Pediatrics and Neonatology (2014) xx, 1–4

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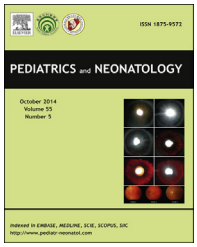

CASE REPORT

Nonocclusive Mesenteric Ischemia after Chemotherapy in an Adolescent Patient with a History of Three Allogeneic Hematopoietic Stem Cell Transplantations for Acute Lymphoblastic Leukemia

Koichi Hirabayashi [a,*], Mitsuho Takatsuki [a], Mitsuo Motobayashi [a], Takashi Kurata [a], Shoji Saito [a], Tomonari Shigemura [a], Yozo Nakazawa [a], Kazuo Sakashita [a], Satoshi Ishizone [b], Hiroyoshi Ota [c], Kenichi Koike [a]

[a] *Department of Pediatrics, Shinshu University School of Medicine, Matsumoto, Japan*
[b] *First Department of Surgery, Shinshu University School of Medicine, Matsumoto, Japan*
[c] *Department of Biomedical Sciences, School of Health Sciences, Shinshu University School of Medicine, Matsumoto, Japan*

Received Feb 10, 2014; received in revised form Jun 13, 2014; accepted Jul 28, 2014

Key Words
acute lymphoblastic leukemia;
adolescent;
allogeneic hematopoietic stem cell transplantation;
chemotherapy;
nonocclusive mesenteric ischemia

Nonocclusive mesenteric ischemia (NOMI) is induced by intestinal vasospasm without thromboembolic occlusion and is associated with high morbidity and mortality. The estimated overall incidence of autopsy-verified fatal NOMI is 2.0 cases/100,000 person-years; however, no pediatric or adolescent cases have yet been reported. An 18-year-old female was diagnosed with B-cell precursor acute lymphoblastic leukemia at the age of 10 years. Our patient received three allogeneic hematopoietic stem cell transplantations but experienced hematological relapse after each. She received combination therapy of prednisolone, L-asparaginase, vincristine, and bortezomib after the third relapse. On Day 16 after the initiation of chemotherapy, she developed NOMI; therefore, we performed a right-sided hemicolectomy on Day 27. Nonocclusive mesenteric ischemia should be considered during the differential diagnosis of intestinal complications after chemotherapy, even in pediatric and adolescent patients.

* Corresponding author. Department of Pediatrics, Shinshu University School of Medicine, 3-1-1, Asahi, Matsumoto, 390-8621, Japan.
E-mail address: hirarinkoichi@gmail.com (K. Hirabayashi).

http://dx.doi.org/10.1016/j.pedneo.2014.07.008

Please cite this article in press as: Hirabayashi K, et al., Nonocclusive Mesenteric Ischemia after Chemotherapy in an Adolescent Patient with a History of Three Allogeneic Hematopoietic Stem Cell Transplantations for Acute Lymphoblastic Leukemia, Pediatrics and Neonatology (2014), http://dx.doi.org/10.1016/j.pedneo.2014.07.008

1. Introduction

Nonocclusive mesenteric ischemia (NOMI) is induced by intestinal vasospasm without thromboembolic occlusion. The typical patient with NOMI is critically ill with severe cardiac disease or sepsis while undergoing inotropic support.[1,2] Thus, NOMI is associated with high morbidity and mortality rates.[3] The estimated overall incidence of autopsy-verified fatal NOMI is 2.0 cases/100,000 person-years,[1] although no pediatric or adolescent cases have yet been reported. In this paper, we report a case of NOMI occurring in an adolescent girl after being administered chemotherapy for a third hematological relapse of acute lymphoblastic leukemia (ALL).

2. Case report

An 18-year-old woman had been diagnosed with B-cell precursor ALL in March 2005 at the age of 10 years. Because of marked leukocytosis (191×10^9/L) and a poor response to prednisolone monotherapy for 7 days, we selected the L04-16 protocol of the Tokyo Children's Cancer Study Group to estimate the risk associated with allogeneic hematopoietic stem cell transplantation (allo-HSCT). In August 2005, she achieved complete remission after induction therapy and then received an allogeneic bone marrow transplant from her human leukocyte antigen (HLA)-matched mother; she had been administered a preparative regimen comprising 8-Gy of total body irradiation, cyclophosphamide at 120 mg/kg, and fludarabine at 150 mg/m^2. In July 2006, she experienced her first relapse. Chemotherapy and donor lymphocyte infusion were administered, but the patient failed to achieve complete remission. In July 2007, she received an allogeneic peripheral blood stem cell transplant from her mother, after conditioning with cytarabine at 10 g/m^2, idarubicin at 36 mg/m^2, cyclophosphamide at 120 mg/kg, and fludarabine at 150 mg/m^2. However, she experienced a second relapse in October 2008. In December 2008, she received a third allo-HSCT a transplant from a sibling with one HLA allele mismatch during the active disease, after she had been conditioned with busulfan at 12.8 mg/kg, cyclophosphamide at 120 mg/kg, and fludarabine at 150 mg/m^2. In September 2009, she developed type 2 diabetes mellitus. After her third relapse in August 2012, she received a combination therapy of prednisolone, L-asparaginase, vincristine, and bortezomib, beginning on September 19, 2012 (Day 1, Figure 1). Physical examination and laboratory findings—which included blood, urine, echocardiography, thoracoabdominal contrast-enhanced computed tomography (CT), and brain magnetic resonance imaging—were normal before chemotherapy with the exception of glucose intolerance and abnormal bone marrow examination results. She received a continuous infusion of insulin after starting chemotherapy. During chemotherapy, only mild neutropenia (500–1000/μL) was present and her general status was relatively good. After the initiation of chemotherapy, the blast count in peripheral blood decreased and disappeared by Day 16. Because of the continuous drip infusion before beginning chemotherapy, she did not develop severe dehydration. However, she often required furosemide to maintain sufficient urine flow during chemotherapy. She complained of severe abdominal pain on Day 16. Contrast-enhanced CT showed thickening of the bowel wall, decreased bowel wall enhancement by contrast media, an elevated CT value around the ascending colon, and accumulation of ascitic fluid (Figure 2A). No obvious thromboembolic occlusion of the mesenteric arteries was evident. An exploratory laparotomy revealed extreme edema of the bowel wall from the ileum to the ascending colon. Pulsation of the ileocolic, right colic, and middle colic arteries was clearly palpable. No bacterial pathogens were detected by cultures of feces and ascitic fluid. Because no macroscopically abnormal intestinal lesions were detected, we decided only to insert an indwelling drainage catheter. However, because her abdominal pain persisted, we again performed abdominal contrast-enhanced CT on Day 27, which revealed thinning of the large bowel without enhancement of the mucosa (Figure 2B). These findings strongly suggested necrosis of the ascending colon; therefore, we performed a right-sided hemicolectomy. Surgical findings confirmed necrosis from the ileum to the ascending colon (Figure 3A). Blood flow within the ileocolic artery that supplied the necrotic colon was confirmed. The colonic mucosa adjacent to the necrotic lesions was characterized by decreased crypts with reduced goblet cells. Furthermore, bleeding to the lamina propria, congestion, edema, and ectasia of the submucosa were present. These findings indicated chronic ischemia of the colon (Figure 3B). There were no findings of vascular lesions, leukemia, arteriosclerosis, or graft-versus-host disease (GVHD). We diagnosed NOMI because there were no findings of vascular lesions, invasion of leukemia cells, or GVHD by contrast-enhanced CT, pathological examination, or surgical findings. No further abdominal complications occurred after restarting chemotherapy. In April 2013, she received unrelated cord blood transplantation. In June 2013, she died of invasive aspergillosis.

3. Discussion

In this paper, we reported a case of an adolescent patient who developed NOMI after chemotherapy for a third

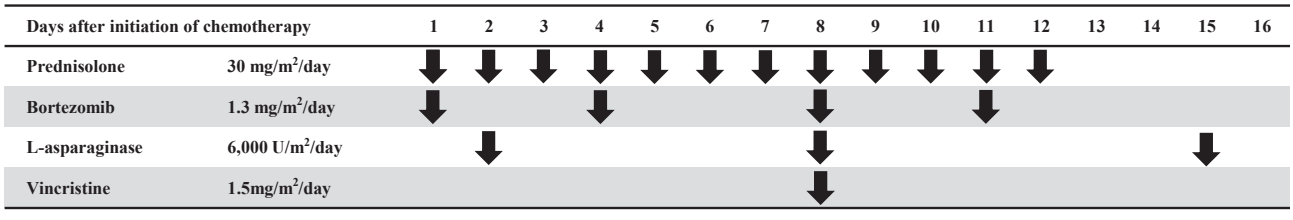

Figure 1 Chemotherapy regimen after the third hematological relapse.

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