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Follicular Pancreatitis: A Distinct Form of Chronic Pancreatitis - An Additional Mimic of Pancreatic Neoplasms

Rajib K Gupta, MD¹,

Department of Pathology and Laboratory Medicine, University of Tennessee Health Science Center, Memphis, TN 38163, rajibgupta2011@gmail.com, Phone (Cell): 901-603-1041

Bill H Xie, MD,

Pathology Group of Midsouth (Trumbull Laboratories), 7550 Wolf River Blvd., Suite 200, Germantown, TN 38138, and attending pathologist, department of pathology, Baptist Memorial Hospital, Memphis, TN 38120, hbup@yahoo.com, Phone: 901-542-6800

Kurt T Patton, MD,

Pathology Group of Midsouth (Trumbull Laboratories), 7550 Wolf River Blvd., Suite 200, Germantown, TN 38138, and attending pathologist, department of pathology, Baptist Memorial Hospital, Memphis, TN 38120, kurt_patton@yahoo.com, Phone: 901-542-6800

Mikhail Lisovsky, MD, PhD,

Department of Pathology, Dartmouth-Hitchcock Medical Center and Geisel School of Medicine at Dartmouth, Lebanon, NH, mikhail.lisovsky@hitchcock.org, Phone: 603-650-7211

Eric Burks, MD,

Department of Pathology, Lahey Clinic, 41 Mall Road, Burlington, MA 01805. eric.burks@lahey.org, Phone: 781-744-8046

Stephen W Behrman, MD, FACS,

Division of Surgical Oncology, Department of Surgery, University of Tennessee Health Science Center, Memphis, TN 38163, and chair, department of surgery, Baptist Memorial Hospital, Memphis, TN 38120, sbehrman@uthsc.edu, Phone: 901-448-7306

David Klimstra, MD, and

Corresponding author. Vikram Deshpande, MD, Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, MA 02114. Phone: 617-726-7741, Vikramdirdeshpande@gmail.com.

¹Currently: Post-doctoral clinical fellow, Department of Pathology, Johns Hopkins Hospital & Johns Hopkins Medical Institute, 600 N. Wolfe Street, Baltimore, MD 21287.

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Department of Pathology, Memorial Sloan-Kettering Cancer Center and Memorial Hospital for Cancer and Allied Diseases, 1275 York Avenue, New York, NY 10065, klimstrd@mskcc.org, Phone: 212-639-5905

Vikram Deshpande, MD

Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, MA 02114, Vikramdirdeshpande@gmail.com, Phone: 617-726-7741

Abstract

Follicular pancreatitis is a recently described variant of chronic pancreatitis characterized clinically by the formation of a discrete pancreatic mass and histologically by the presence of florid lymphoid aggregates with reactive germinal centers. Our aim was to study the clinical and histologic features of follicular pancreatitis, as well as to critically examine potential overlap with autoimmune pancreatitis. Immunohistochemistry for Bcl-2, CD21, kappa and lambda light chains as well as IgG4 and IgG were performed. We found a total of six patients (male:female = 2:1, mean age = 57 years) who fulfilled the diagnosis of follicular pancreatitis in our institutions. Four had an incidental diagnosis while two presented with abdominal pain, fatigue and elevated liver enzymes. On imaging, three patients had a discrete solid mass while 2 cases showed a dilated main pancreatic duct, mimicking an intraductal pancreatic mucinous neoplasm on imaging. One patient had a lesion in the intra-pancreatic portion of the common bile duct. On histopathology, all cases showed numerous lymphoid follicles with Bcl-2 negative germinal centers either in a periductal or in a more diffuse (periductal and intra-parenchymal) fashion, but without attendant storiform fibrosis, obliterative phlebitis or granulocytic epithelial lesions. IgG4/IgG ratio was <40% in all 6 cases. A comparison cohort revealed germinal centers in 25% of type 1 autoimmune pancreatitis and 2% of type 2 autoimmune pancreatitis cases, but none were periductal in location. In conclusion, follicular pancreatitis, an under-recognized mimic of pancreatic neoplasms is characterized by intrapancreatic lymphoid follicles with reactive germinal centers.

Keywords

follicular pancreatitis; autoimmune pancreatitis; IgG4

1. Introduction

Several unique forms of chronic pancreatitis have been described over the last 2 decades including autoimmune pancreatitis and groove pancreatitis, diseases characterized by a dense inflammatory infiltrate [1–3]. Two variants of autoimmune pancreatitis have been identified, type 1 autoimmune pancreatitis, an IgG4 related disease, and type 2 autoimmune pancreatitis, a disease characterized by granulocytic epithelial lesions [1–4]. A 3rd form of pancreatitis characterized by a chronic inflammatory infiltrate and lymphoid follicles bearing prominent germinal centers, follicular pancreatitis, has not been as well characterized [5–10].

Follicular pancreatitis is characterized clinically by a discrete pancreatic mass on imaging, and histologically by the presence of numerous lymphoid follicles with Bcl2-negative

reactive germinal centers [5–10]. The prior descriptions of follicular pancreatitis are in the form of case reports, often designated as ‘pancreatic pseudolymphoma’ (Table 1). However, since the majority of these cases (prior to 2012) were reported prior to the recognition of autoimmune pancreatitis, it remains unclear whether the reported entity truly represented follicular pancreatitis or is merely a variant of autoimmune pancreatitis.

Herein, we report 6 cases of follicular pancreatitis identified at 4 institutions, and compare them with autoimmune pancreatitis. Our goal is to outline the clinical and histologic features of follicular pancreatitis, as well as to critically examine the relationship between follicular pancreatitis and autoimmune pancreatitis. We believe that these observations will assist the practicing pathologist to confidently arrive at a preoperative diagnosis of follicular pancreatitis, and thus facilitate a non-surgical and conservative approach.

2. Materials and Methods

A search for cases of follicular pancreatitis was performed at 2 institutions (Massachusetts General Hospital, Boston, MA and Baptist Memorial Hospital, Memphis, TN). All cases of chronic pancreatitis, both surgical resections and biopsies (MGH only) were re-evaluated for evidence of follicular pancreatitis. Additional cases were identified by two of the authors (VD, DK) from consultation material received by them from two other academic institutions. The study was approved by the institutional review boards of the 4 institutions. Pre-operative clinical history and CT imaging were reviewed from chart analysis. The hematoxylin and eosin stained slides were examined for the presence and location of lymphoid follicles with reactive germinal centers. Type 1 autoimmune pancreatitis was defined by the presence of storiform type fibrosis and obliterative phlebitis: the diagnosis also required the presence of > 50 IgG4 positive plasma cells (>10 per HPF on a biopsy) as well as an IgG4 to IgG ratio of >40%. Type 2 autoimmune pancreatitis was defined by the presence of a periductal lymphoplasmacytic infiltrate and intraductal neutrophilic abscesses [11]. The majority of the autoimmune pancreatitis cases were reported in a study from one of the institutions [11].

Immunohistochemistry for IgG (Dako Inc., 1:3000, Carpinteria, California, USA) and IgG4 (Cell Marque, clone MRQ-44 1:25, Rocklin, California, USA) and Bcl-2 (1:50, 124, Ventana) (Dako Inc., USA) was performed on all 3 cases. Immunohistochemistry for CD20 (L26, 1:300, Ventana) (Dako Inc., USA), CD21 (ready-to-use antibody, using EDTA-based pH 9.0 solution, clone 2G9) (Leica Biosystems, Buffalo Grove, IL, USA), CD3 (prediluted, PS1, Ventana) (Biocare Medical LLC, Concord, California, USA) and kappa (1:50, LIC1, Ventana) and lambda (1:250, Lamb14, Ventana) light chains (Cell Marque Corp., USA) were also performed.

3. Results

3.1 Clinical features

All six cases of follicular pancreatitis occurred in middle-aged to elderly patients with an age-range of 41–68 years and a male:female ratio of 2:1 (Table 2). Significant past medical history included colectomy for ulcerative colitis in one case (case 2), chronic alcoholism and

smoking in two cases each (cases 3 and 6, and cases 4 and 6 respectively) and type 2 diabetes in one case (case 4).. Two patients (cases 2 and 5) presented with epigastric pain and fatigue, had elevated liver enzymes and showed symptoms pointing to a pancreatic mass. The other four lesions were detected incidentally by CT imaging performed for other medical conditions. Three cases (cases 1, 3 and 4) had CT findings suggestive of a solid pancreatic mass (including intense PET positivity in case 3) [Figures 1 and 4A] and two cases (2 and 6) showed diffuse dilatation of the pancreatic duct along its entire course, an appearance suggestive of an intraductal pancreatic mucinous neoplasm (IPMN). Case 5 showed only a mass lesion within the distal common bile duct (CBD).

3.2 Cytology features

EUS-guided FNA was performed in 4 cases (1, 2, 3 and 4) which showed lymphocytes, few neutrophils and scant pancreatic epithelial cells. While the epithelial cells looked mildly atypical, no malignant features were noted in any of the four cases. Immunocytochemistry in case 1 (which was suspected to be an endocrine neoplasm) showed epithelial cells positive for cytokeratin and negative for chromogranin and synaptophysin. ERCP-guided bile duct brushing performed in case 5 revealed glandular cells mainly in sheets and clusters, some of which showed mild cytologic atypia; malignancy could not be excluded.

3.3 Serology and Management

A pancreatoduodenectomy (Whipple surgery) was performed in all cases except for case 3 in which a non-surgical option was pursued. Serum IgG4 levels were normal in the 4 patients where it was obtained (cases 1, 3–5). On a median follow-up of 13 months, there has been no recurrence either within the pancreas or at an extrapancreatic location in any of the studied cases. Case 3 who was treated with steroids showed a 50% reduction in the size of the tumor on imaging.

3.4 Macroscopic features

The resected specimens in cases 1 and 3 revealed 3 cm size firm fleshy tan-gray masses (each) in the pancreatic tail. Cases 2 and 6 showed a dilated main pancreatic duct without evidence of intraluminal mucin or associated mass lesion. Case 5 showed only a lesion within the intrapancreatic portion of the bile duct.

3.5 Microscopic features (Table 2)

Histologic examination in all the cases revealed numerous variable-sized lymphoid follicles with reactive germinal centers and intact mantle zones amidst atrophic or unremarkable pancreatic acini [Figures 2, 3, 4 (B–D) and 5]. The majority of the lymphoid follicles with germinal centers surrounded either pancreatic ducts solely (as in cases 2, 5 and 6), or were more diffusely distributed – that is, around pancreatic acini, blood vessels and nerves in addition to being located adjacent to pancreatic ducts (as in cases 1, 3 and 4). The periductal germinal centers were accompanied by a lymphoplasmacytic infiltrate, similar to that seen in autoimmune pancreatitis. Notably, there was no evidence of injury to the ductal epithelial cells. The germinal centers adjacent to pancreatic acini too did not show any parenchymal destruction. Whatever the location, the germinal centers uniformly showed a compact

network of CD21-positive follicular dendritic cells, and were positive for Bcl-6 and negative for Bcl-2. The plasma cells were polyclonal on immunohistochemistry for kappa and lambda light chains. The germinal centers were composed predominantly of CD20 B-cells, although scattered CD3 positive T cells were also identified. The mean number of intra-lesional IgG4 positive plasma cells varied from 3 to 19 per HPF. The IgG4 to IgG ratio was <40% in all the 6 cases.

Of the two patients with a history of alcoholism (cases 2 and 6), only one (case 6) showed dilated pancreatic ducts with inspissated proteinaceous material. However, the lymphoid aggregates with germinal centers surrounding the main pancreatic duct were distinct from the peripheral dilated ducts containing extravasated material, suggesting two distinct and unrelated diseases.

Neutrophil abscesses (granulocytic epithelial lesions) were conspicuously absent in all cases. Occasional pancreatic ducts showed a periductal collar of fibrosis. Interlobular fibrosis and parenchymal atrophy were frequent in the affected pancreatic segments; however the endocrine component was intact in all the cases and storiform-type fibrosis was consistently absent. Occasional partially obliterated veins were also noted in cases 1 and 4. PanIN1 lesions were additionally seen in all the pancreatectomy specimens (except for case 5) and was particularly prominent in case 2. Peripancreatic nodes were unremarkable except in cases 1 and 2 where they showed reactive changes.

3.6 Autoimmune pancreatitis type 1 and type 2

We also evaluated 20 cases of type 1 and 39 cases of type 2 autoimmune pancreatitis, specifically for the presence of germinal centers. The majority of these cases have been reported in a prior publication [11]. Germinal centers were identified in 5 cases of type 1 autoimmune pancreatitis and one with type 2 disease. However, periductal germinal centers were not identified. All cases of type 1 autoimmune pancreatitis showed storiform type fibrosis and obliterative phlebitis. The cases of type 2 autoimmune pancreatitis showed periductal lymphocytic infiltrates and varying numbers of intraductal neutrophils-granulocytic epithelial lesions.

4. Discussion

Follicular pancreatitis, a term first coined by Zen et al in 2012, is a clinicopathologic entity characterized by clusters of lymphoid follicles with reactive germinal centers presenting usually as a pseudotumor in a single or rarely multiple anatomic segments of the pancreas (Tables 1 and 2). It belongs to the broad class of chronic pancreatitis with prominent lymphoplasmacytic infiltrates, of which autoimmune pancreatitis is the historic prototype [10]. Prior to the report by Zen and co-workers, there have been few reports of a similar entity termed as “pancreatic pseudolymphoma”. However, as the majority of these pseudolymphoma reports were made prior to the recognition of autoimmune pancreatitis, their veracity is difficult to establish (Table 1).

Follicular pancreatitis is a disease of middle-aged to elderly patients (range: 41–71 years, mean = 61 years) with a predilection for males (Tables 1 and 2). Although the disease is

occasionally asymptomatic, in our series the majority of cases were asymptomatic. Historically, the more common presentation is that of obstructive jaundice, epigastric pain, malaise, weight loss and elevated liver enzymes, symptoms similar to a pancreatic tumor. On CT or MRI imaging, the disease frequently mimics either a pancreatic solid neoplasm (carcinoma, neuroendocrine tumor or lymphoma) or an IPMN. Interestingly, in cases where the entity presented as a solid mass (resembling a carcinoma or a neuroendocrine tumor), the lymphoid follicles had a more diffuse distribution involving acini, vessels and nerves besides being periductal (main or branch-ducts), while in those cases where the presentation resembled that of an IPMN, the follicles were usually restricted to the zone immediately surrounding the main pancreatic duct. To the best of our knowledge, this kind of main duct type of follicular pancreatitis has not been described in the English literature [7, 10].

Rarely, there may not be any pancreatic mass. The two most recent cases reported from Japan, as also one of our cases (case 5) lacked a discrete pancreatic mass on imaging and the inflammation appeared to be centered on the intrapancreatic portion of the bile duct [10].

The diagnosis of follicular pancreatitis is predicated on the presence of a prominent lymphoid infiltrate with easily visualized germinal centers, generally with a predilection for ducts. However, given the relative paucity of literature on this topic, we would hesitate to define the number of reactive germinal centers required for this diagnosis. Nevertheless, all our cases demonstrated greater than 10 germinal centers in a single low power field, thus making them easily visible on low power.

Although follicular pancreatitis shares some features with autoimmune pancreatitis such as a pancreatic mass and periductal lymphoplasmacytic inflammation, the preponderance of evidence argues in support of a distinct entity, one characterized by Bcl-2 negative germinal centers within lymphoid follicles [10]. Notably, both forms of autoimmune pancreatitis lack dilation of the pancreatic duct; an irregularly narrowed pancreatic duct is the characteristic feature of this disease. Follicular pancreatitis lacks histologic and immunohistochemical features of type 1 and type 2 autoimmune pancreatitis - type 1 is usually characterized by the presence of storiform type fibrosis, obliterative phlebitis and elevated numbers of IgG4 positive plasma cells (>50 per HPF) as well as an elevated IgG4 to IgG ratio; and type 2 by the presence of periductal inflammation and neutrophilic abscesses [11]. None of our cases had any of the above classical features. Nevertheless, a modest increase in IgG4 positive cells as in case 1 as well as the presence of non-periductal germinal centers in 25% (n=20) of cases of type 1 and 2% (n=38) of cases of type 2 autoimmune pancreatitis raise the question of overlap between the two forms of chronic pancreatitis. Although occasional foci of phlebitis were identified in cases 1 and 4, the resected pancreas lacked the widespread total or near-total obliterated veins invariably seen in type 1 autoimmune pancreatitis [1–3, 10–12]. Finally, none of these cases developed recurrent disease, a common finding in patients with type 1 autoimmune pancreatitis [12]. Although our data suggests that follicular pancreatitis and type 1 autoimmune pancreatitis are distinct diseases, this hypothesis warrants further scrutiny, given the relatively small sample size (although this is the largest reported series of this disease). The two diseases are contrasted in Table 3.

The other forms of pancreatitis, including groove pancreatitis as well as ethanol-associated pancreatitis either lack intrapancreatic (other than intrapancreatic lymph nodes) germinal center formation, or when present, lack periductal reactive germinal centers. Alcohol-related pancreatitis is typically associated with pancreatic lithiasis, a sparse inflammatory infiltrate, as well as dilated ducts with inspissated proteinaceous material. A single case in our series (case 6) with history of alcohol abuse also had histologic evidence of alcohol-related pancreatitis. However, histologically 2 distinct processes were observed in this case - the first was follicular pancreatitis involving the main pancreatic duct with dilatation, an appearance that mimicked an IPMN and secondly, the peripheral portions of the pancreas showed cystically dilated ducts filled with inspissated material. We believe that the 2 diseases, follicular pancreatitis and alcoholic pancreatitis are unrelated since the majority of cystically dilated ducts were not surrounded by reactive germinal centers. Furthermore, prominent germinal center formation around a dilated main pancreatic duct has not been reported in alcohol-related pancreatitis. Groove pancreatitis is characterized by inflammation centered in the region of the groove between the duodenum and the common bile duct [13]. It should be noted that while any form of chronic pancreatitis may show numerous aggregates of mature lymphocytes, reactive germinal center formation is usually uncommon.

In addition to other forms of pancreatitis, the differential diagnosis also includes low-grade B-cell lymphomas associated with prominent germinal center formation such as follicular lymphoma and extranodal marginal zone B-cell lymphoma. The germinal centers in follicular pancreatitis are negative for Bcl-2 which is in contradistinction from the follicles of low-grade follicular lymphoma which are nearly always Bcl-2 positive. Extranodal marginal zone B-cell lymphoma can sometimes produce a striking array of reactive germinal centers which are Bcl-2 negative, however expanded marginal zones and sheets of monocytoid B-cells surrounding these follicles are clues to the diagnosis of marginal zone lymphoma and were not observed in any of the cases of follicular pancreatitis. Immunohistochemistry for kappa and lambda light chains will always show a polyclonal pattern in follicular pancreatitis but many cases of marginal zone lymphoma will show clonal plasmacytic differentiation, allowing a confident diagnostic distinction. Finally, since lymphoma much more commonly involves the pancreas secondarily, a careful review of peri-pancreatic lymph nodes may provide further clues to distinguish low-grade lymphoma from follicular pancreatitis.

Although lymphocytes, albeit modest in number, were recognized on a fine needle aspirate in 3 of the 5 cases (Table 2), the cytologic features were interpreted as non-diagnostic, likely a consequence of the lack of awareness of this disease (significantly lower than autoimmune pancreatitis) as well as the possibility that a lymph node may have been inadvertently sampled during the procedure. The presence of occasional atypical epithelial cells may raise concern of a neoplasm, compounding the difficulties associated with the interpretation of these samples. However, the histologic features are easily appreciated on a core biopsy of the pancreas, as in case 3. Such cyto-histologic discordance has also been noted in core-biopsy diagnosis of autoimmune pancreatitis [14].

The presence of periductal germinal centers in follicular pancreatitis raises the intriguing possibility that this entity is related to a recently described form of cholangitis, follicular

cholangitis as well as the more common gallbladder disease, follicular cholecystitis. Although there is no evidence, other than the histologic overlap, to link these diseases, nevertheless, it is tempting to postulate that the germinal centers represent a reaction to a common pancreaticobiliary-based microbial antigen [10].

5. Conclusion

Follicular pancreatitis is a distinct variant of chronic pancreatitis that mimics either a pancreatic solid neoplasm or an IPMN, joining a growing list of variants of chronic pancreatitis that now includes autoimmune pancreatitis and groove pancreatitis. Grossly, and on imaging, 3 patterns of disease are appreciable: 1) a mass lesion, 2) dilated main pancreatic duct, and 3) obstruction of the intra-pancreatic bile duct. Histologic features of follicular pancreatitis include periductal or diffuse Bcl-2 negative reactive germinal centers within lymphoid follicles in large numbers alongside a low IgG4+ plasma cell count and low IgG4/IgG ratio, as well as the absence of storiform-type fibrosis and obliterative phlebitis. Whether this disease is also steroid responsive, analogous to autoimmune pancreatitis, is yet uncertain, although the mass in case 3 became considerably smaller following steroid therapy. Nevertheless complete resolution of the mass did not occur as is usual in type 1 autoimmune pancreatitis. Awareness of this tumefactive form of pancreatitis is crucial to avert a pancreatic resection, a surgical procedure associated with significant morbidity.

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Figure 1.

Typical imaging findings in a case of follicular pancreatitis reminiscent of a pancreatic neoplasm: Endoscopic ultrasound performed in case #1 reveals a hypoechoic lesion (A); The CT scan of the same reveals a well-circumscribed mass in the tail of the pancreas (B).

Figure 2.

A low-power image showing a major pancreatic duct branch circumscribed on all sides by germinal follicles (case #1). Note a separate germinal follicle also being juxtaposed to a medium-sized arteriole (upper right), and the interlobular collagenous fibrosis in the background, H&E $\times 100$ (Inset: CD21 immunostain highlights the follicular dendritic network within one such periductal germinal follicle, $\times 200$).

Figure 3.

Reactive germinal centers surrounding the main pancreatic duct (case # 2), H&E $\times 200$.

Note also the dense periductal lymphocytic infiltrate (A). Periductal germinal center (case # 1), H&E $\times 200$. Note the ductal epithelium lacks evidence of injury as is commonly seen in type 2 autoimmune pancreatitis (B). A single focus of partial obliteration of a venous channel seen in case # 1, H&E $\times 200$. Although reminiscent of type 1 autoimmune pancreatitis, the vein lacks the total obliteration that is typically seen in type 1 autoimmune pancreatitis (C).

Immunohistochemical stain for IgG4 performed (case # 1) shows only rare IgG4 positive plasma cells, $\times 200$ (D).

Figure 4. Imaging, histopathologic and immunohistochemical findings in case 3: The pancreatic lesion (in case # 3) was hot on PET scan (A). A core biopsy of the same demonstrates the presence of a germinal center, H&E $\times 100$ (B), negative for Bcl-2, $\times 100$ (C), while an IgG4 stain reveals only few IgG4 positive plasma cells, $\times 100$ (D).

Figure 5.
Histopathologic findings in case 4 showing reactive lymphoid follicles with germinal centers around pancreatic acini and a small artery, H&E $\times$ 200

Table 1

A review of prior reported cases of follicular pancreatitis/pseudolymphoma

Case	Age (years)/Sex	Presenting features	Abdominal imaging ^a	Pre-operative diagnosis	Surgical procedure
1. Nakashiro et al, 1991 # [8]	57/F	Jaundice, elevated LFTs	US and CT: 2 cm hypoechoic mass pancreatic head; dilation of the proximal common bile duct and distal pancreatic duct	Pancreatic carcinoma	Whipple procedure
2. Hatzitheoklitos et al, 1994 # [5]	68/F	Weight loss, elevated LFTs	US and CT: 5 cm hypoechoic mass pancreatic body; dilation of the main pancreatic duct in the tail	Pancreatic carcinoma	Segmental pancreatectomy
3. Kim et al, 2011 # [6]	70/M	Incidental, on imaging	CECT: 2 lesions, 2 cm uncinuate process and 1.8 cm in the tail,	Pancreatic neuroendocrine tumor or pancreatic lymphoma	Whipple procedure
4. Nakata et al, 2012 # [9]	51/F	Incidental on imaging	EUS and MRI: Two hypoechoic lesions 1.7 cm pancreatic head and 2.3 mm in the pancreatic body	Pancreatic neuroendocrine tumor	Whipple procedure
5. Zen et al, 2012 [10]	71/M	Jaundice and weight loss	US, CT and MRI: Diffuse enlargement of the pancreatic head with intra-pancreatic bile duct stenosis	Pancreatic carcinoma	Whipple procedure

Case	Age (years)/Sex	Presenting features	Abdominal imaging ^a	Pre-operative diagnosis	Surgical procedure
6. Zen et al, 2012 [10]	61/M	Jaundice	US, CT and MRI: Diffuse enlargement of the pancreatic head with intra-pancreatic bile duct stenosis	Pancreatic carcinoma	Whipple procedure
7. Mizuuchi et al, 2014 [7]	71/M	Elevated LFTs	CECT and MRI: 2 cm mass in the pancreatic head	Pancreatic carcinoma	Whipple procedure

^a – include ultrasound (US), computerized tomography (CT), contrast-enhanced CT (CECT), endoscopic ultrasound (EUS), magnetic resonance imaging (MRI), LFT = Liver function tests, IHC = Immunohistochemistry; # = case-reports where the entity has been designated as “pancreatic pseudolymphoma”

Table 2

Clinical, cytologic, serologic & histopathologic features of our cases

	Age/Sex	Presenting symptoms	Abdominal imaging ^a	EUS-FNA ^b results	Histology	IgG4 cells /HP F	IgG4 /IgG ratio (%)	Serum IgG4 level (mg/dL) ^e
Case 1	60/M	Incidental	EUS and CECT: 3.5 × 3.8 cm hypoechoic mass tail of pancreas	Benign lymphocytes and rare benign-appearing epithelial cells	Lymphoid follicles with Bcl-2 negative germinal centers – periductal & diffuse	19	30	113
Case 2	57/F	Epigastric pain, fatigue	CECT: Diffuse dilation of the pancreatic duct along its entire course without a discrete mass	Mucin and mildly atypical epithelial cells	Lymphoid follicles with Bcl-2 negative germinal centers – periductal	3	4	Not done
Case 3	55/M	Incidental	CECT and EUS: 6 × 4.3 cm mass with microcalcifications in the body of pancreas; PET scan showed a “hot” lesion	Polymorphic lymphoid cells	Lymphoid follicles with Bcl-2 negative germinal centers – periductal & diffuse (core biopsy)	8	10	130
Case 4	66/M	Incidental	CECT, MRI and EUS: 3.3 × 2.8 cm hypoechoic mass in pancreatic tail	Scant acinar cells, mildly atypical ductal cells, rare lymphocytes	Lymphoid follicles with Bcl-2 negative germinal centers – periductal & diffuse	10	Not done ^c	23
Case 5	41/F	Abdominal pain, fatigue and persistent elevated liver enzymes	ERCP ^d and upper EUS: 0.8–1.0 cm bulging lesion into the distal common bile duct	Mildly atypical glandular cells in clusters and sheets	Lymphoid follicles with bcl2-negative germinal centers – periductal (intrapaneatic distal bile-duct)	10	6	28.6
Case 6	68/M	Incidental	CT and MRI: Main pancreatic duct dilatation (1.4 cm), most notable in the head of the pancreas.	Cytology not done	Lymphoid follicles with bcl2-negative germinal centers – periductal	Less than 5	3	Not done

^a – CT, CECT, EUS and ERCP.

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- ^q – EUS-FNA = EUS guided fine needle aspiration,,
- ^c – IgG immunostain was not done, so ratio was unavailable in this case,
- ^d – Endoscopic retrograde cholangio-pancreatogram,
- ^e – Normal serum IgG4 level = 17–153 mg/dL, HPF = High power field.

Table 3

A comparison of the histologic features of follicular pancreatitis and autoimmune pancreatitis

Feature	Follicular pancreatitis	Autoimmune pancreatitis
Storiform fibrosis	Absent	Present (type 1)
Obliterative phlebitis	Rare to absent	Present easily visualized (type 1)
Lymphoid follicles with germinal centers	Prominent periductal or more diffuse throughout the parenchyma	Periductal-absent. Rarely in the lobules (type 1)
Quantitatively significant tissue IgG4 and/or IgG4/IgG ratio ^a	Absent	Present (type 1)
High-serum IgG4 levels ^b	Absent	Present in type 1 (80%)
Granulocytic-epithelial lesions	Absent	Present in type 2 (usually)
Response to steroids	Currently unknown ^c	Good

^a – the presence of > 50 IgG4 positive plasma cells (>10 per HPF on a biopsy) as well as an IgG4 to IgG ratio of >40%

^b – normal value 17–153 mg/dL; at least 2 to 3 times elevation is diagnostically significant (2)

^c – there was partial response in case 3