Sporadic Lymphoplasmacytic Cholecystitis
A Clinicopathologic Entity
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ABSTRACT

Objectives: To describe a sporadic form of lymphoplasmacytic cholecystitis (LPC), a condition known to occur in patients with chronic biliary tract disease.

Methods: One year’s worth of cholecystectomies was reviewed for sporadic cases of LPC. Histologic, radiologic, and clinical findings were reviewed and compared with noninflamed controls. Sporadic cases were also compared histologically with obstructive LPC cases.

Results: Sporadic LPC made up 7% of cholecystectomies, had a male predominance (54.2%), and more often presented with clinical signs of acute inflammation compared with controls. Radiologic findings identified gallstones in 71.4% of patients. The second most common finding was unexplained extrahepatic biliary dilation. There were no unique histologic findings to separate sporadic cases from those associated with pancreatobiliary disease.

Conclusions: While obstructive LPC is traditionally described as acalculous, chronic cholecystitis, we show this inflammatory pattern occurs both in the presence of gallstones and outside of previously described disease categories. In addition, LPC occurs in a unique patient demographic (older men), often presenting similarly to acute cholecystitis.

Lymphoplasmacytic cholecystitis (LPC), as initially described, was a chronic inflammation, usually without gallstones, that occurred in patients with primary sclerosing cholangitis.1-3 Histologically, gallbladders with LPC had a triad of findings, including a diffuse chronic inflammatory infiltrate, with a predominance of plasma cells in the lamina propria accompanied by nodules of mucosal lymphocytes, some of which might have germinal centers.1 Some patients with LPC also had radiologic evidence of gallbladder wall thickening and extrahepatic bile duct stenosis.2 For years, this pattern was thought to be specific for primary sclerosing cholangitis.1 Other studies emerged proving an association of LPC with other forms of chronic biliary tract disease, including neoplastic obstruction and autoimmune pancreatitis.3,5 Many of these studies have examined the relationship between biliary obstruction and this particular pattern of
inflammation, but to our knowledge, no studies have examined this pattern of inflammation outside of extrahepatic biliary obstruction (EHBO), in other words, sporadic LPC. We evaluated all cases of LPC in 2010 from consecutive gallbladder resections for primary gallbladder disease to determine if there are any unique clinical or radiologic associations with the sporadic disorder.

Materials and Methods

In total, 535 histologically adequate gallbladders resected for primary gallbladder disease in 2010 were identified. Forty-one cases of LPC were identified based on the following histologic criteria: the presence of a diffuse lymphoplasmacytic lamina propria infiltrate and the presence of lymphocytic nodules in the mucosa Image 1 and Image 2, as has been similarly described in other studies.1,5 Of those cases, 35 had no pancreatobiliary disease; these formed the study group. Thirty-five consecutive noninflamed gallbladders resected for cholelithiasis were chosen as controls Image 3. Histologic findings evaluated included the intensity of the inflammation, wall thickness, fibrosis, pericholecystic fluid, muscular hypertrophy, and pyloric gland and intestinal mucosal metaplasias.

Clinical features reviewed included age, sex, ethnicity, body temperature, WBC count, and persistent right upper quadrant pain. We evaluated sonographic reports for the presence of bile duct dilatation, gallstones, pericholecystic edema, gallbladder wall thickening, and the presence of pain on inspiration during a sonographic examination (Murphy sign). The surgeons’ intraoperative impressions were also reviewed.

To compare the prevalence, histologic features, and demographics between sporadic and EHBO-associated LPC, we reviewed those gallbladders removed incidentally as part of larger hepatobiliary or pancreatic resections. Thirty-six of these large resection cases were available for review. These diseases included pancreatic adenocarcinoma, ampullary carcinoma, cholangiocarcinoma, cholangitis, pancreatic neuroendocrine tumors with bile duct impingement, and primary sclerosing cholangitis. Statistical significance was calculated using the Fisher exact test and Student t test.

This study was approved by the institutional review board at the University of Michigan, Ann Arbor.

Results

Study patients with sporadic LPC had a mean age of 62.1 years (range, 23-84 years) and had a male predominance (54.2%). Most patients were white (88.6%), with some African American and Asian American representation. Control patients had a mean age of 47.6 years (range, 20-87 years) with a female predominance (68.6%). The control patients had a similar ethnic distribution, with most being white (88.6%), and also with African American, Hispanic, and Asian American representation.

The clinical presentations of patients with LPC were significantly different from those of the control group. The study group patients were more likely to be febrile than were the control patients with cholelithiasis (22.9% vs 0%). They also more frequently had a leukocytosis, although this difference did not reach statistical significance Table 1. These clinical signs did not vary within the study group based on the presence or absence of choleliths (41.4% vs 41.7%). Both study
and control patients had a similar frequency of right upper quadrant pain lasting greater than 24 hours.

There were some radiologic differences between the two groups. Table 2. The most common ultrasound abnormality in the study group was biliary dilatation (17.1%), which was higher than in the control group (8.6%), but this difference was not statistically significant. There were no cases of suspected primary sclerosing cholangitis in either group. A large percentage of patients with LPC had gallstones (71.4%). Radiologic changes did not vary significantly when stratified by the histologic severity of inflammation.

Patients in both the study and control groups had sporadic LPC with mucosal metaplasias, almost all pyloric gland type (P = .1074). This was also true regardless of inflammation severity. Muscular hypertrophy was seen in both study and control patients. Cases of LPC with muscular hypertrophy were all associated with cholelithiasis. No other histologic changes were associated with the presence of cholelithiasis.

Of gallbladders removed as part of larger surgical resections in patients with EHBO, 46% had evidence of lymphoplasmacytic cholecystitis. Similar to those with sporadic LPC, these patients were also predominantly male (63%) and had a mean age of 62 years. No specific histologic findings separated obstructive lymphoplasmacytic cholecystitis from the sporadic LPC cases.

Discussion

Lymphoplasmacytic cholecystitis occurred sporadically in almost 7% of gallbladders resected for primary gallbladder disease, and it was almost seven times as common in gallbladders resected during operations for pancreatobiliary disease. Comparing our study patients with control patients with noninflamed gallbladders allowed us to identify a distinct clinical picture of this sporadic disease. The entity tends to disproportionately affect male patients, unlike most gallbladders resected for cholelithiasis. The age at presentation is about 15 years older than that of patients with cholelithiasis alone. Patients with this syndrome also tend to present more acutely with fever and/or a leukocytosis.

Sporadic LPC has some important radiologic findings. Most patients have sonographic evidence of cholelithiasis. The increased rate of biliary dilatation in this group, compared with controls, also approaches statistical significance. Seventeen percent of the study patients had radiologically unexplained biliary dilatation. There were no differences between rates of pericholecystic fluid, wall thickening, and the sonographic Murphy sign compared with controls.

In our study, we also reviewed gallbladders removed during pancreatobiliary resection as described in previous studies. The types of diseases we encountered were similar to those in other reports. They included predominantly pancreatic adenocarcinomas but also cholangiocarcinomas, primary sclerosing cholangitis, and pancreatic neuroendocrine tumors. The rate of lymphoplasmacytic cholecystitis in these resection specimens was 46%, similar to reported frequencies in other studies. This rate is much higher than in cases of sporadic LPC. There were also no distinguishable

### Table 1
Clinical Signs and Symptoms

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Study</th>
<th>Control</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y</td>
<td>62.1</td>
<td>47.6</td>
<td>.0002</td>
</tr>
<tr>
<td>M:F ratio</td>
<td>19:16</td>
<td>11:24</td>
<td>.0036</td>
</tr>
<tr>
<td>Fever</td>
<td>8:27</td>
<td>0:35</td>
<td>—</td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>11:24</td>
<td>7:28</td>
<td>.09</td>
</tr>
<tr>
<td>RUQ pain</td>
<td>33:2</td>
<td>32:3</td>
<td>.546</td>
</tr>
</tbody>
</table>

RUQ, right upper quadrant.

*Age is calculated as the mean age of each group. Fever represents the proportion of febrile patients to afebrile patients. Leukocytosis represents the proportion of patients with leukocytosis to those without. RUQ represents the proportion of patients with prolonged right upper quadrant pain to those without.

### Table 2
Imaging Findings

<table>
<thead>
<tr>
<th>Finding</th>
<th>LPC, No.</th>
<th>Control, No.</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholelithiasis</td>
<td>25</td>
<td>33</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Biliary dilatation</td>
<td>6</td>
<td>3</td>
<td>.67</td>
</tr>
<tr>
<td>Pericholecystic fluid</td>
<td>1</td>
<td>2</td>
<td>.4665</td>
</tr>
<tr>
<td>Wall thickening</td>
<td>4</td>
<td>5</td>
<td>.2691</td>
</tr>
<tr>
<td>Sludge</td>
<td>1</td>
<td>1</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Murphy sign</td>
<td>2</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Normal</td>
<td>6</td>
<td>0</td>
<td>—</td>
</tr>
</tbody>
</table>

LPC, lymphoplasmacytic cholecystitis.

*Only 33 patients had gallstones demonstrable by radiologic means. All control patients had gallstones present on gross examination.
histologic features between obstructive LPC gallbladders and sporadic cases.

While obstructive lymphoplasmacytic cholecystitis has been described as an acalculous, chronic cholecystitis, our study shows that this pattern of inflammation occurs both in the presence of gallstones and in clinical contexts outside of these previously described disease categories. In addition, the process occurs in a unique patient demographic—namely, older men compared with controls—and often presents with fevers and/or leukocytosis more like acute cholecystitis.

The etiology of this inflammatory pattern remains unknown but may simply be nonspecific, attributable to the same speculative causes as any other inflammations of the gallbladder, whether acute or chronic.

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References