Pancreatic Hyperamylasemia and Hyperlipasemia in Association with Cytomegalovirus Infection following Unrelated Cord Blood Transplantation for Acute Myelogenous Leukemia

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Abstract

Cytomegalovirus (CMV)-associated pancreatitis is rare after allogeneic hematopoietic stem cell transplantation (SCT). We describe a patient who developed pancreatic hyperamylasemia and hyperlipasemia in association with CMV infection after cord blood transplantation (CBT). A 31-year-old man with acute myelogenous leukemia underwent CBT. A neutrophil count consistently greater than 500/μL was achieved on day +21. Positive results for CMV antigenemia on days +35 and +67 prompted 2 courses of preemptive therapy with ganciclovir or foscarnet. The CMV antigenemia value again became positive on day +134. On day +141, serum amylase and lipase activities markedly increased to 1221 IU/L and 894 IU/L, respectively. The patient had no abdominal symptoms. Ultrasonography and computed tomography results showed no abnormalities of the pancreas. A diagnosis of possible pancreatitis was made. After the initiation of foscarnet therapy, the CMV antigenemia results soon became negative, and serum amylase and lipase activities returned to normal. Therefore, CMV infection was considered to play a major role in the development of pancreatic hyperamylasemia and hyperlipasemia in our patient. The present report indicates that CMV infection should be included in the differential diagnosis for patients with pancreatic hyperamylasemia after SCT.

Key words: Hyperamylasemia; Pancreatitis; AML; Cord blood; Transplantation

1. Introduction

Cytomegalovirus (CMV) infection is one of the major complications after allogeneic hematopoietic stem cell transplantation (SCT) [1]. Interstitial pneumonia is the most common clinical presentation of CMV disease. Some patients develop gastroenteritis, hepatitis, and encephalitis. In addition, CMV can cause pancreatitis. There have been several reports of CMV-associated pancreatitis in patients infected with human immunodeficiency virus 1 [2,3]. Rarely, CMV has caused pancreatitis in patients who have undergone kidney, pancreas, or heart transplantation [4-6]. CMV-associated pancreatitis is rare after SCT. We describe a patient who developed pancreatic hyperamylasemia and hyperlipasemia in association with CMV infection after cord blood transplantation (CBT).

2. Case Report

A 31-year-old man with acute myelogenous leukemia in the second complete remission underwent CBT from an unrelated donor in October 2003. The cord blood (CB) donor had 2 mismatches in the HLA-A and HLA-B loci. The number of nucleated cells in the CB unit before freezing was 2.11 x 10^7/kg. The conditioning regimen included 12 Gy total body irradiation, 120 mg/kg cyclophosphamide, and 12 g/m² cytarabine with concomitant administration of granulocyte colony-stimulating factor (G-CSF) [7]. Graft-versus-host
Pancreatic Hyperamylasemia after CBT

Figure 1. Clinical course of the patient. CBT indicates cord blood transplantation; MTX, methotrexate; PSL, prednisolone; CSP, cyclosporine; GCV, ganciclovir; PFA, foscarnet; CMV-Ag, cytomegalovirus antigenemia; AMY, amylase.

disease (GVHD) prophylaxis consisted of cyclosporine and methotrexate. To facilitate myeloid engraftment, we administered 5 μg/kg G-CSF from day +1. A neutrophil count consistently greater than 500/μL was achieved on day +21. Grade II acute GVHD involving the skin occurred from day +23 (Figure 1). On day +32, the patient developed a cough and dyspnea. A chest computed tomography scan showed diffuse infiltrates in the lungs. CMV DNA was not detected in a bronchoalveolar lavage fluid specimen by a quantitative real-time polymerase chain reaction method. Prednisolone therapy at 1 mg/kg per day (60 mg/day) initiated on day +34 led to remarkable improvement of the lung lesions. Because of renal dysfunction, cyclosporine treatment was discontinued on day +34.

On day +35, the CMV antigenemia test result became positive with a value of 7 per 300,000 cells (Figure 1). Therefore, ganciclovir was administered at 10 mg/kg per day. Because the patient’s renal function improved, cyclosporine was readministered on day +47. From day +50, the dose of prednisolone was gradually reduced. The CMV antigenemia result became negative on day +53, and ganciclovir therapy was discontinued on day +67. On day +77, CMV antigenemia again occurred with 1 positive cell detected, and ganciclovir therapy was reinitiated. On day +81, mild diarrhea occurred. A histologic examination of the large intestine revealed the presence of GVHD. Changing cyclosporine administration on day +85 from 75 mg/day orally to 60 mg/day intravenously led to the resolution of the diarrhea on day +88. Despite ganciclovir therapy, the CMV antigenemia value increased to 16 cells on day +98. Therefore, foscarnet (120 mg/kg per day) was administered from day +99. The CMV antigenemia result became negative again on day +102. Foscarnet therapy was discontinued on day +110. Serum immunoglobulin levels on day +116 were as follows: immunoglobulin G (IgG), 744 mg/dL (normal range, 800-1800 mg/dL); IgA, 55 mg/dL (normal range, 90-450 mg/dL); IgM, 42 mg/dL (normal range, 60-230 mg/dL). The patient was followed up as an outpatient from day +121. No apparent GVHD was observed. The doses of oral cyclosporine (50 mg/day) and prednisolone (7.5 mg/day) were not changed after hospital discharge.

On day +134, the CMV antigenemia value again increased, to 31 cells, and increased further to 51 cells on day +141 (Figure 1). In addition, the activity of serum amylase markedly increased from 164 IU/L (normal range, 30-140 IU/L) on day +134 to 1221 IU/L on day +141. An isozyme analysis showed that most of the amylase in the serum was of the pancreas type. The activity of serum lipase also markedly increased to 894 IU/L (normal range, 11.59 IU/L); however, the patient had no obvious symptoms, such as abdominal pain or fever. Abdominal ultrasonography and computed tomography evaluations showed no abnormalities of the liver, gall bladder, bile ducts, or pancreas. Foscarnet (120 mg/kg per day) was administered for the CMV infection from day +146. For the pancreatic hyperamylasemia and hyperlipasemia, no other medications, such as protease inhibitors, were administered. On day +151, the CMV antigenemia result became negative, and serum amylase and lipase activities decreased to 792 IU/L and 548 IU/L, respectively. Because serum amylase and lipase activities subsequently decreased further to 345 IU/L and 211 IU/L, respectively, foscarnet therapy was discontinued on day +167. Serum amylase and lipase activities returned to normal from day +176. At the last follow-up evaluation at 30 months after CBT, the patient was well without disease progression.

3. Discussion

We have described a patient who developed pancreatic hyperamylasemia and hyperlipasemia in association with CMV infection after CBT. Acute pancreatitis is clinically diagnosed on the basis of clinical features, elevated pancreatic amylase activities, and radiographic findings [8]. Despite the markedly high activities of serum amylase and lipase, our patient lacked abdominal symptoms and radiographic changes of the pancreas. According to the criteria, the diagnosis was not definite or probable but possible pancreatitis.

Various factors other than CMV infection may contribute to the development of pancreatic hyperamylasemia or pancreatitis after SCT. These include GVHD, medications, other viral infections, biliary stones, and parenteral nutrition [9]. Nieto et al. [10] described a patient who developed tacrolimus-caused acute pancreatitis following CBT. In our patient, GVHD was inactive, and the dosage of immunosuppressive drugs was not changed at the onset of pancreatic hyperamylasemia. In addition, pancreatic hyperamylasemia, which occurred with increasing values of CMV antigenemia, soon resolved after foscarnet therapy. Therefore, CMV infection was considered to play the primary role in the development of pancreatic hyperamylasemia in our patient. Early antiviral therapy might have been beneficial for preventing the progression to obvious acute pancreatitis in our patient.

Salomone et al. [11] reported that acute pancreatitis occurred in 2 (8%) of 26 patients after bone marrow transplantation (BMT). The 2 patients had severe GVHD of the liver at the onset of pancreatitis. Concomitant CMV infection was observed in one of these patients. The authors...