BRIEF ARTICLE

Focal autoimmune pancreatitis: Radiological characteristics help to distinguish from pancreatic cancer

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Author contributions: Sun GF and Zuo CJ contributed equally to this work; Sun GF and Zuo CJ designed the experiment, acquired, analyzed and interpreted the data, and drafted the article; Shao CW designed the experiment, analyzed and interpreted the data, revised the article, and approved the version to be published; Wang JH and Zhang J acquired, analyzed and interpreted the data, and revised the article.

Supported by National Nature Science Foundation of China No. 30970801; National Nature Science Foundation of China, No. 81170435; the China Post-doctoral Science Foundation, No. 20100480545; and the Shanghai Leading Talent Team Construction Special Funds, No. 2011-036

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Telephone: +86-21-81874178 Fax: +86-21-31162238 Received: February 2, 2013 Revised: April 12, 2013 Accepted: May 18, 2013 Published online: June 21, 2013

Abstract

AIM: To identify the radiological characteristics of focal autoimmune pancreatitis (f-AIP) useful for differentiation from pancreatic cancer (PC).

METHODS: Magnetic resonance imaging (MRI) and triple-phase computed tomography (CT) scans of 79 patients (19 with f-AIP, 30 with PC, and 30 with a normal pancreas) were evaluated retrospectively. A radiologist measured the CT attenuation of the pancreatic parenchyma, the f-AIP and PC lesions in triple phases. The mean CT attenuation values of the f-AIP lesions were compared with those of PC, and the mean CT attenuation values of pancreatic parenchyma in the three groups were compared. The diagnostic performance of CT attenuation changes from arterial phase to hepatic phase in the differentiation between f-AIP and PC was evaluated using receiver operating characteristic (ROC) curve analysis. We also investigated the incidence of previously reported radiological findings for differentiation between f-AIP and PC.

RESULTS: The mean CT attenuation values of f-AIP lesions in enhanced phases were significantly higher than those of PC (arterial phase: 60 ± 7 vs 48 ± 10, P < 0.05; pancreatic phase: 85 ± 6 vs 63 ± 15, P < 0.05; hepatic phase: 95 ± 7 vs 63 ± 13, P < 0.05). The mean CT attenuation values of f-AIP lesions were significantly lower those of uninvolved pancreas and normal pancreas in the arterial and pancreatic phase of CT (P < 0.001, P < 0.001), with no significant difference at the hepatic phase or unenhanced scanning (P = 0.4, P = 0.1). When the attenuation value increase was equal or more than 28 HU this was considered diagnostic for f-AIP, and a sensitivity of 87.5%, specificity of 100% and an area under the ROC curve of 0.974 (95%CI: 0.928-1.021) were achieved. Five findings were more frequently observed in f-AIP patients: (1) sausage-shaped enlargement; (2) delayed homogeneous enhancement; (3) hypoattenuating capsule-like rim; (4) irregular narrowing of the main pancreatic duct (MPD) and/or stricture of the common bile duct (CBD); and (5) MPD upstream dilation ≤ 5 mm.

CONCLUSION: Analysis of a combination of CT and MRI findings could improve the diagnostic accuracy of differentiating f-AIP from PC.

Key words: Focal autoimmune pancreatitis; Pancreatic cancer; Computer tomography; Magnetic resonance imaging; Magnetic resonance cholangiopancreatography

Core tip: At present, focal autoimmune pancreatitis (f-
AIP is still very difficult to differentiate from pancreatic cancer (PC). In this study, we compared the incidence of radiological features, investigated the differences in the triple-phase enhancement pattern of f-AIP and PC, and found that the combination analysis contributed to improve the diagnostic accuracy of f-AIP thus avoiding unnecessary surgery.

Sun GF, Zuo CJ, Shao CW, Wang JH, Zhang J. Focal autoimmune pancreatitis: Radiological characteristics help to distinguish from pancreatic cancer. World J Gastroenterol 2013;19(23): 3634-3641. Available from: URL: http://www.wjgnet.com/1007-9327/full/v19/i23/3634.htm DOI: http://dx.doi.org/10.3748/wjg.v19.i23.3634

INTRODUCTION

Autoimmune pancreatitis (AIP) is a rare form of immune-mediated chronic pancreatitis (CP) due to an autoimmune mechanism and is characterized by a marked infiltration of lymphocytes and plasma cells in pancreatic tissue (lymphoplasmacytic sclerosing pancreatitis) and was first described in 1961[1-8]. It can be classified into two radiological types: the diffuse form (the most frequent, 70% of cases) and the focal form (30% of cases), which is characterized by focal swelling of the pancreas, localized narrowing of the main pancreatic duct (MPD) with an irregular wall on imaging modalities[6-8]. Focal AIP (f-AIP) can be due to a mass formation or swollen pancreas located in one or two segments of the gland. AIP has a variety of manifestations, obstructive jaundice occurs in 76% and weight loss in 35% of patients, usually in combination with pancreatic enlargement, especially with focal pancreatic enlargement on imaging, making it very difficult to differentiate from pancreatic cancer[7,9,10].

Treatment for AIP and pancreatic cancer (PC) are completely different. Autoimmune pancreatitis is a benign disease and steroid therapy can rapidly resolve symptoms; for PC, however, surgical resection is preferred, with the criterion of (1) narrowing of the MPD with enlargement of the pancreas, as determined by a review of an imaging study, is met together with the criterion of (2) an increase in serum markers (g-globulin, IgG, or IgG4) and/or the criterion of (3) pathology. In this study, the diagnosis of AIP was established by the presence of criteria 1 and 2 in 4 patients; criteria 1 and 3 in 3 patients; and criteria 1, 2, and 3 in 12 patients.

The f-AIP group included 19 patients (14 men and 5 women; age range, 41-75 years; mean age, 54 years) with 21 lesions who had undergone contrast-enhanced computed tomography (CE-CT) (n = 19), CE magnetic resonance imaging (MRI) (n = 11), and magnetic resonance cholangiopancreatography (MRCP) (n = 16). One patient had 3 lesions which were located at the pancreatic head, body and tail.

Identification of patients with focal pancreatic carcinoma was performed by reviewing patient records between March 2012 and December 2012 obtained from the hospital’s pathology database. All 30 patients (21 men, 9 women; age range, 43-79 years; mean age, 58.2 years) with pathologically (histopathological examination of the surgically resected or biopsied tumor specimen) confirmed pancreatic ductal carcinoma (n = 30) were included in this study. All 30 patients had undergone CE-CT, 26 had undergone MRCP, and 12 had undergone CE MRI using extracellular MR contrast agents (Gd-DTPA).

Thirty patients (20 men, 10 women; age range, 41–68 years; mean age, 53 years) with normal pancreas were also recruited. They were confirmed by reviewing the radiological images and followed-up for more than 6 months. All 30 patients had undergone CE-CT.

CE-CT

In this study, all 79 patients underwent the triple-phase pancreatic CT protocol (Brilliance 16; PHILIPS Medical System) which included an unenhanced scan followed by triple-phase contrast-enhanced scans of the abdomen. The tube voltage was 120 kV, the tube current was 250 mA, and the rotation period was 0.75 s. A total of 90 mL of IV contrast material (iohexol, Omnipaque 300, GE Healthcare) containing 300 mg/mL iodine was intravenously administered as a bolus via a power injector. The injection rate was 3.5 mL/s. Images were obtained during the arterial, pancreatic and hepatic phases at 20, 40 and 80 s, respectively, after contrast medium injection. The median slice thickness for contrast-enhanced images was 3 mm.
MRI and MRCP

MR imaging and MR cholangiopancreatography were performed using a 1.5-T MR imaging system (AVANTO; SIEMENS Medical Systems) and a pre-contrast coil. Pre-contrast T1-weighted MR imaging [repetition time msec/echo time msec, 150 (R) 200/2.1, 4.2] with and without fat saturation and respiratory-triggered T2-weighted MR imaging (5000-8000/80-135) were performed, followed by dynamic fat-suppressed T1-weighted MR imaging (150-200/2.1) after administration of a gadolinium-based contrast agent. MRCP was performed with a single-shot fast spin-echo thick-slab technique (25000-30000/800-1000).

Imaging analysis

Three board-certified abdominal radiologists (with 9, 10 and 15 years of experience) reviewed all CT and MRI images retrospectively using a picture archiving and communication system (PACS) work station (General Electric Medical Systems). During analysis of the CT and MRI findings, all cases were randomly intermixed. The radiologists were blinded to the patients’ clinical data, official reports, radiological examinations on other dates, and histopathological findings. Decisions were made by consensus.

For each patient, the radiologists were asked to make judgments on the following signs: (1) focal pancreatic enlargement and the location of the lesion; (2) capsule-like rim of the lesion; (3) localized irregular narrowing of MPD; (4) stricture of the distal common bile duct; and (5) other associated findings such as calcification, peripancreatic lymphadenopathy and vascular invasion.

When the lesion was confirmed, CT attenuation values of the f-AIP, PC, the apparently unaffected pancreatic parenchyma, and the normal pancreas were measured by one radiologist using a workstation (Advantage Version 4.2, GE Healthcare). The CT attenuation values were measured using unenhanced images and images obtained from arterial, pancreatic and hepatic phases after contrast administration. Following the placement of a region of interest (ROI) in each segment of the pancreas (head, body and tail), CT attenuation values of the pancreatic parenchyma were measured. The mean value of the three segments was used as the CT attenuation value of the pancreatic parenchyma. In f-AIP and PC patients, ROIs were placed both above the lesion and in the unaffected segments of the pancreas. The largest possible spherical ROI was marked, ruling out the pancreatic duct and partial volume averaging from the extrapancreatic structures. The smallest ROI was approximately 3 mm in diameter when the pancreas was atrophic. Delayed enhancement of the AIP and PC lesions was defined as the change in CT attenuation of the lesion between the arterial phase and the hepatic phase. CT attenuation values of the liver and spleen were similarly measured on unenhanced images (when available) and on images obtained in the arterial, pancreatic and hepatic phases.

The MRCP images were reviewed to identify changes in the common bile duct (CBD) and MPD. The MPD and CBD observations were classified into 1 of 3 categories: as displaying (1) normal appearance; (2) stenosis; and (3) complete obstruction (nonvisualization of the obstructed segment). The MPD upstream diameter was evaluated by a review of MRCP images. The MPD upstream diameter and presence of distal pancreatic atrophy were not evaluated in patients with lesions in the pancreatic tail, while stenosis of CBD was not evaluated for patients with lesions in the pancreatic head.

Statistical analysis

Statistical analysis was performed using the Fisher’s exact test to compare the frequencies of imaging findings. The inter-reader agreement was evaluated by measurement of the kappa value. The mean CT attenuation value of the lesion in patients with f-AIP was compared with that of PC. Similarly, the mean CT attenuation values of unaffected segmental pancreas in f-AIP were compared with those of PC and normal pancreas. A comparison of the mean CT attenuation values of other organs (liver and spleen) was also performed in the three groups of patients.

Statistical analyses were performed with nonparametric tests due to the non-gaussian distribution of the data and smaller sample sizes involved in some comparisons of interest. Wilcoxon’s rank sum test was used to compare the CT attenuation values. When comparing two groups, the Kruskal-Wallis test was performed before Wilcoxon’s rank sum test. Fisher’s exact test was applied to compare frequencies of delayed enhancement of the masses and focal enlarged segments. The diagnostic performance of attenuation value increase between the arterial and hepatic phase in the differentiation between f-AIP and PC was evaluated using receiver operating characteristic (ROC) analysis. From the ROC curves, the appropriate cutoff values were determined by selecting the point at which the Yoden index (sum of sensitivity + specificity - 1) was largest. All tests were two sided, and \( P < 0.05 \) was considered statistically significant. Statistical analysis was performed with SPSS software (version 18.0, SPSS).

RESULTS

The imaging characteristics of f-AIP and PC identified by reviewing the CE-CT and MRI/MRCP results are summarized in Tables 1 and 2.

Focal pancreatic enlargement

Of the 49 f-AIP and PC cases, the affected segments of pancreas differed in the extent of enlargement. Of the f-AIP cases, the affected sites of the pancreas were the head in 5 patients, the body in 5 patients, and the tail in 9 patients. Of the PC cases, these values were 16, 6 and 8, respectively. The sausage-shaped enlargement of the affected segments of the pancreas was observed in 11 patients with f-AIP, but not in PC cases. Atrophy of
Table 1 Comparison of imaging findings

| Imaging features                              | Data of assessable patients | Kappa | P      |
|------------------------------------------------|-----------------------------|-------|--------|
|                                               | f-AIP (n = 19) | f-PC (n = 30) |        |
| Sausage-shaped enlargement                     | 0.58 (11/19) | 0.03 (1/30) | 0.38<0.001|
| Delayed homogeneous enhancement                | 1.00 (19/19) | 0.1 (3/30) | 0.88<0.001|
| Hypoattenuated capsule-like rim                | 0.63 (12/19) | 0.03 (1/30) | 0.64<0.001|
| Distal pancreatic atrophy MPD                  | 0.30 (3/10) | 0.95 (20/22) | -0.55<0.001|
| Normal                                         | 0 (0/19) | 0 (0/30) | NS     |
| Irregular narrowing                            | 0.58 (11/19) | 0.06 (2/30) | 0.05 NS |
| Complete obstruction                           | 0.42 (8/19) | 0.93 (28/30) | -0.06 NS |
| CBD                                            | 0.53 (10/19) | 0.47 (14/30) | -0.36 0.027|
| Stenosis                                       | 0.29 (4/14) | 0 (0/14) | 0.3 0.22|
| Complete obstruction                           | 0 (3/19) | 0.53 (16/30) | -0.38 <0.01|
| MPD upstream dilation ≤ 5 mm                   | 1.00 (10/10) | 0.14 (5/22) | 0.66 <0.001|
| Affected location of pancreas                  |               |       |        |
| Head                                           | 0.26 (5/19) | 0.53 (16/30) | -0.08 NS |
| Body                                           | 0.26 (5/19) | 0.2 (6/30) | -0.27 NS |
| Tail                                           | 0.47 (9/19) | 0.27 (8/30) | 0.11 NS |
| Other findings                                 |               |       |        |
| Vascular invasion                              | 0 (0/19) | 0.13 (4/30) | -0.17 NS |
| Pancreatic lymph node                          | 0.16 (3/19) | 0.87 (26/30) | -0.65 <0.001|
| Calcification                                  | 0 (1/19) | 0 (0/30) | NS     |

Data are percentages and numbers in parentheses refer to numbers of lesions. The Kappa value was negative, the corresponding item was not suitable for differentiation. f-AIP: Focal autoimmune pancreatitis; MPD: Main pancreatic duct; NS: Not significant.

the pancreas was observed in 3 f-AIP and 20 PC cases whose lesions were located in the head and body.

Density or signal abnormalities
CE-CT scans showed hypoattenuated or isointensified lesions in the involved segments of the pancreas in 4 and 15 f-AIP cases on precontrast scans, respectively. In all f-AIP patients, the affected pancreas appeared uniformly enlarged with the absence of pancreatic clefts and with a sharp outline (Figures 1-3). AIP and PC lesions all showed decreased enhancement on arterial phase and delayed enhancement on pancreatic and hepatic phases, however, the degree of delayed enhancement in f-AIP was greater than that in PC (Figures 2 and 4, Table 2). MRI imaging showed that the lesion was isointense or slightly hypointense in T1WI and slightly hyperintense in T2WI (Figure 3A and B). The MR enhancement patterns were similar to those of CE-CT.

CBD and MPD Abnormalities
Of the AIP lesions (n = 21), irregular narrowing of the MPD was observed in 13 lesions (Figure 3E), and the remaining 8 lesions did not display this MPD abnormality. Bile duct dilatation was observed in 5 cases which included 4 patients who had lesions at the pancreatic head and 1 at the tail. The range of dilatation was 9-14 mm (mean, 11 mm). The CBD showed a beak-like stricture (Figure 1C). In 3 patients with lesions in the pancreatic head, the upstream MPD was slightly dilated (less than 5 mm), distal pancreatic atrophy was not observed in 14 patients with lesions in the pancreatic body and tail. Of the PC lesions (n = 30), no irregular narrowing of the MPD was observed. Bile duct dilatation was observed in all 8 patients with lesions located in the pancreatic head, and the distal CBD showed an abrupt interruption sign.

Capsule-like rim
Capsule-like rims were observed in f-AIP cases (n = 11), which were shown continuously or discontinuously as hypodense peripancreatic strands on the precontrast CT and delayed enhanced on the delayed phase of dynamic CT (Figure 2). On MR imaging, the capsule-like rim appeared as a T1WI isointense and T2WI hypointense area surrounding the pancreas (Figure 3A and B).

Other associated findings
Other associated findings included calcification (f-AIP, n = 1; PC, n = 0), peri pancreatic lymphadenopathy (f-AIP, n = 3; PC, n = 26) and vascular invasion (f-AIP, n = 0; PC, n = 4).

Comparison of CT attenuation values
The results of the mean CT attenuation values of the f-AIP lesions and uninvolved segments in f-AIP patients and normal pancreas are shown in Table 2. The mean CT attenuation values of f-AIP lesions in enhanced phases were significantly higher than those of PC (P < 0.05, P < 0.05, P < 0.05) (Figure 5). The mean CT attenuation values of the f-AIP lesions were significantly lower than those of uninvolved pancreas and normal pancreas in the arterial and pancreatic phase of CT (P < 0.001, P < 0.001), however, there were no significant differences in the hepatic phase or unenhanced scanning (P = 0.4, P = 0.1). The mean CT attenuation values of normal and unaffected pancreatic parenchyma in the three groups showed no significant differences in the arterial, pancreatic, and hepatic phases (P = 0.1, P = 0.8, P = 0.2). When the attenuation value increase was equal or more than 28 HU this was considered diagnostic for f-AIP, and a sensitivity of 87.5%, specificity of 100% and an area under the ROC curve of 0.974 (95%CI: 0.928-1.021) were achieved (Figure 6).

DISCUSSION
Although the diagnosis of AIP has improved due to a growing awareness of the condition and proposed diagnostic criteria[9], there is no practical strategy to differentiate PC from f-AIP. One must distinguish between the two disorders to prevent unnecessary surgery or delayed
initiation of corticosteroid therapy. A review of the CE-CT and MRI data indicated five imaging features of AIP: (1) delayed homogeneous enhancement; (2) hypoattenuating capsule-like rim; (3) the absence of distal pancreatic atrophy; (4) irregular narrowing of the MPD; and (5) stenosis of the CBD in patients with lesions in the body or tail. The analysis also indicated that those imaging features could be used to differentiate AIP from PC with high accuracy.

Some studies have reported that the head of the pancreas is involved in most AIP cases[^15,20], which is consistent with the study by Woo Ik Chang who showed that the affected site was the pancreatic head in 5 (62.5%) of 8 patients[^13]. However, in our study, the affected site was the pancreatic head in only 4 patients (21.1%). This difference may be due to the following reasons: (1) the pancreatic head may not be the most commonly involved site in f-AIP; and (2) the number of patients studied may have been too small.

In our study, we identified the homogeneous good
enhancement during the delayed phases as useful in differentiating between f-AIP and PC. Similarly, in the study by Kamisawa et al., delayed enhancement was observed in 17 of 17 (100%) AIP patients, while Wakabayashi et al. described delayed homogeneous enhancement in 9 of 9 (100%) AIP patients. In addition, Chang et al. described homogeneous enhancement during the hepatic phase in six of seven AIP patients. The consistency of delayed homogeneous enhancement in this and previous studies shows one of the common imaging features of AIP, but the absence of a further quantitative analysis.

We found that the attenuation values of AIP were significantly higher than those of PC in the enhanced phases, lower than those of unaffected pancreatic parenchyma in the arterial and pancreatic phase, however, no significant differences were observed in the hepatic phase (95 ± 7 HU vs 95 ± 7 HU, 75 s). Takahashi found significantly higher CT attenuation values for AIP (90 ± 19 HU) than for pancreatic carcinoma (64 ± 19 HU) during the hepatic phase (60-70 s). They also found greater enhancement during the pancreatic phase (71 ± 22 HU vs 59 ± 20 HU), although the difference between the two groups was not statistically significant. The difference between the CT attenuation values obtained in this study and those by Takahashi may be related to differences in the timing of scan acquisition, contrast injection rates and CT scanners.

Irregular narrowing of the MPD is one of the most important features of AIP. In our study, 79% of AIP patients (15 of 19) showed segmental irregular narrowing of the MPD, while the number was 6% (2 of 30) in PC patients. Moreover, no or minimal upstream dilatation can also be helpful to differentiate AIP from PC. In the current study, upstream MPD dilatation (≥ 5 mm)
Autoimmune pancreatitis (AIP), a rare form of chronic pancreatitis (CP), can be classified as the diffuse form and the focal form. Although AIP is well-known among radiologists, focal AIP (f-AIP) is still very difficult to differentiate from pancreatic cancer (PC).

**Research frontiers**

F-AIP has a variety of manifestations and is very difficult to differentiate from PC. Improving the diagnostic accuracy can help avoid unnecessary surgery in f-AIP patients.

**Related publications**

The analysis of combined imaging with computed tomography and magnetic resonance to improve the diagnostic accuracy of differentiating f-AIP from PC has rarely been reported.

**Innovations and breakthroughs**

This is the first study to report that the triple-phase enhancement pattern of f-AIP is different from that of PC. Three imaging features are more frequently found in f-AIP, including focal pancreatic enlargement with a capsule-like rim, irregular narrowing of the main pancreatic duct and stricture of the common bile duct in patients with lesions not located in the pancreatic head. The combination of these findings could further improve the diagnostic accuracy of f-AIP and avoid unnecessary surgery.

**Applications**

The study results suggest that a combination of imaging findings will help improve the diagnostic accuracy of f-AIP and avoid unnecessary surgery.

**Peer review**

It is a good clinical study in which the authors analyzed the radiological characteristics of f-AIP. The results are interesting and suggest that the combination of triple-phase enhancement pattern and imaging features of f-AIP can help for the differential diagnosis of f-AIP from PC.

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