CASE REPORT

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Acute Myeloid Leukemia Presenting as Obstructive Jaundice Caused by Granulocytic Sarcoma

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We report a rare case of granulocytic sarcoma infiltrating the bile duct in a patient with acute myeloid leukemia. A 23-year-old man presented with jaundice and weight loss. A peripheral blood smear revealed blast cells, and the results of an examination of bone marrow aspirate were consistent with acute myeloid leukemia. The bilirubin level increased gradually after induction chemotherapy with cytarabine. Magnetic resonance cholangiopancreatography (MRCP) revealed dilatation of the intrahepatic bile ducts and smooth tapering off at the level of the common hepatic bile duct. Endoscopic retrograde cholangiopancreatography (ERCP) also revealed diffuse narrowing of the proximal common hepatic bile duct. Obstructive jaundice resolved after endoscopic nasobiliary drainage. Remission induction chemotherapy with cytarabine and idarubicin was administered, and the patient remained complete hematological remission with normal liver function tests. **(Gut and Liver 2007;1:182-185)**

Key Words: Leukemia, Myelocytic, Acute; Jaundice, Obstructive; Bile ducts; Retrograde cholangiopancreatography, Endoscopic

INTRODUCTION

Extramedullary manifestations of acute myeloid leukemia include leukemia cutis, gingival hypertrophy, organomegaly, meningeal leukemia and tumorous masses at any body sites. Among them, granulocytic sarcoma is a rare extramedullary tumor that is composed of immature cells of myeloid progenitor series, which are found in patients with myelodysplastic syndrome, chronic myelogenous leukemia, and acute myeloid leukemia and usually involves bone, periosteum, soft tissue, lymph nodes and skin.[1,2] A wide variety of symptomatic and asymptomatic processes is related to a leukemic blast infiltration or mass lesions of granulocytic sarcoma, abscess, hematomas and secondary malignancies.[3] Rarely, jaundice is a presenting feature in a patient with leukemic infiltrate of the liver or tumorous aggregate of the perihepatobiliary ductal structure. Here, we report a patient who presented with obstructive jaundice resulting from leukemic infiltration of extrahepatic bile duct, which improved after endoscopic biliary drainage combined with chemotherapy.

CASE REPORT

A 23-year-old man was admitted to our hospital due to one-month history of jaundice and weight loss. He complained of fatigue, nausea and dyspepsia as well. His past medical history was unremarkable. Physical examination revealed pale conjunctivae, icteric sclerae and a few palpable nodes at the cervical region. Peripheral blood tests revealed hemoglobin 6.1 g/dl, platelet count 124,000/μL and white blood cell count 30,880/μL. Differential count in a peripheral blood smear showed 10% of neutrophils, 12% of lymphocytes, 6% of monocytes and 72% of circulating blasts. Bone marrow aspirate and biopsy revealed that the blast cells with relatively abundant cytoplasm and prominent nucleoli were counted up to 75.6% of all nucleated cells. Immuohistochemical studies of the blast cells were positive for myeloperoxidase, CD13 and CD33 but negative for periodic acid Schiff. Abnormalities in

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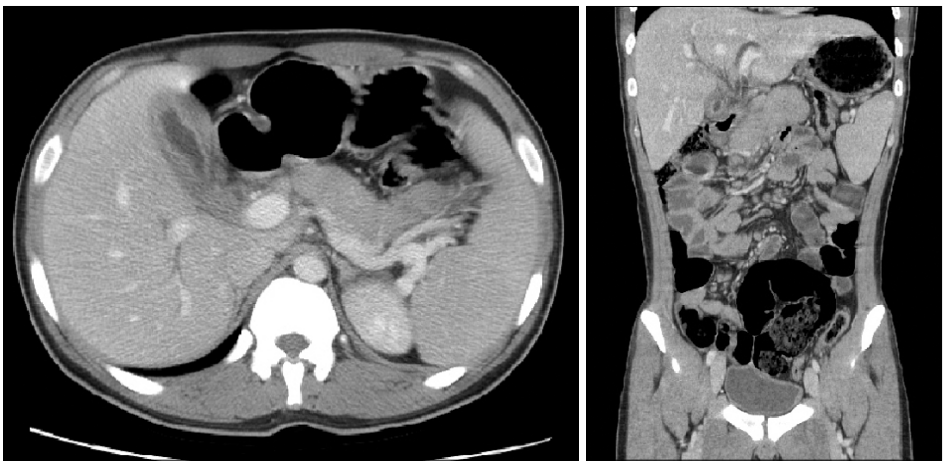

Fig. 1. Computed tomogram demonstrates a low density rim around the extrahepatic bile duct with no definitive abnormal enhancing lesion or mass.

chromosome number or structure were not found. These results were compatible with the diagnosis of M2, acute myeloid leukemia with maturation according to the classification of World Health Organization. Initial laboratory tests on admission showed aspartate aminotransferase 113 U/L, alanine aminotransferase 234 U/L, alkaline phosphatase 558 U/L, gamma glutamyltranspeptidase 505 U/L and total bilirubin 4.9 mg/dL with 3.5 mg/dL of direct fraction. Serologic tests for hepatitis viruses, Epstein Barr and cytomegalovirus were all negative. Abdominal ultrasonography revealed hepatosplenomegaly, mild dilatation of intrahepatic bile ducts and mild distension of the gallbladder. Abdominal computed tomography revealed a low density lesion around extrahepatic bile duct, but no definitive abnormal enhancing lesion of the wall or mass was recognized (Fig. 1). The patient immediately received induction chemotherapy with cytarabine. After the ninth day of chemotherapy, the level of total bilirubin was increased gradually up to 13.5 mg/dL and laboratory tests at that point were hemoglobin 8.5 g/dL, platelet count 48,000/μL, white blood cell count 2,700/μL with 8% of blast cells, aspartate aminotransferase 72 U/L and alanine aminotransferase 90 U/L. Magnetic resonance cholangiopancreatography revealed dilatation of the intrahepatic bile ducts and smooth tapering off at the common hepatic bile duct (Fig. 2). Endoscopic retrograde cholangiopancreatography revealed diffuse narrowing of the proximal common hepatic bile duct and endoscopic nasobiliary drainage was performed (Fig. 3). Over the next 11 days, the level of total bilirubin continued to regress constantly to 2 mg/dL and jaundice eventually disappeared. Because of thrombocytopenia after induction chemotherapy, we could not obtain tissue for pathologic diagnosis. But the low density lesion around the extrahepatic duct showed radiologic and clinical features consistent with granulocytic sarcoma. And then the patient received remission induction chemotherapy with cytarabine and idarubicin. Subsequent cholangiography revealed decompression of the extrahepatic bile ducts and endoscopic nasobiliary drainage was removed four weeks later (Fig. 3). The patient continued to receive consolidation chemotherapy and remained in complete hematological remission with normal liver function tests.

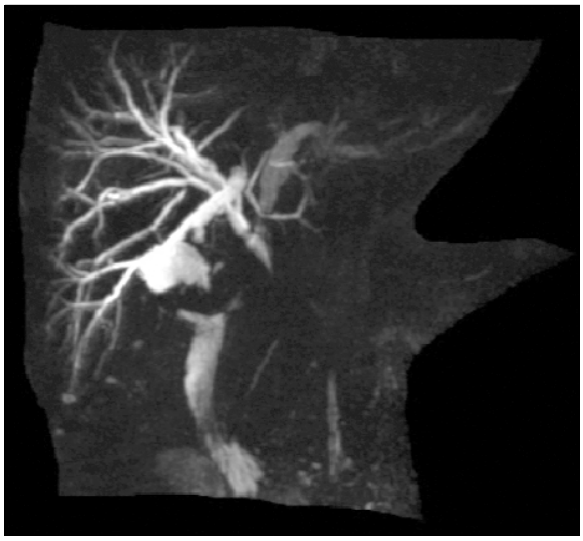

Fig. 2. Magnetic resonance cholangiopancreatography reveals dilatation of intrahepatic bile ducts and smooth tapering off at the common hepatic bile duct.

DISCUSSION

Extramedullary leukemia used together with extramedullary myeloid cell tumors encompass all forms of nonmedullary leukemic infiltrates and can occur throughout any body sites in different configurations of tumorous

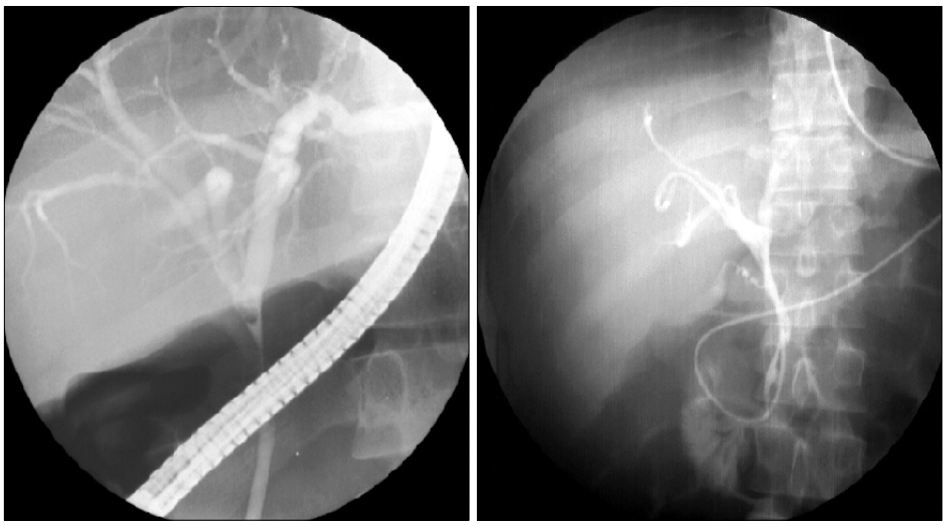

Fig. 3. Left; endoscopic retrograde cholangiopancreatogram reveals a diffuse narrowing of the proximal common hepatic bile duct with dilatation of the intrahepatic bile ducts. Right; after remission induction chemotherapy, follow-up cholangiogram reveals no luminal narrowing at proximal common hepatic duct.

masses.[3] Granulocytic sarcoma refers to extramedullary solid destructive tumorous infiltrates of malignant myeloid precursor cells. The term granulocytic sarcoma was initially introduced by Rappaport strictly to describe tumorous masses associated with cells of the granulocytic series. Since the lesion was first described by Burns[4] in 1811, it was King[5] in 1853 that designated the term chloroma based on the green color of the tumorous masses. The green color is due to myeloperoxidase, an enzyme found in a majority of extramedullary myeloid tumors. Neiman et al[1] described 4 of 61 granulocytic sarcomas presenting as gastrointestinal tract lesions and involvement of the biliary tract was presumed to be extremely rare. Granulocytic sarcomas may precede or occur concurrently with acute myeloid leukemia, or may be revealed in the absence of clinical evidence of acute myeloid leukemia or myeloproliferative disorder. They may also develop in a relapse in treated patients, even after bone marrow transplantation. The incidence of extramedullary leukemic infiltrate during the course of acute myeloid leukemia has not yet been properly described. However, it is often resistant to standard chemotherapy and might predispose patients to a higher incidence of both medullary and extramedullary relapse of acute myeloid leukemia. Cytogenetic abnormalities such as t (8;21), blast differentiation, cell-surface markers, lack of Auer rods, French-American-British classification (M2, M4 and M5), high presenting leukocyte count, and cellular immune dysfunction have been associated with a higher incidence of extramedullary leukemia. Although many factors influence the inclination to complete remission and the curability of acute myeloid leukemia, extramedullary infiltrate should not be present prior to the assessment of complete remission. The progression of granulocytic sarcoma in patients with acute leukemia has the same prognosis as the underlying leukemia. Obstructive jaundice with leukemic infiltration of the hepatobiliary territory has been infrequently reported in the circumstance of simultaneous acute myeloid leukemia. Diffuse hepatic sinusoidal infiltration of leukemic cells may be expected to bring about cholestatic jaundice, which may respond to chemotherapy with appropriate dosage modification.[6] In most cases jaundice was ascribed to leukemic infiltrate of the gallbladder or of the pancreas and still more to granulocytic sarcomas compressing the bile ducts.[7,8] Because leukemia is a rapidly progressive disease, contemporary hepatic dysfunction accompanied by jaundice may impair tolerance to a rigorous therapy and lessen the probability of survival. To reduce inevitable loss of lives, immediate intensifying chemotherapy with well-timed supportive therapy for jaundice should be warranted.[9,10] Ascani et al. described a woman who had undergone a right hepatectomy for stenosis of extrahepatic bile ducts mimicking the presentation of Klatskin tumor.[9] A diagnosis of granulocytic sarcoma and bone marrow biopsy showing acute myelomonocytic leukemia could not retard her fatal progress. Rajesh et al. reported a man with acute myeloid leukemia presenting as obstructive jaundice.[10] Biliary drainage failed to improve malignant stricture of the common bile duct before definitive chemotherapy could be instituted. Obstructive jaundice arising from merely leukemic infiltrate of the bile ducts has been rarely reported to show a favorable response to systemic therapy and mandate further local intervention.[10,11] Goor et al reported a patient who presented with obstructive jaundice and a rapid rise in bilirubin level.[11] Prompt chemotherapy without temporary drainage procedures resolved presumptive biliary leukemic infiltration. Mano et al., in the report on

a patient who presented with jaundice in whom computed tomography disclosed thickening of the common bile duct, noted possible institution of chemotherapy after placement of endoscopic nasobiliary drainage.[12] In our patient, immediate administration of chemotherapy resulted in a gradual increment in bilirubin level and rapid vanishing of the blast cells from the peripheral blood. Even though the jaundice may reflect that therapy induced hepatocellular damage, gradual decline of the aminotransferase level and finding of narrowing of the common hepatic bile duct in magnetic resonance cholangiopancreatography are consistent with biliary leukemic infiltrate resulting in bile duct wall thickening. Endoscopic nasobiliary drainage relieved jaundice and induction chemotherapy with full doses could be administrated.

In summary, we present a rare case report showing biliary leukemic infiltrate giving rise to obstructive jaundice associated with acute myeloid leukemia and found that endoscopic biliary drainage combined with chemotherapy might prove to be a feasible therapeutic strategy for leukemic bile duct obstruction.

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