A Case of Primary Mucosa-Associated Lymphoid Tissue Type Lymphoma of the Gallbladder

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Primary lymphomas of mucosa associated lymphoid tissue (MALT) lymphoma of the gallbladder is exceedingly rare. A 67-year-old man was admitted to our hospital presenting with epigastric pain and vomiting. Abdominal computed tomography (CT) and magnetic resonance cholangiopancreatography (MRCP) revealed dilatation of the gallbladder, thickening of the gallbladder wall, and biliary sludge formation in the gallbladder. Thus, the patient was diagnosed with acute cholecystitis and underwent laparoscopic cholecystectomy. Microscopically, we noted that lymphoid cells had infiltrated the mucosa of the gallbladder and formed a lymphoepithelial lesion (LEL). On polymerase chain reaction analysis, the reconstituted immunoglobulin heavy chain was detected. Therefore, a diagnosis of MALT lymphoma of the gallbladder was made. We report a case diagnosed with primary MALT lymphoma of the gallbladder after cholecystectomy.

Key words: Mucosa-associated lymphoid tissue type lymphoma, Gallbladder, Cholecystectomy

INTRODUCTION

Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue type (MALT lymphoma) was first reported by Isaacson and Wright in 1983 [1]. MALT lymphoma originates from marginal zone B-cells and accounts for 7%-8% of non-Hodgkin lymphomas [1]. Most cases of MALT lymphoma were thought to develop in association with autoimmune diseases or chronic infectious diseases, and were considered to mostly occur in the stomach; however, MALT lymphomas have since been reported in a number of mucosal sites including the salivary glands, thyroid gland, lungs, thymus, and breasts [2-5]. Primary MALT lymphomas of the gallbladder are exceedingly rare with only 14 reported cases in the English medical literature. Here we report the rare case of primary MALT lymphoma of the gallbladder with a review of the relevant literature.

CLINICAL CASE SUMMARY

A 67-year-old man was admitted to our hospital presenting with epigastric pain and vomiting in March 2014. The patient’s blood pressure was 93/59 mmHg, his heart rate was 65 bpm, and his body temperature was 36.8°C. Peripheral blood examination revealed a total white blood cell count of 4670/μl. The patient’s aspartate aminotransferase value was 416 U/L, alanine aminotransferase was 263 U/L, lactase dehydrogenase was 562 U/L, leucine aminopeptidase was 178 U/L, alkaline phosphatase was 431 U/L, and C-reactive protein was 0.96 mg/dL. Abdominal computed tomography (CT) and magnetic resonance cholangiopancreatography (MRCP) revealed dilatation of the gallbladder, thickening of the gallbladder wall, and biliary sludge.
formation in the gallbladder (Fig. 1a, b). In addition, a right renal tumor was detected on the abdominal CT scan by chance. Thus, the patient was diagnosed with acute cholecystitis and underwent laparoscopic cholecystectomy without complications.

PATHOLOGIC FINDINGS

Grossly, the gallbladder measured $75 \times 55$ mm in length, with a smooth serosal surface, prominent cholesterolosis, and a slightly incrassated wall (Fig. 2a, b). Microscopically, we noted that lymphoid cells had infiltrated the mucosa of the gallbladder and formed a lymphoepithelial lesion (LEL) (Fig. 3a, b, c, d). However, monocytoid cells and lymphoid follicles were not particularly noticeable. Kappa and lambda light chain restrictions could not be proven with immunohistochemistry. For the polymerase chain reaction (PCR) isolated DNA from the paraffin-embedded samples was used in order to demonstrate clonal rearrangements of immunoglobulin genes. The primer for V-domain was

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**Fig. 1a.** An abdominal CT scan demonstrated a dilatation of the gallbladder, thickening of the gallbladder wall, and biliary sludge formation in the gallbladder.

**Fig. 1b.** A magnetic resonance cholangiopancreatography demonstrated a dilatation of the gallbladder, thickening of the gallbladder wall, and biliary sludge formation in the gallbladder.

**Fig. 2a.** Photography of the gallbladder; The gallbladder measured $75 \times 55$ mm in length and the serosal surface was smooth and revealed prominent cholesterolosis.

**Fig. 2b.** Photomicrograph of the gallbladder; Mucosal layer was thickening with inflammatory cell infiltration, however, polypoid lesions were absent (H&E, 20x).
FR2a (Hokkaido System Science Ltd.) and for J-domain was LJH (Hokkaido System Science LTD.) and VJLH (Hokkaido System Science Ltd.). The Taq polymerase for PCR was Go Taq (Promega). Nested PCR was assayed twice; first using the primers set of FR2a and LJH and second using the primer set of FR2a and VJLH. The PCR-based assay showed two distinct band at 232bp and 258bp and the PCR analysis detected the reconstitution of the immunoglobulin heavy chain (IgH) (Fig. 4).

![Fig. 3a. A dense lymphoid infiltration composed of small lymphoid cells into the mucosa and the muscle layer were revealed (H&E, 100x).](image)

![Fig. 3b. Small lymphoid cells which infiltrated the mucosa of the gallbladder formed a lymphoepithelial lesion (H&E, 200x).](image)

![Fig. 3c. The destroyed epithelium was positive for AE1/AE3 (Immunoperoxidase stain, 200x).](image)

![Fig. 3d. The neoplastic cells are small with small amount of cytoplasm. (H&E, 200x).](image)

![Fig. 4. Lane M; DNA bp size marker. Lane 1; positive control from malignant lymphoma. Lane 2; negative control. Lane 3; the present case. Note the distinct two bands.](image)
Therefore, MALT lymphoma of the gallbladder was diagnosed. The patient underwent further lymphoma staging, including upper and lower gastrointestinal endoscopy and a full-body CT, none of which revealed any evidence of lymphoma. Two months after discharge, the patient underwent partial nephrectomy and histopathological diagnosis of the renal tumor was clear cell carcinoma. At 5 months after discharge, the patient shows no evidence of disease.

DISCUSSION

MALT lymphoma was reported as a particular type of B-cell lymphoma originating from organs containing glandular epithelium and has been shown to exhibit distinct clinical and histopathological characteristics. MALT lymphoma is one of an extranodal lymphoma which usually but not necessarily presents in a mucosal site. It is potentially curable with local therapy such as surgery and radiation therapy because it is often localized at presentation and indolent. Furthermore, it is associated with chronic inflammation and autoimmune disease such as Helicobacter pylori gastritis, Hashimoto thyroiditis and Sjogren’s syndrome. In the point of histopathology, three main components make up histological pattern: (1) Atypical and small-sized follicular cells with abundant cytoplasm (centrocytoid cells; CCL cells) and medium-sized cells with pale cytoplasm and irregular nuclei (monocytoid cells), which infiltrate around reactive B-cell follicles in the marginal zone and spread to the interfollicular area. (2) Invasion of epithelial structures to form LEL; invading B cells are at various stages of differentiation including monocytoid cells, small lymphocytes, plasma cells, centroblasts, and a small number of immunoblasts. (3) Follicular colonization of neoplastic cells that resemble follicular lymphoma [6]. There are two points of attention in the diagnosis of MALT lymphoma. Firstly, histopathological differentiating between MALT lymphoma and reactive lymphoid hyperplasia (RLH) is not so easy because intraepithelial lymphocytic infiltration is shown in both of them. Because monoclonality of infiltrating lymphocytes must be demonstrated in the diagnosis of MALT lymphoma, demonstration of immunoglobulin light chain restriction or IgH chain reconstitution is important. Secondary, diffuse large B cell lymphoma (DLBL) which is one of high grade of malignancy occasionally arises during the course of MALT lymphoma. However, differentiating between MALT lymphoma and DLBL is also difficult. It gives an indication that if sheet proliferation composed of over 20 of large lymphoblastic cells is present or large lymphoblastic cells account for more than 5% of all cells, DLBL is put down with MALT lymphoma [7]. In the present case, MALT lymphoma of the gallbladder was diagnosed based on LEL, absence of large lymphoblastic cells and the reconstituted IgH chain. Fourteen cases of primary MALT lymphoma of the gallbladder have been described in the English medical literature [8-21]. MALT lymphoma of the gallbladder most commonly occurs in women in their 60s and 70s. In the majority of cases, pain is noted in the right upper quadrant and cholecystectomy is performed for diagnoses of acute cholecystitis. In some cases the gallbladder wall were diffusely thickened and multiple polypoids were noted on the entire mucosal surface [11, 14, 21], however, in some another cases the mucosal surface were smooth as shown in the present case [13, 17]. As for the etiology of MALT lymphomas involving the gallbladder, it is important to note that the gallbladder is normally devoid of lymphoid tissue. For a MALT lymphoma to form, migration of lymphocytes to the gallbladder mucosa is necessary. Furthermore, it has been hypothesized that lymphomas may occur secondary to chronic cholecystitis or bacterial infection that cause lymphocyte migration [14, 16]. MALT lymphomas of the gallbladder have a better prognosis than other nonHodgkin lymphomas, and in the majority cases where the lesion is localized to the gallbladder, cholecystectomy alone is considered curative and offers an excellent prognosis [8, 14, 16]. Conflict of interest: None to declare.

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