

Case Report

Gallbladder with chronic calculous cholecystitis, reactive lymphoid hyperplasia and pyloric metaplasia

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Received - 20 March 2019

Initial Review - 03 April 2019

Accepted - 30 April 2019

ABSTRACT

The lymphoid hyperplasia of the gallbladder is a rare condition, which can be diagnosed only by performing a histological examination. Here, we present the case of a 62-year-old woman with complaints of repeatable pain in the area of the right hypochondrium for a few months. Ultrasonography revealed chronic cholecystitis with a concrement in the lumen. A cholecystectomy was then performed. Histology shows nests of cells with lymphoid origin in the lamina propria, a multitude of lymphoid follicles and areas with pyloric metaplasia in the gallbladder wall. The case presented herein is of reactive lymphoid hyperplasia resembling a lymphoma combined with chronic cholecystitis, pyloric metaplasia, and cholelithiasis.

Keywords: *Chronic cholecystitis, Lymphoid hyperplasia, Lymphoma, Metaplasia.*

Lymphoid hyperplasia is a rare but benign lesion. Histologically, it comprises hyperplastic lymphoid follicles with germinal centers. It can occur in the lungs, the gastrointestinal tract (GIT), the orbit and the skin [1,2]. The lymphoid hyperplasia in the mucosa and the gallbladder wall is an extremely rare kind of lesion. Chronic inflammation or an autoimmune reaction are considered to be the pathogenic basis for the development of this condition [3]. There have been several reported cases of lymphoid hyperplasia with chronic cholecystitis not exceeding 2% of the cholecystectomies [4,5]. We, hereby report a rare case of chronic cholecystitis with reactive lymphoid hyperplasia, pyloric metaplasia, and cholelithiasis.

CASE REPORT

A 62-year-old woman reported to the emergency department of our hospital with complaints of strong gripping pain in the right hypochondrium, nausea, and vomiting. The pain was recurring in nature occurred for a period of some years with shorter intervals. There was no other history of fever or a change in skin coloration. The patient also reported darker urine color on several occasions. On clinical examination, there was an absence of icterus. The vitals were stable. On palpation, there was a pain in the right hypochondrium and Murphy's sign was positive.

On further investigations, total bilirubin level was $6.8 \mu\text{mol/l}$ and direct bilirubin was $1.7 \mu\text{mol/l}$. Other biochemical tests like alpha-amylase, aspartate aminotransferase (AST), alanine aminotransaminase (ALT), electrolytes and other were in the normal range. The hematological parameters were within normal values with the exception of a lightly accelerated erythrocyte

sedimentation rate (ESR). Ultrasound examination of the abdominal organs showed a slightly thicker wall of the gallbladder with a single concrement sized 1 cm.

Based on the above observations, a clinical diagnosis of chronic calculous cholecystitis was established. Cholecystectomy was performed and the gallbladder sent for histological study.

Macroscopically, the gallbladder was sized 7.2 x 3 cm, wall thickness within 0.8 to 1 cm. Single greenish concrement sized 1 cm was located in the lumen of the collum vesicaefelleae of the gallbladder (Fig. 1).

Histology examination was performed using 3μ slices and colored with H&E. The slices showed the characteristics of chronic cholecystitis. Infiltration was mainly present in the lamina propria with chronic inflammatory monomorphic cells



Figure 1: Gross photograph of the gallbladder with solitary stone present

- lymphocytes, macrophages, and plasmocytes. There was a presence of numerous reactive lymphoid follicles with germinal centers (Fig. 2a and b) and more than three lymphoid follicles per 0.5 cm². Occasional mitosis was also seen. Rokitansky Aschoff sinuses in some place nests of pyloric metaplasia (Figure 2c). The presence of round cellular lymphoid infiltration and a multitude lymphoid follicles therein (Figure 2d) eliminated the possibility of the lymphoproliferative lesion.

Immunohistochemistry (Dako, Glostrup, Denmark) was performed using CD20, Bcl-2, CD5, CyclinD1, and CD23 in conformity with reactive change. The results do not comply with a lymphoproliferative lesion as follicular lymphoma, a mantle cell lymphoma, a CLL/SLL nor a mucosa-associated lymphoid tissue (MALT) lymphoma. After analyzing the histopathological and immunohistochemical indexes, a final diagnosis of gallbladder with chronic calculous cholecystitis, reactive lymphoid hyperplasia, and pyloric metaplasia was made. Postoperative period was without complications.

DISCUSSION

Follicular cholecystitis is a very rare gallbladder pathology. A few cases have been published with an occurrence frequency of less than 2% [6]. It comprises hyperplastic lymphoid follicles with germinal centers consisting of the polymorphic lymphoid population distributed throughout the whole gallbladder wall [7,8]. Five cases with chronic cholecystitis and focal lymphoid hyperplasia were described in previous research [1]. The combination of chronic cholecystitis, cholelithiasis, benign lymphoid hyperplasia,

and pyloric metaplasia as reported in the present case was not published before. Three lymphoid follicles with germinal centers were observed in the muscle layer in our case.

Lymphoid hyperplasia can be located in the lungs, orbit, skin and the GIT [2]. The presence of lymphoid tissue in the gallbladder mucosa is extremely rare, and there is a lack of any lymphoid follicles whatsoever. There were intraepithelial lymphocytes located among the superficial epithelial cells [9]. The presumption is that the reactive lymphoid hyperplasia occurs either after a prolonged inflammation or as a result of autoimmune disease [3]. In the reported case, the reactive lymphoid hyperplasia and pyloric metaplasia in the gallbladder developed in association with cholelithiasis and chronic cholecystitis. There is a possible association for lymphoid hyperplasia with a malignant tumor [3]. The exact reason for the lymphoid hyperplasia is still unclear due to the very low number of reported cases and the absence of throughout studies. Typically, the diseased are middle-aged or elderly women suffering from various chronic inflammatory conditions such as chronic hepatitis, thyroiditis and primary biliary cirrhosis [5].

The reactive lymphoid hyperplasia must always be differentiated from malignant lymphoma. Frequently they are disguised from cholecystitis. The most common ones are mucosa-associated lymphoid tissue (MALT) lymphoma, follicular lymphoma, mantle cell lymphoma and CLL/SLL [10]. MALT lymphoma of the gallbladder is described with diffuse infiltration of cells which resemble small follicular cells and a great number of plasmocytes as well as epithelial invasion of the lymphoid cells. This differentiates it from the reactive changes [11]. MALT

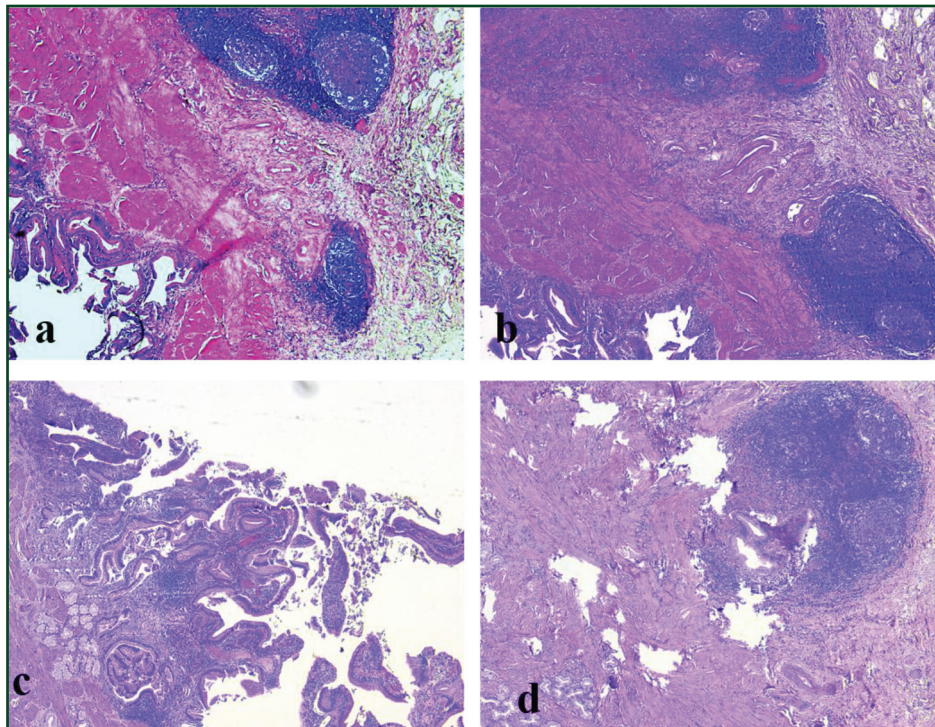


Figure 2: Histology (H&E) sections showing (a) Three Lymphoid follicles in the wall of the gallbladder (enlargement x100); (b) Two Lymphoid follicles in the gallbladder wall with proliferation centers (enlargement x100); (c) Mucosa and part of the gallbladder wall with infiltration of the lamina propria with mononuclear cells. The area with pyloric metaplasia (enlargement x50); (d) Gallbladder wall with reactive lymphoid follicle and an area with pyloric metaplasia (enlargement x200)

lymphoma represents 38% of all previously reported cases of primary lymphoma and is the most common non-Hodgkin's lymphoma of the gallbladder. If the lesion is located in the gallbladder, then there is a good prognosis after cholecystectomy [12]. Lymphoid cells are clearly positive for CD20, CD79a, CD43, and Bcl-2.

In cases of follicular lymphoma, the follicles are the same size, without the presence of clearly-outlined mantle zone and monomorphic cell population. During the reactive changes, the follicles become of different size, distinctly outlined mantle zone and polymorphic lymphoid population – as in the case reported herein. IHC detection of bcl-2 oncoprotein shows diffuse and intensive positivity in follicular lymphoma while the normal germinal centers do not show bcl-2 positivity as well as the reduced intensity in the mantle zone and interfollicular cells. The follicular infiltrations are composed of cells which test negative for CD20 and CD3; but positive for CD10, bcl-6, bcl-2. Follicular dendritic networks are positive for CD21 [13]. Mantle cell lymphoma consists of small to medium-sized centrocytes CD5 and cyclin D1 positive as well as a bcl-2 expression [14]. Chronic lymphocytic leukemia (CLL) which affects the gallbladder is extremely rare. There have been only a few presented cases [15].

Histologically, there is an unvaried population of small monoclonal lymphoid cells, infiltrating the gallbladder wall. IHC shows a distinctly positive response certainly for CD20, CD79a, CD23, BCL2, but CD5 and BCL6 tests turn negative [15]. Our case was negative for CD5 and bcl-2 markers.

CONCLUSION

A rare case of chronic cholecystitis with benign lymphoid hyperplasia and pyloric metaplasia is presented herein. Malignant lymphoma of gallbladder should be eliminated as a possibility for cases with lymphoid hyperplasia. When located in the gallbladder, the cholecystectomy is of curative nature and the prognosis is good. IHC staining tests in the combination of morphology are necessary in order to confirm the diagnosis.

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Funding: None; Conflict of Interest: None Stated.

How to cite this article: Shopov ST. Gallbladder with chronic calculous cholecystitis, reactive lymphoid hyperplasia and pyloric metaplasia. *Indian J Case Reports*. 2019;5(3):232-234.

Doi: 10.32677/IJCR.2019.v05.i03.011