Human Pathology (2016) **48**, 154–162

ELSEVIER

Human PATHOLOGY

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Original contribution

Follicular pancreatitis: a distinct form of chronic pancreatitis—an additional mimic of pancreatic neoplasms☆,☆☆,★,★★

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Received 16 February 2015; revised 13 September 2015; accepted 16 September 2015

Keywords:
Follicular pancreatitis;
Autoimmune pancreatitis;
IgG4;
Pancreatitis;
Lymphoma

Summary 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, κ and λ light chains as well as IgG4 and IgG were performed. We found a total of 6 patients (male-female ratio, 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, 3 patients had a

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☆ Presented as a poster at the 2015 USCAP meeting at Boston on Tuesday, March 24 by the first author (R.K.G.).

☆☆ Financial support for the manuscript (if any): None.

★ Conflict of interest for this paper (for all authors): None.

★★ IRB approval: All procedures were performed in compliance with relevant laws and institutional guidelines (Massachusetts General Hospital, Boston, MA; Baptist Memorial Hospital Memphis, TN; Dartmouth-Hitchcock Medical Center, Lebanon, NH; and Lahey Clinic, Burlington, MA) and were approved by appropriate institutional committee(s) at all the abovementioned hospitals.

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http://dx.doi.org/10.1016/j.humpath.2015.09.017

discrete solid mass, whereas 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-to-IgG ratio was <40% in 5 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.

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 third 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 Bcl-2–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 most of these cases 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 (Massachusetts General Hospital only) were re-evaluated for evidence of follicular pancreatitis. Additional cases were identified by 2 of the authors (V.D. and D.K.) from consultation material received by them from 2 other academic institutions. The study was approved by the institutional review boards of the 4 institutions. Preoperative clinical history and computed tomographic (CT) imaging were reviewed. The hematoxylin and eosin (H&E)–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 high-power field [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 (1:3000; Dako Inc, Carpinteria, CA) and IgG4 (Cell Marque, clone MRQ-44 1:25; Rocklin, CA, USA) and Bcl-2 (1:50, 124, Ventana) (Dako Inc) was performed on all 3 cases. Immunohistochemistry for CD20 (L26, 1:300, Ventana) (Dako Inc), CD21 (ready-to-use antibody, using EDTA-based pH 9.0 solution, clone 2G9) (Leica Biosystems, Buffalo Grove, IL), CD3 (prediluted, PS1, Ventana) (Biocare Medical LLC, Concord, CA) and κ (1:50, LIC1, Ventana) and λ (1:250, Lamb14, Ventana) light chains (Cell Marque, Rocklin, CA, USA) were also performed.

3. Results

3.1. Clinical features

All 6 cases of follicular pancreatitis occurred in middle-aged to elderly patients with an age range of 41 to 68 years and a male-female ratio of 2:1 (Table 2). Significant past medical history included colectomy for ulcerative colitis