

ORIGINAL ARTICLE

Influence of pre-operative diagnosis and frozen section on operative management of pancreatic cystic lesions

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Abstract

Background. Frozen section analysis of cyst wall has been advocated as standard of care prior to surgical drainage of pancreatic pseudocysts. Recent studies have indicated that frozen section may be unreliable. Our aim was to investigate the role and accuracy of frozen section analysis of the cyst wall in the operative management of pancreatic cystic lesions. **Methods.** A retrospective review was performed of 44 patients who underwent operation for a cystic lesion of the pancreas. **Results.** Of the 25 patients with a diagnosis of pseudocyst, 9 patients had frozen section intra-operatively. Eight frozen sections demonstrated pseudocyst, and correlated with final pathology. One frozen section demonstrated a true cyst. Twenty-three patients had a final diagnosis of pseudocyst. Nineteen patients had a diagnosis of cystic neoplasm, and six patients had frozen sections. Three frozen sections were consistent with cystic neoplasm and correlated with final pathology. Three frozen sections demonstrated characteristics of pseudocyst, two correlated with final pathology, and one showed cystic neoplasm on final pathology. **Conclusion.** Routine use of frozen section may not be necessary; however, frozen section is useful when the intra-operative appearance does not correlate with pre-operative diagnosis.

Key Words: *Frozen section, pseudocyst, cystic neoplasm*

Introduction

Cystic lesions of the pancreas are often the consequence of pancreatitis or represent a neoplastic process. The surgical management of pseudocysts differs from that of cystic neoplasms. The operative management of pseudocysts is often internal drainage, whereas pancreatic resection may be required for cystic neoplasms.

Distinguishing pseudocysts from cystic neoplasms pre-operatively can be challenging. Pseudocysts represent 70–80% of cystic pancreatic lesions and can often be differentiated from cystic neoplasms using patient history and imaging modalities [1,2]. Pseudocysts arise as a consequence of acute or chronic pancreatitis, usually seen in middle-aged men with a history of alcohol abuse or other causes of pancreatitis [3]. Cystic neoplasms, on the other hand, are usually seen in female patients with no history of pancreatitis or identifiable risk factors for pancreatitis [4]. On imaging studies, pseudocysts do not generally have central scarring, septae, solid components, or

loculations that are characteristic of cystic neoplasms on computed tomography (CT) and ultrasonography (US) [1,5,6]. In addition, endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasound (EUS), and cyst aspiration can aid in differentiation of cystic lesions. O'Connor et al. demonstrated communication between the ductal system and a pseudocyst at least 65% of the time using ERCP [7]. With the exception of intraductal papillary mucinous neoplasms, most cystic neoplasms are independent of the pancreatic duct [7]. Also, cystic fluid indices are different between pseudocysts and cystic neoplasms. Fluid from pseudocysts is commonly high in amylase, and low in viscosity, CEA, CA15-3 and CA 72-4 [1]. Fluid from cystic neoplasms is commonly low in amylase, cytology is usually positive, and may have elevated levels of CEA, CA15-3 and CA 72-4 [1].

Frozen section has previously been considered standard of care in distinguishing cystic neoplasm from pseudocyst at the time of operation [8]. However, recent studies have shown that frozen section may not

add information to aid in surgical decision making [9,10]. The presence of epithelium in the cyst wall of major cystic tumours has been stated to be incomplete in 40–72% of cases, and the denuded areas may comprise 5–98% of the wall [10]. These findings could contribute to the misdiagnosis of cystic neoplasms as pseudocysts when epithelial lining is not biopsied. The purpose of this study was to investigate the role and accuracy of frozen section in the operative management of pancreatic cystic lesions.

Patients and methods

Between March 1994 and March 2004, 44 patients underwent surgical intervention for a cystic lesion of the pancreas at the University of Nebraska Medical Center. A retrospective review was done to determine pre-operative diagnosis, type of operation performed, frozen section results and final pathology results (Table I). Pre-operative diagnosis was determined using the patient's clinical history of pancreatitis or presenting symptoms, and a combination of imaging techniques including CT, magnetic resonance imaging (MRI), ERCP, US and EUS. Some patients also had fine-needle aspiration of the cyst or biopsy of the lesion to aid in diagnosis. Frozen section of the cyst wall was performed intra-operatively at the discretion of the individual surgeon.

Results

Of the 25 patients diagnosed with pancreatic pseudocyst, 23 patients (92%) had clinical and radiographic findings suggestive of a pseudocyst. Twenty-one patients had a clinical history of acute or chronic pancreatitis. Nineteen patients were diagnosed with a cystic neoplasm, 17 of which were suspected pre-operatively.

Frozen section of the cyst wall was performed in a total of 15 patients. Eleven of these demonstrated inflammatory tissue with no epithelial lining; however, in one patient, final pathology demonstrated a cystic neoplasm. This patient underwent a distal

pancreatectomy. All four frozen sections of the cyst wall that demonstrated an epithelial lining were corroborated on permanent histological examination as being a cystic neoplasm.

Frozen section changed operative management in one patient. In two cases, frozen section differed from pre-operative assessment. The sensitivity of frozen section of cyst wall for diagnosing pseudocyst was 100%, specificity was 80%, and positive predictive value was 90%.

Operative management

Eighteen patients with a pre-operative diagnosis of pseudocyst underwent an internal drainage procedure, one patient underwent an external drainage procedure and six underwent distal pancreatectomy. All patients who underwent a drainage procedure had final pathology of pseudocyst. Of the patients who underwent an internal drainage procedure for a pre-operative diagnosis of pseudocyst, 12 patients had follow-up ranging from 2 months to 5 years. One patient had pseudocyst recurrence requiring re-operation. This patient initially underwent a cyst gastrostomy, but had recurrence of the pseudocyst, by CT, 5 years later when the patient presented with abdominal pain. The recurrence required further operative intervention with a roux-en-Y cyst jejunostomy, and final pathology showed pseudocyst. No patients required operative intervention for a previously misdiagnosed cystic neoplasm. All patients who underwent a drainage procedure for a pseudocyst had a cyst wall biopsy and in all cases were confirmed under permanent evaluation.

Discussion

Biopsy of cyst wall and frozen section has previously been considered fundamental to a decision as to whether resection or drainage is the treatment of choice of cystic lesions [8]. More recently, Warshaw et al. reported that cystic lesions have absence of epithelial lining in 40–72% of cases, causing misdiagnoses on frozen section and even permanent sections [10]. Therefore, a pseudocyst may be ruled out if frozen section of the cyst wall contains epithelium, but absence of epithelium does not rule out cystic neoplasm. Studies looking at accuracy of frozen section in cystic lesions of the pancreas are lacking. We realize the limitations of this study's small sample size; however, frozen section of cystic lesions was 93.3% accurate. There was one false negative frozen section identified, for a rate of 6.6%. Frozen section at our institution was used at the discretion of the individual surgeon, with frozen section deferred in 50% of cases, which also limited this study.

In one case, a patient had a pre-operative diagnosis of pseudocyst, based on history of acute pancreatitis and CT findings, but frozen section demonstrated epithelial lining, and the patient had a distal

Table I. Patient characteristics and results based on final pathology

Parameter	Pseudocyst (n=25)	Cystic neoplasm (n=19)
Gender		
Male	10	6
Female	15	13
History of pancreatitis	18	4
Pre-operative diagnosis		
Pseudocyst	23	2
Cystic neoplasm	2	17
Operation		
Distal pancreatectomy	6	12
Pancreaticoduodenectomy	0	7
Internal drainage	18	0
External drainage	1	0

pancreatectomy. Frozen section in this case may have changed operative management from an internal drainage procedure to resection.

In other cases, the surgeon acted on intra-operative impression instead of using frozen section. For example, a patient had a pre-operative diagnosis of pseudocyst, however, intra-operative impression did not correlate with this initial diagnosis. Frozen section was sent for margins only, the patient underwent resection, and final pathology showed a mucinous cystadenoma. In addition, one patient with a pre-operative diagnosis of a cystic neoplasm had frozen section, which showed inflammation, and this patient underwent resection. Final pathology in this patient showed cystic duct ectasia with extensive ductal squamous metaplasia. Frozen section did not change operative management in this case.

In one patient with a pre-operative diagnosis of cystic neoplasm, frozen section reported benign true cyst, but final pathology was cystadenoma. Despite both lesions being benign cystic lesions, the frozen section was inaccurate in the diagnosis in this case.

Two patients with a pre-operative diagnosis of cystic neoplasm had frozen section demonstrating characteristics of pseudocysts. In these cases, lack of epithelium on frozen section cannot rule out a cystic neoplasm, as epithelium can be denuded in up to 98% of the wall [10]. The first patient had an unresectable mass involving the portal vein. A fluctuant mass in the pancreatic head was noted, and wall of the cyst was sent for pathology. This patient underwent a gastrojejunostomy. The second case was a patient who had CT and US findings correlating with a pseudocyst; however, because the patient did not have risk factors or a history of pancreatitis, a cystic neoplasm was suspected. Despite frozen section demonstrating pseudocyst characteristics, the patient underwent a distal pancreatectomy.

In conclusion, the routine use of frozen section may not be necessary. Nevertheless, frozen section is useful when intra-operative appearance of a cystic lesion does not correlate with pre-operative diagnosis. A prospective clinical trial would be needed to assess the role of frozen section of the cyst wall in patients with pancreatic cystic lesions.

References

- [1] Castillo C, Warshaw A. Cystic tumors of the pancreas. *Surg Clin North Am* 1995;75:1001–16.
- [2] Hsieh C, Tseng J, Huang S. Co-existence of a huge pseudocyst and mucinous cystadenoma: report of a case and the value of magnetic resonance imaging for differential diagnosis. *Eur J Gastroenterol Hepatol* 2002;14:191–4.
- [3] Andren-Sandberg A, Dervenis C. Pancreatic pseudocysts in the 21st century. Part I: classification, pathophysiology, anatomic considerations and treatment. *J Pancreas* 2004;5:8–24.
- [4] Lumsden A, Bradley E. Pseudocyst or cystic neoplasm? Differential diagnosis and initial management of cystic pancreatic lesions. *Hepatogastroenterology* 1989;36:462–6.
- [5] Demos T, Posniak H, Harmath C, Olson M, Aranha G. Cystic lesions of the pancreas. *Am J Roentgenol* 2002; 179:1375–88.
- [6] Cohen-Scali F, Vilgrain V, Brancatelli G, Hammel P, Vullierme M, Sauvanet A, et al. Discrimination of unilocular macrocystic serous cystadenoma from pancreatic pseudocyst and mucinous cystadenoma with CT: initial observations. *Radiology* 2003; 228:727–33.
- [7] O'Connor M, Kolars J, Ansel H. Pre-operative endoscopic retrograde cholangiopancreatography in the surgical management of pancreatic pseudocysts. *Am J Surg* 1986; 151:18–24.
- [8] Howard J. Cystic neoplasms and true cysts of the pancreas. *Surg Clin North Am* 1989;69:651–63.
- [9] Martin I, Hammond P, Scott J, Redhead D, Carter DC, Garden OJ. Cystic tumours of the pancreas. *Br J Surg* 1998; 85:1484–6.
- [10] Warshaw A, Compton C, Lewandrowski K, Cardenosa G, Mueller P. Cystic tumors of the pancreas. *Ann Surg* 1990; 212:432–45.