Nonneoplastic Lesions of the Pancreas: A Retrospective Analysis of 20 Cases

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Abstract

Objectives: In the pancreatic lesion cases, surgery is often planned based only on imaging results and without a preoperative histological diagnosis, due to the high risk of malignancy in combination with the difficulty of invasive interventions and limited cytopathological evaluation. In this study, the records of 20 patients who had undergone a pancreatectomy procedure and who were diagnosed with nonneoplastic pancreatic lesions were retrospectively evaluated according to the clinical and histopathological findings.

Methods: A total of 122 cases of patients who underwent a pancreatectomy with suspicious lesions between 2004 and 2016 were retrospectively assessed in detail using the clinical and histopathological findings.

Results: Nonneoplastic lesions were observed in 20 (16%) of 122 patients who underwent a pancreatectomy. Histopathological examination revealed 11 cases of chronic pancreatitis, 1 hematoma, 1 instance of hemorrhagic necrosis secondary to trauma, 1 pseudocyst, 1 granulation tissue, 1 retention cyst, 1 bile duct cyst, 1 patient with Castleman disease, and 1 instance of fat necrosis were seen. In 1 patient, no evidence of disease was found. In addition, among the patients with chronic pancreatitis, autoimmune pancreatitis was observed in 1, adenomyoma of the ampulla of Vater was present in 1, and a pseudocyst was found in 1 patient.

Conclusion: A clinical and histopathological analysis of nonneoplastic lesions found in pancreatectomy patients was performed.

Keywords: Nonneoplastic; pancreas; retrospective analysis.

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In the pancreas, a variety of conditions may form solid masses that may mimic cancer. Lesions of the pancreas are classified in 2 categories: nonneoplastic and neoplastic lesions. Nonneoplastic lesions include congenital anomalies (annular pancreas, heterotopic pancreas), pancreatitis, abscess and granulomatous inflammation, pseudocysts, and cysts. Neoplastic lesions consist of ductal adenocarcinoma, anaplastic carcinoma, cystic pancreatic lesions, intraductal papillary mucinous neoplasms and pancreatic intraepithelial neoplasia, acinar cell tumors, solid-pseudopapillary tumor, pancreatoblastoma, other epithelial exocrine tumors, lymphoid tumors, mesenchymal tumors, and metastatic tumors. This study is a clinical and histopathological evaluation of nonneoplastic lesions reported in pancreatectomy cases from a period of 12 years.
Methods
The clinical findings and histopathological diagnoses of 112 pancreatectomies performed between January 2004 and June 2016 in a single clinic were retrospectively evaluated for nonneoplastic lesions of the pancreas. The data analyzed, including the initial diagnosis, procedure performed, and final histopathological results, are provided in Table 1.

Results
Nonneoplastic lesions of the pancreas were observed in 20 (16%) of 122 pancreatectomy cases. Clinicians were initially concerned about the possibility of a malignancy due to the appearance of a mass lesion. Since invasive interventions are difficult and limited cytopathological evaluation is available, due to inherent characteristics of this region, in addition to the high risk of malignancy, surgery was planned. Histopathological examination revealed the presence of chronic pancreatitis (n=11), hematoma (n=1), hemorrhagic necrosis secondary to trauma (n=1), pseudocyst (n=1), granulation tissue (n=1), retention cyst (n=1), choleoductal cyst (n=1), Castleman disease (n=1), and fat necrosis (n=1). No pathology was seen in the final case. Among the cases with chronic pancreatitis, 1 was diagnosed with autoimmune pancreatitis because of increased serum immunoglobulin G levels, histopathologically diffuse lymphoplasmocytic cell infiltration, and fibrosis. Adenomyoma of the ampulla of Vater was observed in another, and a pseudocyst was found in a third.

Discussion
The term chronic pancreatitis describes various progressive fibroinflammatory diseases that cause glandular damage in the exocrine pancreas.[1] Although the incidence of chronic pancreatitis is not precisely known, Yadav et al.[2] determined an incidence and a prevalence of chronic pancreatitis of 4.05/100,000 and 41.76/100,000, respectively. Domínguez-Muñoz et al.[3] reported an incidence of chronic pancreatitis of 4.66/100,000. Chronic pancreatitis is more frequently detected in men.[2, 4] In our study, there were 6 male and 5 female patients with chronic pancreatitis.

Alcohol intake is the most important risk factor in chronic pancreatitis.[1-3, 5] Frulloni et al.[5] found alcohol as an etiological factor in 43% of 893 cases of chronic pancreatitis. Other important risk factors include genetic factors, ductal obstruction, and smoking.[1, 4, 6, 7]

Clinically, the most prevalent and characteristic surgical indication for chronic pancreatitis is abdominal pain, which sometimes becomes very severe.[8, 9] Fully developed pancreatitis can lead to failure of both the exocrine and endocrine functions of pancreas.[9]

Chronic pancreatitis is characterized by a grossly enlarged

| Age (years) | Gender | Initial diagnosis | Procedure performed | Pathological diagnosis | Right/ex | Survey |
|------------|--------|-------------------|---------------------|----------------------|---------|--------|
| 45         | M      | Firearm injury    | Wedge resection     | Hematoma             | Right   | 11 years |
| 55         | M      | Insulinoma        | Pancreatectomy      | Normal               | Right   | 11 years |
| 37         | M      | Penetrating stab wound | Subtotal pancreatectomy | Necrosis congestion | Right   | 11 years |
| 50         | F      | Carcinoma         | Pancreatectoduodenectomy | Chronic pancreatitis | Right   | 10 years |
| 49         | M      | Carcinoma         | Pancreatectomy      | Pseudocyst            | Right   | 10 years |
| 61         | M      | Carcinoma in fistula tract | Fistula tract excision | Granulation tissue   | Right   | 12 years |
| 75         | F      | Carcinoma         | Biopsy              | Chronic pancreatitis  | Right   | 12 years |
| 47         | F      | Cystadenoma       | Excision            | Retention cyst        | Right   | 7 years  |
| 5          | M      | Cystadenoma       | Whipple procedure   | Choleoductal cyst     | Right   | 1 year   |
| 53         | M      | Carcinoma         | Whipple procedure   | Chronic pancreatitis  | Right   | 1 year   |
| 54         | F      | Carcinoma         | Excision            | Castleman disease     | Right   | 1 year   |
| 50         | M      | Carcinoma         | Subtotal pancreatectomy | Chronic pancreatitis | Right   | 1 year   |
| 45         | M      | Carcinoma         | Whipple procedure   | Chronic pancreatitis  | Right   | 4 months |
| 56         | F      | Periampullary region tumor | Whipple procedure   | Chronic pancreatitis  | Right   | 4 months |
| 45         | M      | Carcinoma         | Excision            | Chronic pancreatitis  | Right   | 3 months |
| 39         | F      | Cushing disease   | Bilateral adrenalectomy and distal pancreatectomy | Fat necrosis | Right | 2 years |
| 50         | F      | Cyst              | Subtotal pancreatectomy | Chronic pancreatitis | Right   | 2 years |
| 67         | M      | Carcinoma         | Whipple procedure   | Adenomyoma            | Right   | 2 years |
| 56         | M      | Carcinoma         | Whipple procedure   | Chronic pancreatitis  | Right   | 2 years |
| 54         | F      | Papilloma         | Whipple procedure   | Chronic pancreatitis  | Right   | 2 years |
or atrophic, nodular, hard, and misshapen pancreas. In some cases, ductal obstruction by a stone or a tumor may be seen. In our study, there was an instance of an obstructive, ampullary-region adenomyoma that led to chronic pancreatitis (Fig. 1). Ampullary-region adenomyoma, which generally causes a biliary system obstruction, is a benign nodular lesion with a proliferation of both epithelial (gland and ductus) and smooth muscle components.\(^{[10, 11]}\)

In chronic pancreatitis, microscopically, the main characteristics are ductal and acinar dilation, squamous metaplasia, intraluminal eosinophilic mucoprotein plugs, acinar atrophy, and sclerosis (Figs. 2, 3). Mononuclear inflammatory cell infiltration accompanied by mast cells around the lobules and ducts is seen (Fig. 4).\(^{[12]}\) Islets of Langerhans may be sclerotic, lost, or may proliferate in an invasive cell pattern in the peripancreatic adipose tissue. Manifestations of pancreatitis detected in 1 patient in this study, a 45-year-old male, were characterized by diffuse lymphoplasmacytic infiltrate and fibrosis (Fig. 5).

Treatment modalities for chronic pancreatitis include drainage of the pancreatic duct, partial pancreatic resection, and near total pancreatectomy.\(^{[1, 13-18]}\) In our study, of 11 cases with pancreatitis, 6 underwent a Whipple procedure, 2 a pancreaticoduodenectomy, 1 a subtotal pancreatectomy, 1 an excision, and a biopsy was performed in 1 case.

Cystic lesions of the pancreas may be classified in 3 groups: true cysts, pseudocysts, and cystic neoplasias.\(^{[19, 20]}\) Pseudocysts are the most frequently seen cystic lesions of the pancreas. In our study, pseudocysts were detected in a 49-year-old male and a 50-year-old male patient with chronic pancreatitis. Pseudocysts are nonepithelial cystic lesions associated with acute or chronic pancreatitis, trauma, and...
rarely, neoplastic obstruction of large ducts.\textsuperscript{[21, 22]} They are more frequently seen in men, with a variable mean age.\textsuperscript{[22]} Microscopically, the wall of the pseudocyst consists of non-epithelialized granulation or fibrotic tissue (Fig. 6). It usually contains tissue rich in intraluminal amylase and hemorrhagic debris.\textsuperscript{[24]} In our study, a 47-year-old female patient who underwent excision of a cyst with an initial diagnosis of serous cystadenoma had definitive diagnosis of a retention cyst based on histomorphological findings. Retention cysts are true cysts lined with pancreatic duct epithelium that create cystic dilations of the pancreatic duct due to intraluminal obstruction.\textsuperscript{[24]}

A 5-year-old male patient underwent a Whipple procedure with the initial clinical diagnosis of serous cystadenoma, but received a histomorphological diagnosis of choleductal cyst. Choleductal cysts are a rarely seen congenital anomaly that involves dilation of the intra- and/or extrahepatic bile duct.\textsuperscript{[25]} Microscopically, discrete areas of destruction and inflammation are seen. Forny et al.\textsuperscript{[25]} reported the notable finding of choleductal cyst fibrosis in 45.5\% of the liver biopsies in a retrospective analysis of 30 pediatric cases. Analysis of a series of excision material sections from a 54-year-old female patient who presented with an initial clinical diagnosis of lymphoma did not reveal findings specific to the pancreas; however, Castleman disease involving the peripancreatic lymph node was noted. Castleman disease is a rarely seen lymphoproliferative disease characterized by an enlarged hyperplastic lymph node.\textsuperscript{[26]} It is most frequently seen in the mediastinum, followed by the cervical region, and rarely, in the pelvic cavity, axilla, or retroperitoneum.\textsuperscript{[26]} In our study, it was observed in the unusual location of the retroperitoneal peripancreatic lymph node (Fig. 7).

In the present study, a hematoma was detected in a 45-year-old male patient who underwent a wedge resection following a firearm injury, and necrosis and congestion were observed in a 37-year-old male patient who underwent a subtotal pancreatectomy due to a penetrating stab wound. Histomorphological analysis of the excision material retrieved from a pancreatic fistula tract of a 61-year-old male patient with suspected malignancy revealed granulation tissue. Fat necrosis of a pancreas specimen was seen in a 39-year-old female patient who underwent a bilateral adrenalectomy and distal pancreatectomy with the indication of Cushing disease. No pathology was detected in the pancreatic tissue material of a 55-year-old male patient who underwent a pancreatectomy with the initial clinical diagnosis of insulinoma.

This study was a retrospective analysis of nonneoplastic lesions of the pancreas from the clinical and histopathological perspectives.

\textbf{Figure 5.} Autoimmune pancreatitis (H\&Ex400).

\textbf{Figure 6.} Pseudocyst (H\&Ex40).

\textbf{Figure 7.} Castleman disease (H\&Ex200).
References

1. Majumder S, Chari ST. Chronic pancreatitis. Lancet 2016;387:1957–66.
2. Yadav D, Timmons L, Benson JT, Dierkhising RA, Chari ST. Incidence, prevalence, and survival of chronic pancreatitis: a population-based study. Am J Gastroenterol 2011;106:2192–9.
3. Domínguez-Muñoz JE, Lucendo A, Carballo LF, Iglesias-García J, Tenías JM. A Spanish multicenter study to estimate the prevalence and incidence of chronic pancreatitis and its complications. Rev Esp Enferm Dig 2014;106:239–45.
4. Coté GA, Yadav D, Slivka A, Hawes RH, Anderson MA, Burton FR, et al.; North American Pancreatitis Study Group. Alcohol and smoking as risk factors in an epidemiology study of patients with chronic pancreatitis. Clin Gastroenterol Hepatol 2011;9:266–73.
5. Frulloni L, Gabbielli A, Pezzilli R, Zerbi A, Cavestro GM, Marotta F, et al.; PanCroInfAISP Study Group. Chronic pancreatitis: report from a multicenter Italian survey (PanCroInfAISP) on 893 patients. Dig Liver Dis 2009;41:311–7.
6. Yadav D, Hawes RH, Brand RE, Anderson MA, Money ME, Banks PA, et al.; North American Pancreatic Study Group. Alcohol consumption, cigarette smoking, and the risk of recurrent acute and chronic pancreatitis. Arch Intern Med 2009;169:1035–45.
7. Andreiulli A, Botteri E, Almasio PL, Vantini I, Uomo G, Maisonneuve P; ad hoc Committee of the Italian Association for the Study of the Pancreas. Smoking as a cofactor for causation of chronic pancreatitis: a meta-analysis. Pancreas 2010;39:1205–10.
8. Proca DM, Ellison EC, Hibbert D, Frankel WL. Major pancreatic resections for chronic pancreatitis. Arch Pathol Lab Med 2001;125:1051–4.
9. Lankisch PG, Löhr-Happe A, Otto J, Creutzfeldt W. Natural course in chronic pancreatitis. Pain, exocrine and endocrine pancreatic insufficiency and prognosis of the disease. Digestion 1993;54:148–55.
10. Kwon TH, Park DH, Shim KY, Cho HD, Park JH, Lee SH, et al. Ampullary adenomyoma presenting as acute recurrent pancreatitis. World J Gastroenterol 2007;13:2892–4.
11. Higashi M, Goto M, Saitou M, Shimizu T, Rousseau K, Batra SK, et al. Immunohistochemical study of mucin expression in periampullary adenomyoma. J Hepatobiliary Pancreat Sci 2010;17:275–83.
12. Esposito I, Friess H, Kappeler A, Shrikhande S, Kleeff J, Ramesh H, et al. Mast cell distribution and activation in chronic pancreatitis. Hum Pathol 2001;32:1174–83.
13. Traverso LW, Kozarek RA. The Whipple procedure for severe complications of chronic pancreatitis. Arch Surg 1993;128:1047–50.
14. Sherman S, Lehman GA, Hawes RH, Ponich T, Miller LS, Cohen LB, et al. Pancreatic ductal stones: frequency of successful endoscopic removal and improvement in symptoms. Gastrointest Endosc 1991;37:511–7.
15. Rösch T, Daniel S, Scholz M, Huijbrcsvte K, Smits M, Schneider T, et al.; European Society of Gastrointestinal Endoscopy Research Group. Endoscopic treatment of chronic pancreatitis: a multicenter study of 1000 patients with long-term follow-up. Endoscopy 2002;34:765–71.
16. Morrow CE, Cohen JL, Sutherland DE, Najarian JS. Chronic pancreatitis: long-term surgical results of pancreatic duct drainage, pancreatic resection, and near-total pancreatectomy and islet autotransplantation. Surgery 1984;96:608–16.
17. Friess H, Berberat PO, Wirtz M, Büchler MW. Surgical treatment and long-term follow-up in chronic pancreatitis. Eur J Gastroenterol Hepatol 2002;14:971–7.
18. Alvarez C, Widdison AL, Reber HA. New perspectives in the surgical management of chronic pancreatitis. Pancreas 1991;6 Suppl 1:S76–81.
19. Ryu DH, Sung RH, Kang MH, Choi JW. Lymphoepithelial cyst of the pancreas mimicking malignant cystic tumor: report of a case. Korean J Hepatobiliary Pancreat Surg 2015;19:129–32.
20. Karim Z, Walker B, Lam E. Lymphoepithelial cysts of the pancreas: the use of endoscopic ultrasound-guided fine-needle aspiration in diagnosis. Can J Gastroenterol 2010;24:348–50.
21. Matussue E, Fujihara Y, Maeda K, Okamoto M, Yanagitani A, Tanka K, et al. Three cases of mediastinal pancreatic pseudocysts. Acta Radiol Open 2016;5:2058460116647213.
22. Layfield LJ, Jarboe EA. Cytopathology of the pancreas: neoplastic and nonneoplastic entities. Ann Diagn Pathol 2010;14:140–51.
23. Parra-Herran CE, Garcia MT, Herrera L, Bejarano PA. Cystic lesions of the pancreas: clinical and pathologic review of cases in a five year period. JOP 2010;11:358–64.
24. Molvar C, Kayhan A, Lakadamyali H, Oto A. Nonneoplastic cystic lesions of pancreas: a practical clinical, histologic, and radiologic approach. Curr Probl Diagn Radiol 2011;40:141–8.
25. Forny DN, Ferrante SM, Silveira VG, Siviero I, Chagas VL, Méio IB. Choledochal cyst in childhood: review of 30 cases. Rev Col Bras Cir 2014;41:331–5.
26. Xu J, Zhou BO, Cao HL, Wang BO, Yan S, Zheng SS. Surgical management of isolated retroperitoneal Castleman’s disease: A case report. Oncol Lett 2016;11:2123–2126.