Acute Recurrent Pancreatitis Curtaining an Intraductal Papillary Mucinous Tumor of the Pancreas

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Abstract

Intraductal papillary mucinous tumor (IPMN) of the pancreas is a rare pancreatic tumor characterized by intraductal proliferation of mucin producing cells with hypersecretion of mucin that leads to cystic dilatation of the involved ducts. The usual clinical presentation is recurrent episodes of pancreatitis due to hypersecretion of mucin and temporary obstruction of the main pancreatic duct.

Key words

Pancreatic cancer - pancreatitis - IPMT

Introduction

Intraductal papillary mucinous tumors (IPMN) of the pancreas are a relatively new entity among mucinous cystic tumors. Described for the first time in 1982 by Ohhashi et al (1) as neoplasms with mucin hypersecretion, dilatation of the main and/or collateral pancreatic ducts and protruding papilla (the Ohhashi triad), there has been a true epidemiologic " explosion" in recent years (2).

Although these neoplasms are usually slow–growing tumors, approximately 30% may eventually become invasive and metastasize. In contrast to the ductal adenocarcinoma, IPMNs have in general a better clinical prognosis and can be cured by surgery(3). Therefore the correct diagnosis has an important clinical impact.

Case report

A 54-year old man presented at our pancreas clinic because of recurrent episodes of acute pancreatitis, almost 30 episodes in the last two years. Particular in the history of the patient was that these recurrent pain episodes were reminiscent of colic, because the pain rapidly vanished 1-2 days after onset without further treatment.

The patient denied any previous history of similar symptoms. He was a non-smoker and drank very little alcohol.

The physical examination was normal with a vague epigastric pain at palpation.

The laboratory findings showed a slight increase of lipase (329 U/l) and amylase (140 U/l) with a normal serum level of CA 19-9, CEA. The other parameters (CRP, white blood cell count, ALT, AST, gammaGT, alkaline phosphatase, bilirubin) were within normal limits.

The abdominal ultrasound showed a 3cm pancreatic cyst in the head of the pancreas and findings suggestive for chronic pancreatitis. The MRT showed similar findings (Fig.1). The EUS showed an echodense 2.2x1.1 cm tumor near the papilla, and a dilatation of the proximal major pancreatic duct to 9mm (Fig.2).

ERCP demonstrated an enlarged papillary orifice of the major papilla ("fish mouth" sign) with mucus exceeding from it (Fig.3). The Wirsung duct was dilated (12 mm) and presented a 2 cm filling defect in the head of the pancreas (at 3 cm proximally from the papilla) (Fig.4). The histology of the secretion prelevated from the Wirsung showed eosinophilic mucus with no signs of dysplasia or malignity. These findings suggested an IPMN.

The subsequent pancreatoscopy showed a papillary growth near the papilla over 3 cm and a grossly dilated Wirsung and the side branches further proximal.

The patient was referred to surgery with the indication of partial pancreatectomy given the malignant potential. A pylorus-preserving pancreatic head resection (Traverso) was performed.

Histology revealed, in the head of the pancreas, a 6.5 cm intrapapillary mucinous tumor which arose from a secondary duct, without dysplasia or invasive growth (Fig.5). The immunhistochemistry was positive for MUC1 and negative for MUC 2.

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Fig.1 The "MRCP" (RARE = short rapid acquisition with relaxation enhancement technique, TR=2.800 ms, TE=1.100 ms, TA=5,3 sec.) demonstrates a large cystic mass in the head of the pancreas (arrow) as well as a persistent duct of Santorini (arrow head). The main duct is widened up to 4 mm.

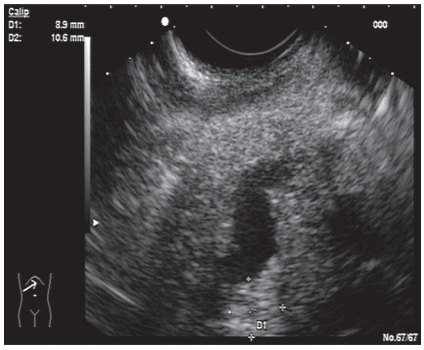

Fig.2 EUS demonstrating the echodense cystic pancreatic tumor.

The tumor was completely resected. Thirteen peripancreatic lymphnodes presented no signs of malignancy.

Discussion

IPMN is a rare pancreatic tumor originating from the epithelium of the pancreatic duct, characterized by intraductal proliferation of mucin producing cells (2,3). In many IPMNs, hypersecretion of mucin leads to cystic dilatation of the involved ducts. In a few IPMNs, focal or diffuse intraductal papillary growth causes duct dilatation (4). The cytologic atypia in IPMNs ranges from minimal to severe and can be divided into adenomas, borderline tumors and intraductal carcinomas. Although these neoplasms are usually slow-growing tumors, about 30% may eventually become invasive and metastasize (5). In 2004, a new classification of IPMN in 4 subtypes, based on histological features and immunohistochemical reactivities with antibodies to specific types of mucin (MUCs) was developed (6). The gastric-type IPMN (MUC 1-; MUC2-, MUC5AC +) usually show low-grade atypia corresponding to intraductal pappilary-mucinous adenoma. The intestinal-type IPMN (MUC1-, MUC2+, MUC5AC+) usually shows moderate- or high-grade atypia corresponding to borderline or in situ carcinoma and can progress in 30-50%of cases to colloid carcinoma (7).

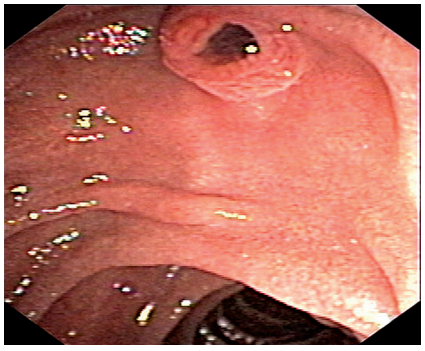

Fig.3 Endoscopic picture of the papilla Vateri during ERCP prior to intubation (fish-mouth sign).

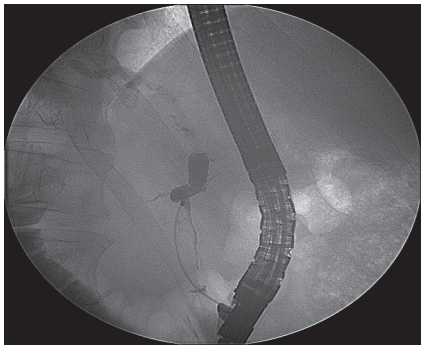

Fig.4 Filling defect in the distal (prepapillary) part of the main pancreatic duct over 3 cm. Neither the cystic deformation in the uncinate process nor the Santorini duct are visualized (blocked by the mucinous masses).

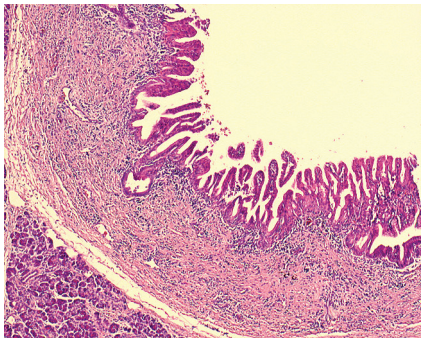

Fig.5 Histopathology of the pancreas demonstrating intraductal papillary-mucinous neoplasia of the pancreas with thickened fibrotic wall (HE stain 75x).

The pancreatobiliary and the oncocytic types IPMN (MUC1+, MUC2-, MUC5AC+) usually show severe/high-grade atypia corresponding to carcinoma in situ and can progress in 50% to an invasive ductal adenocarcinoma of the pancreas (as in our patient).

IPMNs are most frequently localized in the main duct of the head region of the pancreas (8). There, IPMNs that arise from secondary ducts (as in our patient) seem to have an even better prognosis than IPMN of the main duct.

Clinical symptoms of IPMN are different from those of the usual pancreatic cancer. About one-fourth of the patients

have pancreatitis-like symptoms (episodes of epigastric pain, hyperamylasemia), often for many years (9). Symptoms of acute pancreatitis are especially observed in patients with mucin-hypersecreting tumors and are due to temporary complete obstruction of the main pancreatic duct by viscous mucin (as in our patient). About half of the patients develop pancreatic insufficiency with weight loss, diabetes and/or steatorrhea (10). These symptoms of chronic pancreatitis are due to permanent or prolonged occlusion of the main duct in the pancreatic head or by large amounts of viscous mucin that cannot be washed off by pancreatic secretion (11). The main clinical problem is to differentiate IPMN from chronic pancreatitis with relapsing episodes. Most undiagnosed IPMNs are, in fact, wrongly interpreted as chronic pancreatitis (as happened with our patient).

There is no reliable serum tumor marker that can diagnose IPMN. CA 19-9 and CEA levels may be moderately elevated but usually they are within normal limits (7). There also is no reliable marker to differentiate IPMN from chronic pancreatitis (12).

Abdominal ultrasound, CT, EUS may detect a cystic mass of the pancreas (13). It is very important to differentiate it from pseudocysts and cystic tumors. Especially when the cystic mass shows thin septae, calcifications, or the presence of papillary proliferations arising from the wall, or septal, it is necessary to perform ERCP, MRT/MRCP or, in unclear cases, a surgical resection to exclude malignancy (14,15).

ERCP shows an enlarged papilla with a wide opened orifice ("fish mouth" sign) and a dilated main pancreatic duct or his branches with filling defects caused by the mucin plugs or by the papillary tumor (16,17).

Although IPMN of the main duct can simulate chronic pancreatitis, tumors involving the secondary ducts must be differentiated from other cystic tumors. The differential diagnosis with serous cell adenoma is difficult and particularly important because the last one is almost always benign (18). When imaging is not relevant, pancreatic biopsy preferably EUS-guided should be considered (19). The differences between IPMN and mucinous cystic tumors are less important, because the malignant potential of all these forms has been always an indication for surgery. Mucinous cystic tumors are usually localized in the body-tail of the pancreas (20) and are almost always asymptomatic, whereas IPMN is almost always symptomatic, mimicking chronic pancreatitis.

In conclusion, because the presence of malignancy cannot be excluded by clinical and radiological features, surgical resection is recommended for suspected IPMN.

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