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Per Oral Pancreatotomy Identification of Main-Duct Intraductal Papillary Mucinous Neoplasms and Concomitant Pancreatic Duct Stones: Not Mutually Exclusive

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Abstract

Objectives—Per oral pancreatotomy (POP) assists in the evaluation and treatment of select benign and neoplastic pancreatic disorders including main-duct intraductal papillary mucinous neoplasm (MD-IPMN). While pancreatic duct stones are classically thought of as pathognomonic for chronic pancreatitis, its co-occurrence with MD-IPMN as identified via POP may help identify an alternative etiology for presumed idiopathic chronic pancreatitis.

Methods—This was a multicenter retrospective case series of patients found to have pancreatic duct stones with concomitant MD-IPMN by POP.

Results—Thirteen patients with presumed idiopathic chronic calcific pancreatitis were found on POP to have both pancreatic duct stones and MD-IPMN. All patients had a dilated pancreatic duct and the majority (92.3%) were symptomatic.

Conclusions—Per-oral pancreatotomy may identify MD-IPMN as an etiology for patients with presumed idiopathic chronic calcific pancreatitis and associated dilated pancreatic duct. Larger prospective studies are needed to validate these findings.

Keywords

intraductal papillary mucinous neoplasm; chronic pancreatitis; pancreatic duct stones; pancreatotomy; ERCP

Introduction

Intraductal papillary mucinous neoplasm (IPMN) may be misdiagnosed as chronic pancreatitis as patients can present with abdominal pain, nausea/vomiting, steatorrhea and a

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dilated pancreatic duct on imaging.¹ While the risk of developing pancreatic cancer from main-duct IPMNs (MD-IPMN) is well-known, chronic pancreatitis associated with IPMN has been reported only in limited series.^{2–4} Zapiach et al reported an initial series without the use of per oral pancreatoscopy (POP) that identified calcific obstructive pancreatitis with IPMN but it was unclear how many of the patients had actual intraductal stones. The authors offered three potential explanations of IPMN associated with calcifications: 1) tumoral calcification, 2) the IPMN develops as a complication of long-standing chronic calcifying pancreatitis, or 3) chronic partial ductal obstruction from IPMNs may predispose to intraductal calcifications.²

Per-oral pancreatoscopy enables detection of intraductal lesions with sensitivity up to 95% in diagnosing MD-IPMN.^{5, 6} In our multicenter case series spanning 14 years, we describe thirteen patients with previously incorrectly presumed idiopathic chronic pancreatitis associated with a dilated pancreatic duct who underwent intraductal mucosal inspection with POP and were found to have concomitant main pancreatic duct stones (PDS) and MD-IPMN.

MATERIALS AND METHODS

This was a retrospective review at two tertiary medical centers of patients that underwent POP for evaluation of idiopathic calcific chronic pancreatitis and a dilated pancreatic duct. The patients included in the analysis were found to have PDS and a MD-IPMN. Per-oral pancreatoscopy was performed during endoscopic retrograde cholangiopancreatography (ERCP) utilizing two different platforms including 1) the Olympus CHF-BP 30 system (Olympus, Inc. Tokyo, Japan) and 2) the Spyglass DS™ system (Boston Scientific, Marlborough, Mass). Intraductal biopsies were performed using cholangioscope-compatible miniature forceps (Olympus, Inc. and Boston Scientific, Inc) under direct visualization. Main-duct IPMNs (Fig. 1) were classified as described by Hara et al.⁷ Institutional review board approval was obtained for this study.

RESULTS

A total of 13 patients with PDS were found to have concomitant MD-IPMN on POP (Table 1). The mean age was 62.5 years (standard deviation [SD], 11.9), seven (53.8%) patients were male and one (7.7%) patient had a family history of pancreatic cancer. The most common presenting symptoms were abdominal pain (84.6%) and weight loss (61.5%). Seven (53.8%) patients had experienced a prior episode of pancreatitis with work-ups revealing no clear etiology for the pancreatitis and one (7.7%) patient was asymptomatic. In the 7 patients who had experienced a prior episode of pancreatitis, a median of 33 months (range, 10–202 months) passed from initial episode of pancreatitis to diagnosis of MD-IPMN. The median follow-up time was 1 year (range, 0.5–9 years) after POP.

All patients underwent cross-sectional imaging via either computed tomography or magnetic resonance cholangiopancreatography with all found to have dilated main pancreatic ducts. Pancreatic duct stones were detected on imaging in five (38.5%) patients and six (46.2%) patients had a prior endoscopic retrograde cholangiopancreatography (ERCP). The median

time from prior ERCP to diagnosis of MD-IPMN was 13 months (range, 7–28 months). Endoscopic ultrasound was performed on all patients prior to POP, confirming a dilated pancreatic duct while revealing PDS in eight (61.5%) patients.

Pancreatotomy found a mean number of 2.6 PDS (SD, 1.5) per patient. In 4 patients, POP-guided intraductal lithotripsy (3 cases of laser lithotripsy and 1 case of electrohydraulic lithotripsy) was required to fragment and remove stones with the goal of improving symptoms and better visualizing the duct to ultimately identify IPMN. Pancreatotomy-guided biopsies were performed in all patients with pathology demonstrating IPMN in all cases. Type I IPMNs were most commonly found (53.8%), followed by Type III IPMNs (Fig. 2, 23.1%) and Type IV IPMNs (Fig. 3, 15.4%) with one case of a Type IV IPMN (7.7%). Surgical resection was performed in six patients. Surgical pathology found early focal cancer in 2 patients, high-grade dysplasia in 2 patients, low-grade dysplasia in 1 patient, and no dysplasia in 1 patient, all in the setting of MD-IPMN.

DISCUSSION

Pancreatic ductal adenocarcinoma can obstruct the main duct and small ductules thereby activating pancreatic stellate cells upstream to the lesion resulting in the development of fibrosis and changes of chronic pancreatitis.^{8–10} Similarly, mucin-producing IPMN involving the main duct may also result in chronic ductal and ductule obstruction that produces changes consistent with chronic pancreatitis. This ductal obstruction can predispose to stasis of pancreatic juice flow, and subsequently ductal dilatation and intraductal stones, which in conjunction with fibrotic changes, may lead to a misdiagnosis of idiopathic chronic pancreatitis. As noted in our case series, none had a clear etiology for chronic pancreatitis and we propose that in patients with presumed idiopathic chronic pancreatitis and a dilated PD, POP be considered to exclude IPMN due to its high diagnostic accuracy in detecting MD-IPMN.¹¹ Furthermore, should there be obstructing PDS, pancreatotomy-guided lithotripsy may assist in reducing stone burden, permitting a thorough examination of the duct.^{12,13}

In conclusion, this study gives insight into a rare subset of patients who seemingly have classic chronic calcific pancreatitis with intraductal stones but were found to have occult MD-IPMN as an etiology not detected by non-invasive imaging, endoscopic ultrasound, or pancreatography. This is an important finding that can alter patient management given the malignant potential of MD-IPMN. Future, larger studies involving multiple centers are required to validate these findings in a broader population to determine whether patients with idiopathic chronic calcific pancreatitis and a dilated PD will benefit from investigation with pancreatotomy.

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FIGURE 1.
Patulous “fish mouth” pancreatic duct orifice suggestive of intraductal papillary mucinous neoplasm.

FIGURE 2.
Characteristic “fish eggs” seen on pancreatoscopy.

FIGURE 3.
Villous mass with finger-like projections consistent with Type 4 IPMN on pancreatoscopy.

TABLE 1.

Characteristics of Patients

Patient No.	Presenting Symptoms	No. of Prior Episodes of Acute Pancreatitis	Imaging Findings	Type of IPMN
1	None	0	MRCP: Dilated PD	III
2	Abdominal pain and weight loss	2	CT: Dilated PD, pancreatic mass, atrophic tail	V
3	Abdominal pain and weight loss	>3	CT: Dilated PD, parenchymal calcifications, and PD stones	IV
4	Weight loss	0	MRI: Dilated PD, side duct dilation, pancreatic atrophy, and mural nodularity	IV
5	Abdominal pain	>3	CT: Dilated PD, pancreatic mass	III
6	Abdominal pain and weight loss	1	MRCP: Dilated PD, calcifications in head of the pancreas	III
7	Abdominal pain and weight loss	0	CT: Dilated PD, PD stones	I
8	Abdominal pain and weight loss	0	CT: Dilated PD, PD stones	I
9	Abdominal pain	2	MRCP: Dilated PD	I
10	Abdominal pain	>3	MRCP: Dilated PD, PD stones	I
11	Abdominal pain	1	MRCP: Dilated side branches	I
12	Abdominal pain and weight loss	0	CT: Dilated PD, PD stones	I
13	Abdominal pain and weight loss	0	CT: Dilated PD, PD stones	I

MRCP indicates magnetic resonance cholangiopancreatography; PD, pancreatic duct; CT, computed tomography.