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Review

MRI findings of intraductal papillary mucinous neoplasms (IPMNs)

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Summary. Cystic lesions of the pancreas are relatively frequent imaging findings due to the improvement of imaging technologies. They may be secondary to both benign and malignant disease processes and their prevalence increases with age. In most cases, these lesions are detected incidentally by computed tomography and magnetic resonance imaging (MRI) performed for other reasons. Intraductal papillary mucinous neoplasms (IPMNs) represent 25% of the cystic neoplasms, morphologically classified into "main pancreatic duct IPMN" (MPD-IPMN), "side branches IPMN" (SB-IPMN) and mixed forms. Magnetic Resonance Cholangiopancreatography (MRCP) is a multiparametricity not invasive radiological technique that doesn't use ionizing radiation or organ iodinized contrast agents; it allows an accurate characterization of the lesions (number and size of cystic lesions, internal features of a cyst, ducts dilation, communication with main pancreatic duct) that is important to guide the differential diagnosis and establish a correct follow-up. International guidelines consider IPMN of MPD and mixed forms to be an indication for surgery, while clinical and radiological follow-up is indicated in asymptomatic patients with SB-IPMN, especially when lesions are < 2,5-3 cm in diameter and there are no mural nodules or dilation of MPD. (www.actabiomedica.it)

Key words: IPMN, CPRM, pancreatic duct

Introduction

Intraductal papillary mucinous neoplasms (IPMNs) are nearly 25% of the cystic neoplasms of the pancreas (1); they arise from the epithelium of pancreatic ducts at any level of the pancreatic ductal system, with an intraductal papillomatous growth; so, they can develop from the main pancreatic duct (MPD), from the side branches (SB) or both and they are thus morphologically classified into MPD-IPMN, SB-IPMN and mixed forms respectively (2, 3). They are mucin-producing tumors and the excessive secretion of mucin can lead to occlusion of the pancreatic duct and result in progressive ductal dilation or cyst development, due to tumor's growth that can lead to a bulging of the wall of the affected duct, giving the neoplasm the appearance of a pancreatic cystic lesion. The impaired outflow of pancreatic juice may cause clinical symptoms such as pain and produces the laboratory test abnormalities of pancreatitis.

Benign (adenoma), borderline (IPMN with moderate dysplasia) or malignant forms (invasive or not invasive carcinoma) can exist; different degrees of dysplasia can also be found in the same tumor (4, 5), with possible progression from adenoma to carcinoma (6). Malignant transformation risk is more frequent in MPD-IPMN than SB-IPMN; for this reason, the international guidelines consider IPMN of MPD or mixed forms to be an indication for surgery (total re-

section is the treatment of choice in these cases), while clinical and radiological follow-up is indicated in SB-IPMN (7), especially when lesions are <2,5-3 cm in diameter in asymptomatic patients (8, 9) and there are no mural nodules or dilation of MPD, because these lesions are usually benign and grow very slowly (2); patients should undergo observation with magnetic resonance cholangiopancreatography (MRCP) with an interval of 6 months for the first 2 years and annually thereafter; any increase in tumor size, changes in radiological aspects and the appearance of symptoms must be evaluated; total resection should be performed when the main duct is dilated (3).

The goals of imaging are: the diagnosis of lesions, their follow-up and the detection of malignant forms or the initial stages of malignant transformation (10); MRCP is the main radiological method used for this purpose.

Examination technique and MRI protocol

MR examination is performed using a 1,5-Tesla magnet.

Before the investigation, patients must be fasting for 4-6 hours; then, 15-20 minutes before the examination, they are given about 200 ml of superparamagnetic contrast agent (ananas juice) orally, in order to reduce the signal of gastroduodenal fluids on T2-weighted sequences.

Following sequences are used:

- T2-weighted Turbo Spin Echo (TSE) or Single Shot TSE sequence acquired in axial and coronal planes;
- T1-weighted gradient echo (GRE) in-phase and out-of-phase sequence acquired in the axial plane;
- Diffusion Weighted Imaging (DWI) (b value=0; 100; 500; 800) acquired in the axial plane and ADC map;
- T1-weighted GRE 2D with fat saturation (fat-sat), centered on the pancreatic parenchyma;
- Cholangiographic sequences: T2-weighted Single Shot TSE 2D (radial) fat-sat sequences and/or T2-weighted volumetric (3D) TSE fat-sat sequences (with possible MIP reconstructions).

The dynamic study is obtained during the intravenous administration of gadolinium chelates (Multihance=0,1 ml/Kg of body weight; Dotarem=0,2ml/kg of body weight) at a rate of 2-2,5 ml/s with quadriphasic technique: pre-contrast, pancreatic (35-45 s), portal venous (80-90s) and late phase (>180 s), followed by saline injection. The dynamic study is performed with T1-weighted volumetric GRE sequences, with selective fat saturation acquired in the axial plane.

The slice thickness has to include the entire biliary tree and pancreatic ductal system.

Main duct IPMN

The involvement of MPD can be segmental or diffuse. It has the same frequency in male and female patients, more frequently in the 6th decade.

Differential diagnosis between IPMN and chronic pancreatitis is important because both of them may be associated with MPD dilation. Clinical symptoms are not specific: abdominal pain, diabetes, frequent episodes of acute pancreatitis, which is typical of chronic pancreatitis. In the presence of one such clinical picture, the only elements that can indicate the diagnosis of IPMN rather than chronic pancreatitis are the late onset (patients affected by IPMN are generally 20 years older than those with chronic pancreatitis) and the absence of alcohol abuse history.

Segmental involvement of MPD

Typical lesion is confined to a small portion of the MPD, with dilation of the interested segment and normal or atrophic adjacent pancreatic parenchyma. In this type the differential diagnosis with some kind of obstructive chronic segmental pancreatitis could be difficult.

MRI/MRCP findings are:

- segmental ductal dilation that can evolve into a cystic appearance; in this cases, tumor resembles a peripheral mucinous cystic tumor (cystadenoma, cystadenocarcinoma). However, MPD is almost normal in cystadenoma or cystadenocarcinoma; on the contrary, IPMN with a cystic appearance causes upstream MPD dilatation.

- intraductal filling defects that appear hypointense in comparison to the surrounding fluid in T2-weighted sequences; these represent papillary tumor or mucin globs and they are usually difficult to visualize; demonstration of these intraductal filling defects are useful for differentiation of IPMN from chronic pancreatitis with pseudocysts. Papillary excrescences and mucin globs are difficult to be distinguished, but the first are clearly attached to the wall, the second are located in the gravity-dependent portion of the duct or isolated from the wall (11). Moreover, in dynamic MR sequences, mural nodules have enhancement while mucin does not; malignant mural nodules are characterized by restricted diffusion in DWI, so they appear hyperintense at high b value and hypointense in ADC map.
- communication between the dilated ductal segment and Wirsung duct.

Segmental ectasia of MPD can be followed by its diffused dilation, so the lesion becomes indistinguishable from diffuse form; this happens more frequently when the focal segmental lesion of origin is located in the pancreatic head.

Diffuse involvement of MPD

Full length of MPD is involved (12, 13). In these forms differential diagnosis with chronic pancreatitis is difficult. The suggestive sign of IPMN is ductal obstruction in the absence of stenosis.

MRI/MRCP findings are:

- diffuse dilation of MPD with homogeneus duct content, hyperintense in T2-weighted sequences and hypointense in T1-weighted sequences (14-16);
- parenchymal atrophy, which is first localized, then becomes progressively diffused (12, 17);
- mural nodules or mucin globs within the dilated duct;
- dilation of the major duodenal papilla with protrusion into the duodenal lumen (pathognomonic sign, useful for differentiation between IPMN and chronic pancreatitis).

In advanced disease, excessive mucin production can lead to cystic dilation of collateral branches and common biliar duct obstruction. A pancreatobiliari or pancreatoduodenal fistula could develop (17-19). Advanced disease signs are dissemination within the peritoneum or retroperitoneum (pseudomyxoma peritonei) and direct invasion of adjacent viscera; lymphadenopathy or distant metastases are rarely observed.

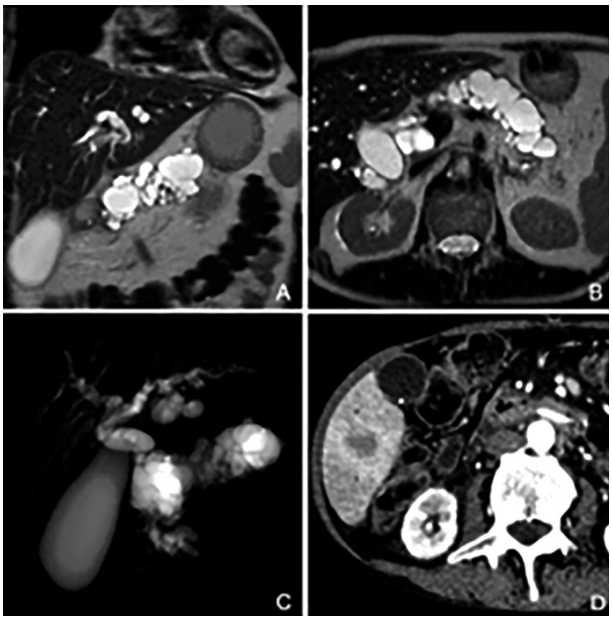

Figure 1. Main duct dilation. Coronal (A), axial (B) T2-weighted images and MRCP image (C) show multiple pancreatic cystic lesions. In the same patient, abdomen Computed Tomography (CT) acquired in arterial phase (D) shows the appearance of a metastatic lesion one month later

Branch duct IPMN

SB-IPMNs appear as cystic dilations of the ducts in communication with the MPD, the latter characterized by normal caliber. It is most frequently located in the uncinate process, but it can be found throughout the pancreas, particularly in pancreatic tail (12, 20).

They can have multifocal growth responsible of an increased cumulative risk of neoplastic degeneration; for this reason, patients should be monitored over time in order to detect early signs of malignancy.

Patients with SB-IPMN are generally older than those with MPD-IPMN (21).

MRI/MRCP findings:

- round or oval cystic masses; grapelike clustered and small cystic lesion with lobulated margins and septa is more frequent than single unilocular macrocyst (22-28);
- communication of the cystic lesion with MPD (the more suggestive sign of SB-IPMN);
- normal or slightly dilated MPD.

In later stages, SB-IPMN can involve MPD; tumor growth and MPD involvement usually require a long time to develop.

In benign lesions both wall and septa are thin. Imaging signs related to malignancy are: irregular and thick wall, presence of mural or septa nodules (especially if larger than 2 mm), abnormal contrast-enhancement of ductal wall and mural nodules, cyst size greater than 3 cm, coexistence of dilation of MPD. Severe dilation of the MPD is more frequent in the malignant forms and bulging of duodenal papilla may be also occur.

Some studies demonstrate that an increase in the average number of cystic dilations of the side branches over time is not a sign of malignant transformation, so it should not increase the level of suspicion nor any change in follow-up program is required in consideration of the long growth times. On the contrary, the increase of the average diameter of the cystic dilations or of the caliber of MPD in the head-uncinate process could be indicative of an extention and progression of the cancer from the side branches to MPD. (1).

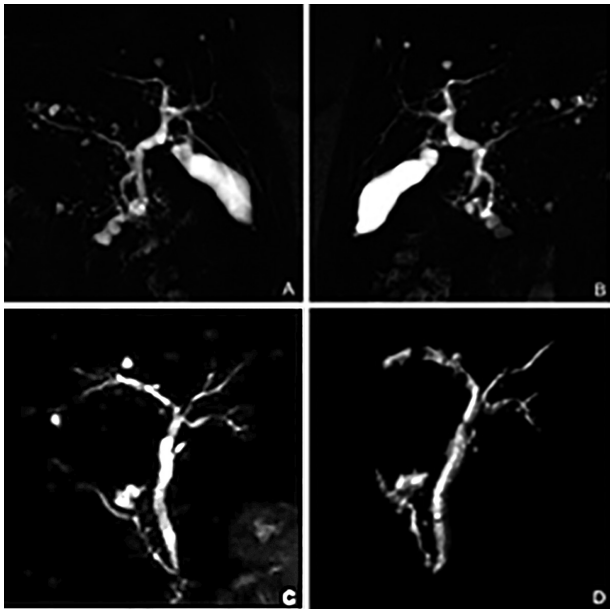

Figure 2. Branch-duct IPMN. MRCP images (A, B) show multiple pancreatic cysts in communication with MPD. MRCP (C) and Volume Rendering (VR) images (D) in a 60 years-old female (different patient from A, B case) with a single cystic lesion of pancreatic head in communication with MPD

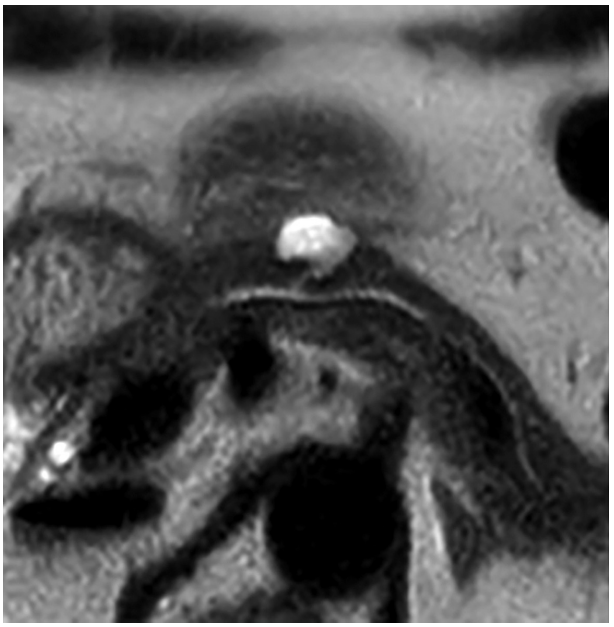

Figure 3. Branch-duct IPMN. Axial T2-weighted image in a 77 years old male shows a pancreatic cyst in communication with MPD

Furthermore, factors related to malignancy are: age over than 70 years, presence of clinical symptoms (onset of pain, weight loss, diabetes) and laboratory signs (tumor markers CA19-9 and CEA).

IPMN Combined type

In this type, both branch ducts of the uncinate process and the MPD are involved. In some cases, the branch-ducts along the body and tail may also be affected.

Conclusions

MRCP is a valid and not invasive radiological method for the diagnosis and follow-up of IPMNs

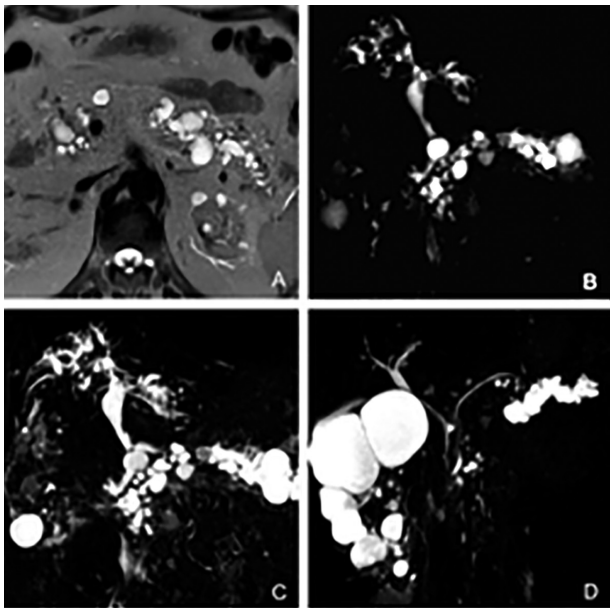

Figure 4. Combined IPMN. Axial T2-weighted image (A), MRCP (B) and MIP (C) images in a 83 years-old male patient. MIP (D) image (different patient from A, B case) shows a combined IPMN with segmental dilation of MPD localized in pancreatic head

that doesn't use ionizing radiation or organ iodinized contrast agents. Being a multiparametricity technique, MRI allows a good characterization of the lesion and diffusion weighted sequences are very useful for a better evaluation of any sign of malignancy; magnetic resonance imaging detects the characteristic ducts dilation, their content and allows differential diagnosis between papillary tumors and mucin globs. The communication of the cystic lesions with MPD in cholangiographic images suggests IPMN, rather than mucinous tumors.

Finally, MRCP is considered the best modality to evaluate the upstream duct of stenosing tumors that can't be investigated through endoscopical exam (ERCP).

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