Natural Evolution of an Intraductal Papillary Mucinous Neoplasm of the Pancreas. A Case Report

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Abstract

Intraductal papillary mucinous neoplasms include a large spectrum of lesions communicating with the Wirsung duct, having a variable invasiveness from benign or borderline, to malignant (carcinoma in situ and invasive cancer). Final diagnosis is based on endoscopic ultrasound (EUS)-guided fine needle aspiration and histopathologic exam of surgical specimens. We present the case of a 28-year-old woman, with several episodes of acute recurrent pancreatitis in the past 6 months, admitted for dyspepsia, nausea and loss of appetite. Imaging studies (transabdominal ultrasonography, CT scanning, MR cholangiopancreatography) showed a macrocystic, multilocular, corporeal tumor, communicating with the retrograde dilated Wirsung duct. EUS revealed hypoechoic material inside the cysts, raising the suspicion of an intraductal papillary mucinous neoplasm. Diagnosis was confirmed by EUS-guided fine needle aspiration, which found columnar mucinous cells within a mucin-rich fluid. The imaging evaluation was repeated after two years, showing a rapid evolution of the tumor. The patient refused surgical exploration and caudal pancreatectomy. In the context of the absence of clinical symptoms, the indolent evolution of these tumors and the excellent prognosis after resection, we consider that early identification and regular follow-up by EUS with fine needle aspiration is imperative, especially because of the limited success of other imaging methods.

Key words

Intraductal papillary mucinous neoplasm – MRCP - endoscopic ultrasound - EUS-FNA

Introduction

Intraductal papillary mucinous neoplasms (IPMNs) of the pancreas are characterized by papillary proliferation of the pancreatic duct epithelium, with secretion of mucin that usually determines cystic dilatation of the main pancreatic duct or its branches. Both the characteristic filling defects produced by mucin, as well as the swelling of the papilla caused by excessive intraductal secretion of mucin, were initially described during endoscopic retrograde colangio-pancreatography (ERCP). IPMNs are divided into benign (adenomatous), low-grade malignant (borderline) and malignant (noninvasive carcinoma in situ or invasive cancer) (1). Although IPMNs are considered important precursors of invasive carcinoma of the pancreas, the natural history of these cystic neoplasms is currently unclear, with a slow rate of progression from adenoma to carcinoma.

Imaging examinations are very important to establish the diagnosis, with two or more tests usually required (2). We report a case of an IPMN, which initially presented with recurrent attacks of acute pancreatitis.

Case report

A young woman (28-year old) with several episodes of recurring acute pancreatitis in the past six months, first presented (March 2004) with vague epigastric pain, nausea and loss of appetite. Clinical examination was unremarkable, with slight pain during profound palpation of the upper abdominal region. The biological investigations were within normal limits. Initial imaging (transabdominal ultrasonography TUS, CT and MRCP) performed in another tertiary care center suggested chronic pancreatitis with pseudocysts. ERCP was performed, with visualization of the first portion of the pancreatic duct and complete stop of the contrast substance at the level of the pancreatic isthmus. The patient was referred in June 2004 to our department of gastroenterology for diagnostic work-up and treatment.

A complex imaging evaluation raised the suspicion of IPMN or solid pseudopapillary neoplasm. TUS showed atrophy of the pancreatic parenchyma, and dilation of the
main pancreatic duct (up to 6-7 mm), which communicated with three cystic lesions of 14, 12 and 11 mm, respectively. Helical CT showed a dilated main pancreatic duct in the body and tail with atrophy of the parenchyma. Several cysts in the body and tail of the pancreas were also depicted, with a larger cystic area in the isthmus communicating with the main pancreatic duct (Fig.1). A solid contrast-enhancing component was also visible on the CT scans, at the level of the pancreatic isthmus. MRCP revealed the tubular nature of the cysts which represented dilated ducts (Fig.2). T1-weighted (100/4) and T2-weighted (2760/106) MR images of the pancreas demonstrated the cystic lesions in the body and tail of the pancreas and the markedly dilated pancreatic duct.

EUS showed insufficient criteria of chronic pancreatitis (only hyperechoic foci in the pancreatic head), and multicystic lesions that communicated with a distally dilated main pancreatic duct. One of the three cysts contained hypoechoic material inside, suspicious of mucus (Fig.3). EUS-guided fine needle aspiration (FNA) performed inside the multiloculated cystic lesion found high amylases (200 IU/mL) and normal CEA and CA 19-9. The final diagnosis was established by cytological examination which showed mucinous columnar cells, as well as fluid with high mucin content.

**Fig.1** Helical CT: the dilated main pancreatic duct, with several cysts communicating with the duct.

**Fig.2** MRCP: three cysts (blue arrows) communicating with the dilated pancreatic duct (red arrowheads).

**Fig.3** EUS better delineated the three cysts and showed the presence of hypoechoic material inside one of the cysts.

**Fig.4** Helical CT scanning of the abdomen after two years, showing cystic dilations of the side branches in the pancreatic body and tail.

**Fig.5** MRCP after two years, showing the full extent of ductal involvement at the level of pancreatic body and tail.

**Fig.6** EUS after two years: dilated pancreatic ducts, with cystic aspect, and mural nodules less than 5 mm.
The patient refused surgical intervention and was followed up with serial imaging tests, over a period of two years.

After two years, in June 2006, TUS showed a completely different picture, with marked pancreatic atrophy at the level of the pancreatic body and tail, with multiple cystic lesions that replaced the pancreatic parenchyma of the body and tail. The three cystic lesions at the level of the pancreatic isthmus and body increased in size (22, 14 and 12 mm, respectively). The pancreatic duct was markedly dilated (9 mm). The helical CT scan showed that the cystic lesions had increased in size, with cystically dilated side branches that replaced completely the normal pancreatic structure of the body and tail of the pancreas (Fig.4). MRCP showed the full extent of ductal involvement starting from the cysts of the isthmus, and continuing at the level of the body and tail of the pancreas (Fig.5). A lateral viewing endoscope was used to visualize the papilla, which was proeminent with mucus oozing from the orifice. EUS depicted multiple dilated pancreatic ducts and communicating cysts, some of them filled with hypoechoic material (mucus), other with mural nodules (less than 5 mm) (Fig.6). EUS-FNA was negative for malignancy, but due to the high false negative rate of this procedure and the malignant potential of these tumors, a surgical caudal pancreatectomy was again proposed. The patient refused any surgical exploration and is still undergoing follow-up by imaging methods.

**Discussion**

Most (over 95%) epithelial tumors of pancreas are solid ductal adenocarcinomas. The remaining are represented by serous cystadenomas, mucin producing tumors (mucinous cystic neoplasms and IPMNs), cystic endocrine tumors, solid pseudopapillary neoplasms and other rare tumors (2). Pancreatic cystic neoplasms usually represent less than 5 to 10 percent of all pancreatic neoplasms (1,2). However, mucin producing tumors should be considered in the differential diagnosis of every cystic lesion in the pancreas, due to their malignant potential. There are two types of mucin producing tumors: mucinous cystic neoplasms (cystadenomas and cystadenocarcinomas) and IPMNs (2). Mucinous cystic neoplasms do not communicate with the pancreatic ductal system, whereas IPMNs characteristically communicate with the ductal system (3), as in our patient.

Pancreatic cystic neoplasms are usually asymptomatic, being discovered during US or CT examinations with other indications (2). The patients may be symptomatic, with recurrent acute pancreatitis, chronic abdominal pain, nausea or vomiting and jaundice, indicating a lesion that obstructs the biliary or pancreatic ducts. Advanced IPMNs with invasive carcinoma have a similar clinical presentation with pancreatic ductal adenocarcinoma, including intractable pain, weight loss and progressive jaundice. Due to the similar clinical presentation and imaging characteristics, the differential diagnosis of IPMNs and pseudocysts consecutive to acute or chronic pancreatitis may be extremely difficult in the absence of tissue confirmation (2). Our patient was diagnosed with chronic pancreatitis in another center, after an extensive evaluation (US, CT, ERCP), because it may be difficult to differentiate between an IPMN with ductal dilatation favored by mucin plugs that causes pancreatitis and small pseudocysts formed as a consequence of pancreatitis (2). Imaging examinations are highly important to establish the diagnosis, with TUS, CT and MRI increasingly used for the initial evaluation of these patients (2). TUS was the initial examination of choice, which indicated the extent of pancreatic involvement in our case and allowed the selection of further imaging methods. New techniques such as contrast-enhanced US might further improve the differential diagnosis between benign and malignant IPMNs, with a higher accuracy as compared with EUS (4). CT is currently considered a better test, both for detection of cystic pancreatic neoplasms, as well as for characterization of cyst wall, septa, mural nodules, and findings suggestive of chronic pancreatitis (5). New techniques, such as multidetector row CT with 2D curved reformations (6), CT virtual pancreatography or 3D CT pancreatography (7), were recently reported to provide detailed imaging similar to MRCP.

MRCP plays a definite role in the diagnosis of IPMNs, showing clearly the communication between the cystic lesions and dilated pancreatic ducts (8). The presence of mural nodules and extreme dilatation of the main pancreatic duct (> 15 mm) might indicate an increased risk of malignancy (9). MRCP offers a non-invasive alternative to ERCP for follow-up studies. This was proven by our case, because MRCP raised the suspicion of an IPMN, while TUS and CT indicated possible chronic pancreatitis changes with pseudo-cysts. However, neither CT nor MRCP can accurately diagnose a specific lesion and establish if malignancy is present (2).

EUS has an enhanced image resolution and consequently allows a better delineation of IPMNs. The findings include dilatation of the main pancreatic duct or side branches, with detection of intraductal nodules (main duct type IPMN) or multiple cysts (branch duct type IPMN). EUS is more accurate than ERCP in differentiating IPMN from cystic pancreatic lesions (10). The high accuracy of EUS is based on the paucity of parenchymal features of chronic pancreatitis, while dilatation of the main pancreatic duct, the presence of cysts and pancreatic atrophy are quite common in IPMNs. Intraductal filling defects are less common, although they are characteristic for IPMNs, but were observed in one of the cystic dilatations in our patient. Another study found that preoperative EUS has an accuracy of 86% for distinguishing between benign and malignant lesions (11). The most suggestive features of malignancy were a main duct diameter > 10 mm, side branches > 4 mm with irregular septa and the presence of mural nodules > 10 mm. The presence of an additional hypoechoic mass does not represent an indication for malignancy (12).

EUS clear advantage is that it allows the guidance of EUS-FNA of mural nodules and pancreatic juice from the dilated pancreatic duct or cysts, for cytological analysis, as
well as tumor markers (2). IPMNs have distinct cytological features, which allow a correct diagnosis based on conventional cytology techniques with a high accuracy reaching 100% (13). In our case, EUS-guided FNA established the diagnosis. EUS-FNA of mural nodules is considered to be superior to EUS without puncture for diagnosing malignancy (14). Moreover, certain cytologic features allow an estimation of the histological grade of IPMN. These include smear background (presence of mucin, inflammation or necrosis), epithelial architectural features (hypercellularity, papillary fragments, tight epithelial clusters, single dysplastic cells, etc.) and cellular details (prominent nucleoli, parachromatin clearing etc.) (15).

The natural evolution of IPMNs is not still clear and consequently the management is still evolving. Although most of the studies report a mean time of progression for IPMNs ranging from 5.5 to 6.9 years (16), the evolution was faster in our case, with major imaging changes encountered only in two years. All suspected IPMNs should be resected, due to their malignant potential. Several factors should be taken into consideration when deciding a surgical intervention that carries a risk of significant morbidity and mortality. These include the patients’ age and symptoms, the degree of surgical risk, as well as the location and size of the tumor. We indicated surgery because of the chance of a complete cure for a young, symptomatic patient with a low risk of complications after potential curative intervention. The patient denied surgery, and close follow-up by EUS was recommended (17), which showed a rapid evolution of the disease.

Conclusion

Our case report showed the potential pitfalls encountered during the diagnosis of IPMNs, even by using state-of-the-art diagnostic imaging methods. The role of EUS and EUS-FNA was emphasized as a miniminvasive diagnostic and staging method that provides further detail of the morphologic features and replaces ERCP for tissue sampling, with aspiration of both the fluid from the dilated pancreatic duct, as well as solid components (intramural nodules, cyst wall etc.).

References