Mucosa-Associated Lymphoid Tissue Type Lymphoma of the Gallbladder Associated with Acute Myeloid Leukemia

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We describe a patient with mucosa-associated lymphoid tissue (MALT) type lymphoma of the gallbladder who developed concurrent acute myeloid leukemia (M2). She was admitted because of progressive jaundice and underwent cholecystectomy. Histologic examination of the gallbladder showed diffuse proliferation of atypical lymphoid cells and a formed lymphoepithelial lesion. Because of progressive thrombocytopenia, a bone marrow tap was performed 25 days after the operation. Bone marrow contained 65.5% blasts, and was positive for peroxidase, CD33 and HLA-DR, and negative for lymphoid markers. We discuss the rare association of these disorders.

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Introduction

Mucosa-associated lymphoid tissue (MALT) type lymphoma often originates from the salivary gland (1), thyroid gland (2) or stomach tissue (3, 4). We present a rare case of MALT type lymphoma arising from the gallbladder. Interestingly, the patient developed acute myeloid leukemia (AML, M2) within one month after the diagnosis of lymphoma. There have been some reports of therapy-related leukemia (5) after administration of anticancer drugs with carcinogenic effects, but the concurrent presentation of malignant lymphoma with AML is extremely rare (6-9) and the pathogenesis of this association is unclear. We believe this rarity suggests that the simultaneous development of both disorders in this case was a chance event.

Case Report

An 82-year-old woman was admitted to our hospital because of progressive jaundice and right upper abdominal pain in July 1996. Peripheral blood tests revealed hemoglobin 10.5 g/dl, total white blood cell count 3.5x10^7/ with no abnormal cells, and platelets 15 1x10^9/. The patient's total serum bilirubin was 8.8 mg/dl, alkaline phosphatase 1,024 U/l, aspartate aminotransferase 278 U/l, and alanine aminotransferase 269 U/l. An abdominal computed tomography (CT) scan demonstrated a dilatation of intra- and extra-hepatic bile ducts and thickening of the gallbladder wall (Fig. 1). A percutaneous transhepatic cholangiogram showed narrowing of the common bile duct, and we diagnosed obstructive jaundice due to a tumor of the common bile duct. The patient’s advanced age precluded a curative operation, therefore palliative choledocho-jejunostomy and cholecystectomy were performed on August 21, and the common bile duct tumor was not resected. Histologic examination of the gallbladder showed diffuse proliferation of atypical medium and large-sized lymphoid cells in the walls (Fig. 2A); the lymphoid cells which infiltrated the mucosa formed a lymphoepithelial lesion (Fig. 2B). Immunohistochemically, the cells were positive for B cell marker, clgG and k, and we diagnosed MALT type lymphoma. After the operation, the platelet count gradually decreased and reached a nadir of 26x10^9/. Bone marrow contained 65.5% blasts (Fig. 3A). Interestingly, the cells were positive for peroxidase (Fig. 3B), CD33 and HLA-DR, and negative for lymphoid markers. Karyotypic analysis revealed 46, XX, del (13) (q12q14) in 20 of 20 cells. Prior myelodysplastic syndrome is observed often in the elderly patients of acute myeloid leukemia, however the patient’s bone marrow examination showed no dysplastic change. We diagnosed this patient with de novo acute myeloid leukemia (AML M2 type) on September 15. The patient refused chemotherapy. Her leukocyte count gradually increased to 12x10^9/l, then she
Lymphoma with Myeloid Leukemia

Figure 1. Abdominal computed tomography showed a thickening of the gallbladder wall.

Figure 2. A) Lymphoid infiltration of the gallbladder mucosa extending into the muscularis and the submucosal tissue (HE stain, x40). B) Small lymphoid cells infiltrating the mucosa and forming a lymphoepithelial lesion (HE stain, x400).

Figure 3. A) Bone marrow blast cells with folded nuclei, distinct nucleoli, varying numbers of azunophilic granules and occasional Auer rods (May-Grünwald-Giemsa stain, x1,000). B) Strong positive staining of blasts for peroxidase, x1,000.

developed sepsis and died on October 19, 1996.

Discussion

Extranodal lymphomas often involve Waldeyer’s ring or the gastrointestinal tract. Primary lymphoma of the gallbladder is extremely rare (10–13). Most cases of lymphoma occurring in the biliary tract are high-grade lesions and low-grade MALT lymphoma in this region is rare (12, 13). Our case showed the thickening of the gallbladder wall and an obstructive lesion in the common bile duct. We performed only palliative choledocho-jejunostomy and cholecystectomy, therefore the relationship of these two lesions remained unclear. But we believe this lymphoma arose from the gallbladder, based on its MALT type histology. The term malignant lymphoma of MALT was first proposed by Isaacson and Wright (3, 4). The tumor cells are “centrocyte (small cleaved cells)-like "cells and origi-
nate from MALT. A feature of MALT lymphoma is the presence of lymphoepithelial lesions formed by the invasion of these centrocyte-like cells into the epithelium. MALT lymphoma tends to remain localized and seldom involves the bone marrow. Interestingly, the present patient developed acute myeloid leukemia at almost the same time. The simultaneous occurrence of lymphoid and myeloid malignancies is rare. Most myeloid malignancies are chronic myelogenous leukemia (14–16) or myelodysplastic syndrome (17). These disorders involve stem cells capable of multilineage differentiation. There are some reports of therapy-related AML after treatment of lymphoma, especially with alkylating agents (5), but the association of malignant lymphoma with AML is extremely rare (6–9). A few reports have investigated cell origins by using monoclonal antibody methods (9). The pathogenesis of the simultaneous development of these disorders is unclear. The present patient's lymphoma arose from MALT of the gallbladder and MALT lymphoma tends to remain localized. Therefore, it is unlikely that both AML and MALT lymphoma originated from a common stem cell. Although immune deficiency associated with lymphoma may favor the development of other malignancies, there is no evidence for this phenomenon. To our knowledge, there is no tendency for MALT lymphoma to be accompanied by other malignancies, still less, by AML. Therefore, we cannot preclude the possibility that the association in the present case was a chance event.

References