Cholecystitis Caused by Infiltration of Immature Myeloid Cells: A Case Report

Tetsuya Shimizu¹, Takashi Tajiri¹, Koho Akimaru¹, Yasuo Arima¹, Shigeki Yokomuro¹, Hiroshi Yoshida¹, Yasuhiro Mamada¹, Nobuhiko Taniai¹, Yoshiaki Mizuguchi¹, Yutaka Kawahigashi¹ and Zenya Naito²

¹Graduate School of Medicine, Surgery for Organ Function and Biology Regulation, Nippon Medical School ²Department of Pathology, Nippon Medical School

Abstract

A 59-year-old man with myelodysplastic syndrome who was hospitalized for evaluation of fever and generalized fatigue had elevated levels of C-reactive protein and pancytopenia. A search for a site of infection and empiric treatment with antibiotics were unsuccessful. Over 5 to 6 weeks right upper quadrant pain and rebound tenderness developed. Sonographic Murphy's sign was present. Computed tomography showed thickening of the gallbladder wall, and repeated ultrasonography demonstrated changes consistent with cholecystitis. Open cholecystectomy was performed as an emergency procedure. Macroscopically the resected gallbladder showed an edematous and thickened wall. Histopathologic examination revealed transmural infiltration by atypical mononuclear cells with distinct nuclei. The cells showed immunohistochemical staining for CD15, indicating myeloid lineage. By 10 days after surgery, counts of leukocytes and leukoblasts had markedly increased, reaching 36,700/µL and 76.0%, respectively. The blast crisis was thought to indicate progression from myelodysplastic syndrome to leukemia. The patient died of progressive disease 12 days after surgery. We have described a rare case of acute cholecystitis caused by infiltration of immature myeloid cells to the gallbladder. An acute abdomen complicating hematologic disorders is life-threatening and requires prompt and appropriate treatment.

(J Nippon Med Sch 2006; 73: 97–100)

Key words: cholecystitis, myelodysplastic syndrome, leukemic transformation

Introduction

The clinical course of patients with hematologic disorders is often complicated by events presenting as an acute abdomen¹. Although the gastrointestinal tract may be involved by hematological diseases,

such as leukemia, blast cell infiltration of the gallbladder is extremely rare²³.

We describe a patient with acute cholecystitis caused by infiltration of immature myloid lineage cells to the gallbladder wall.

Correspondence to Tetsuya Shimizu, MD, Graduate School of Medicine, Surgery for Organ Function and Biology Regulation, Nippon Medical School, 1–1–5 Sendagi, Bunkyo-ku, Tokyo 113–8603, Japan E-mail: tetsuya@nms.ac.jp

Journal Website (http://www.nms.ac.jp/jnms/)



Fig. 1 Abdominal CT demonstrated a diffusely thickened gallbladder wall and a calcified 2.5-cm gallstone.

Case Report

A 59-year-old man with myelodysplastic syndrome (MDS) was admitted to the internal medicine service at our hospital for evaluation of pyrexia and generalized fatigue. Initial laboratory tests showed elevation of C-reactive protein (10.18 mg/dl) and pancytopenia (leukocyte count, 2,900 / μl with 14.0% blasts, 0.0% neutrophils, 19.5% lymphocytes, and 18.0% monocytes; red blood cell count, $167 \times 10^4 / \mu l$ with a hemoglobin value of 5.4 g/dl and a hematocrit of 15.3%, and a platelet count of 36,000 / μ l). Pyrexia and elevated levels of C-reactive protein indicated infection, but both a search for a site of infection and treatment with antibiotics were unsuccessful. Although C-reactive protein decreased transiently with broad-spectrum antibiotic treatment, the fever persisted. Pancytopenia was treated with transfusions of red blood cells and platelets, and the infection was treated with injections of granulocyte colony-stimulating factor (G-CSF).

On the 36th hospital day, the patient complained of mild pain in the right upper quadrant. This pain gradually worsened until the 45th hospital day, when guarding and rebound tenderness developed over the gallbladder and the patient was referred to the department of surgery. Physical examination then disclosed palpable enlargement of the liver and tenderness over the gallbladder. Murphy's sign was present.

Ultrasonography showed gallbladder wall thickening and a hyperechoic 2-cm gallstone.



Fig. 2 Macroscopically the resected gallbladder presented an edematous and thickened wall and contained two 2.5-cm gallstones.

Gallbladder distention, intrahepatic bile duct dilation, and fluid accumulation around the gallbladder were not seen. Severe pain was elicited by pressure of the transducer over the gallbladder.

Abdominal computed tomography (CT) demonstrated a diffusely thickened gallbladder wall, a calcified 2.5-cm gallstone (Fig. 1), and marked hepatosplenomegaly.

Percutanous biliary drainage could not be performed because neither the gallbladder nor the intrahepatic biliary tree was dilated. Open cholecystectomy was performed as an emergency procedure on the 45th hospital day. Marked hepatomegaly and edema of the gallbladder were seen, but accompanying inflammatory findings, such as adhesion and distension of the gallbladder, were not prominent.

Macroscopically the resected gallbladder showed an edematous and thickened wall and contained two 2). 2.5-cm gallstones (Fig. Histopathologic examination of this specimen at low magnification showed intramural infiltration of atypical mononuclear cells (Fig. 3A). At high magnification this area showed atypical blastoid cells with distinct nuclei (Fig. 3B). The cells demonstrated immunohistochemical staining for CD15, suggesting myeloid lineage (Fig. 3C). These immature myeloid cells presumably were the cause of cholecystitis. Cultures of bile and blood obtained intraoperatively were negative for bacteria, because broad-spectrum antibiotic treatment had continued.



Fig. 3 A: Histopathologic examination of this specimen at low magnification showed intramural infiltration of atypical mononuclear cells (hematoxylin-eosin, ×50).
B: Examination of this area at high magnification revealed atypical blastoid cells with distinct nuclei (hematoxylineosin, ×400).
C: The cells demonstrated immunohistochemical staining for CD15, suggesting myeloid lineage cells. (×200)

The persistent fever did not resolve after surgery. On day 10 after surgery, counts of leukocytes and blasts were greatly increased, reaching $36,700/\mu l$



Fig. 4 Perioperative clinical course. WBC, white blood cell counts; POD, post operative day

and 76.0%, respectively (**Fig. 4**), while erythrocytopenia and thrombocytopenia worsened. The blast crisis was thought to indicate progression from MDS to leukemia. Myelosuppressive chemotherapy failed to affect the clinical condition or laboratory abnormalities.

Severe pneumonia developed, with subsequent disseminated intravascular coagulopathy and multiple organ failure. The patient died 12 days after surgery.

Discussion

Acute abdominal complications are not rare in patients with hematologic disorders. Hawkins et al. have found acute abdominal disorders in 5.3% of 412 patients with acute leukemia⁴. Blast cell infiltration of the gastrointestinal tract can occur, but gallbladder infiltration is reportedly rare. Several case reports describe relapse of acute lymphoblastic leukemia presenting as leukemic infiltration of the gallbladder wall^{2,35}. Recently, de novo acute leukemia was reported to present as symptomatic gallbladder involvement⁶. Cholecystitis related to chemotherapy is reported to occur in a significant proportion of patients with acute leukemia. Gorschluter et al. have reported cholecystitis in 4.8% of patients with leukemia undergoing chemotherapy¹. Acalculous cholecystitis may be associated with physiologic and pathophysiologic stresses, such as major surgery, multiple injuries, burns, sepsis, childbirth, and blast cell infiltration⁵⁷. Although stones were present in this case, blast cell infiltration may have been the main cause of cholecystitis, considering the severe immature myeloid cell infiltration seen at autopsy in

other organs, such as liver, spleen, lung, and kidney.

Patients with MDS commonly have refractory anemia accompanied by various degrees of granulocytepenia and thrombocytopenia. The G-CSF used in this case is effective for increasing the granulocyte count and for treating infections⁸⁻¹⁰, but MDS includes potentially malignant bone marrow disorders¹¹, and G-CSF might provoke progression to leukemia. The prognosis of MDS is variable and depends on the presence of infection and the progression of leukemia¹².

Abdominal complications in patients with hematologic disorders can be life-threatening. A report from the 1970s indicated that without surgery, intrabdominal complications in patients with leukemia are nearly always fatal¹³. Emergency surgery when patients with leukemia present with an acute abdomen is also associated with high reported mortality rates of 29%¹⁴ and 17%¹⁵. Vaughn et al have found all deaths after surgery to have resulted from uncontrolled sepsis¹⁴. Because patients with hematologic disorders are severely immunocompromised, treatment of infection with intensive antibiotic therapy is extremely important after surgery. Although the timing and indications for surgery in these patients remain controverial, Chirletti et al. have advocated prompt surgical treatment in the presence of an acute abdomen and have suggested that appropriate early surgery contributes to general recovery; the operative mortality rate in their patients with hematologic disorders was 5.5%¹⁶. If a patient's general condition does not permit immediate surgery, intensive preoperative care is required to prepare the patient for surgery.

We have described a rare case of acute cholecystitis in a patient with MDS. An acute abdomen complicating hematologic disorders is lifethreatening and requires prompt, appropriate treatment.

References

1. Gorschluter M, Marklein G, Hofling K, et al.: Abdominal infections in patients with acute leukaemia: a prospective study applying ultrasonography and microbiology. Br J Haematol 2002; 117: 351–358.

- Hurley R, Weisdorf DJ, Jessurun J, Vercellotti GM, Miller WJ: Relapse of acute leukemia presenting as acute cholecystitis following bone marrow transplantation. Bone Marrow Transplant 1992; 10: 387–389.
- Finlay DE, Mitchell SL, Letourneau JG, Longley DG: Leukemic infiltration of the gallbladder wall mimicking acute cholecystitis. AJR Am J Roentgenol 1993; 160: 63–64.
- Hawkins JA, Mower WR, Nelson EW: Acute abdominal conditions in patients with leukemia. Am J Surg 1985; 150: 739–742.
- Buyukasik Y, Kosar A, Demiroglu H, Altinok G, Ozcebe OI, Dundar S: Acalculous acute cholecystitis in leukemia. J Clin Gastroenterol 1998; 27: 146–148.
- Bloom SH, Coad JE, Greeno EW, Ashrani AA, Hammerschmidt DE: Cholecystitis as the presenting manifestation of acute myeloid leukemia: report of a case. Am J Hematol 2002; 70: 254–256.
- Pitkaranta P, Haapiainen R, Taavitsainen M, Elonen E: Acalculous cholecystitis after bone marrow transplantation in adults with acute leukaemia. Case report. Eur J Surg 1991; 157: 361–364.
- 8. Yamagishi T, Fuse K, Saito T, et al.: Successful coronary artery bypass grafting for a patient with myelodysplastic syndrome: report of a case. Surg Today 1996; 26: 740–743.
- Yamamoto K, Maruyama Y, Namura O, Hayashi J, Koyama S: Mycotic abdominal aortic aneurysm associated with myelodysplastic syndrome (MDS): report of a case. Surg Today 1998; 28: 430–432.
- Miyagi Y, Yamauchi S, Suzuki S, et al.: Investigation of coronary artery bypass grafting for a patient with myelodysplastic syndrome. Ann Thorac Cardiovasc Surg 2001; 7: 250–253.
- 11. Steensma DP, Tefferi A: The myelodysplastic syndrome(s): a perspective and review highlighting current controversies. Leuk Res 2003; 27: 95–120.
- Sanz GF, Sanz MA: Prognostic factors in myelodysplastic syndromes. Leuk Res 1992; 16: 77– 86.
- Bjornsson S, Yates JW, Mittelman A, Holland JF: Major surgery in acute leukemia. Cancer 1974; 34: 1272–1275.
- Vaughn EA, Key CR, Sterling WA Jr: Intraabdominal operations in patients with leukemia. Am J Surg 1988; 156: 51–53.
- Villar HV, Warneke JA, Peck MD, Durie B, Bjelland JC, Hunter TB: Role of surgical treatment in the management of complications of the gastrointestinal tract in patients with leukemia. Surg Gynecol Obstet 1987; 165: 217–222.
- 16. Chirletti P, Barillari P, Sammartino P, et al.: The surgical choice in neutropenic patients with hematological disorders and acute abdominal complications. Leuk Lymphoma 1993; 9: 237–241.

(Received, December 13, 2005) (Accepted, February 22, 2006)