatic duct obstruction is usually present, even with small tumours; hence, dual-duct symptoms are used as specific features to diagnose DAC. Unlike DAC, ductal obstruction may be either mild or even absent in large ACCs in the pancreatic head. Among our ten patients, only one lesion in the pancreatic head led to ductal dilatation (Fig. 5c). This is considered a characteristic but not a specific feature of this type of tumour. DAC could also be differentiated from ACC by indirect signs, such as atrophic distal parenchyma, interrupted duct sign, infiltration of the peripheral nerve and encasement of an artery and/or vein [21].

The majority of authors describe ACC as a hypovascular mass on CT, typically heterogeneously enhanced, but less so than the surrounding pancreatic parenchyma [6, 7]. However, some authors report hypervascular ACC in the pancreatic phase that then become isodense in the portal venous phase; tumours that present this enhancement pattern may mimic a neuroendocrine neoplasm [22, 23]. In our review, solid components of ACC tumours presented intermediate enhancement in the pancreatic phase and continuous enhancement in the portal phase. Therefore, portal-phase imaging could provide a better way of differentiating ACC from DAC. One case exhibited hypervascular enhancement (Fig. 5a, b). Compared with other pancreatic neoplasms, the degree of ACC enhancement is usually better than that of DAC but poorer than that of pancreas neuroendocrine tumours. This helps in ACC diagnosis. However, occasionally, ACC appears as a hyperdense mass and the tumours present isodense masses in enhanced imaging.

When ACC is considered as a diagnosis, solid masses with cystic necrosis should be differentiated from solid pseudopapillary tumours (SPTs) of the pancreas, which easily produce intratumoural haemorrhage. Young age and female gender are helpful in discriminating SPT from ACC [23]. Cystic ACC lesions could sometimes be misdiagnosed as mucinous cystadenomas of the pancreas, which occurs predominantly in perimenopausal women (average age at presentation, 47 years) [24]. They may be unilocular or multilocular and be variable in size. The surrounding thick, fibrous wall, which may be calcified, helps differentiate them from ACC. The mucinous cyst content also aids in the differential diagnosis.

In conclusion, CT imaging may be a useful tool for diagnosing pancreatic ACC based on the following characteristics: larger size; solid or cystic masses with well-circumscribed, thin, enhanced encapsulation and hypovascular mass on CT; solid masses with hypodense area in large masses; cystic lesions with mural nodules or a small solid component; enhancement in the cystic wall; mural nodules; and solid component.

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Conflict of interest None

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