

## Case Report

# Acute pancreatitis developed after allogeneic hematopoietic stem cell transplantation: a case report and literature review

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**Abstract:** The goal of this study was to reveal a rare complication of allogeneic hematopoietic stem cell transplantation (allo-HSCT). Herein, a case is presented of a 16-year-old female patient, who developed acute pancreatitis after allo-HSCT, presenting with severe abdominal pain, nausea, and vomiting. Laboratory evaluation showed marked elevated serum amylase and computed tomography scan confirmed the diagnosis of acute pancreatitis. To observe the patient's clinical characteristics, potential etiology for this patient was analyzed. Some specific medicines might be the cause of acute pancreatitis after transplantation, such as cyclosporin A and tigecycline in this case. Patients suspected to have pancreatitis should consider discontinuing the administration of tigecycline and cyclosporin A and at the same time, monitor the concentration of patients' blood glucose, blood calcium, amylase and their abdominal pain symptoms. An awareness of this circumstance is crucial for the hematologic transplantation doctors and the approach to prevent acute pancreatitis is also needed, as well as exploring the pathogenic mechanism of this complication.

**Keywords:** Acute pancreatitis, allogeneic stem cell transplantation

### Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains the most promising curative option for variety of hematologic disorders. [1, 2] There could be a range of complications after transplantation, such as graft failure, infection, bleeding, and graft-versus-host disease (GVHD). GVHD is still the major complication after allo-HSCT, which can result in liver damage to the skin, gastrointestinal tract, unusually the bone marrow, thymus, and lungs, increasing the morbidity and mortality of allo-HSCT patients. [3-5] However, acute pancreatitis after stem cell transplantation is a very rare complication and few pertinent documents can be numbered.

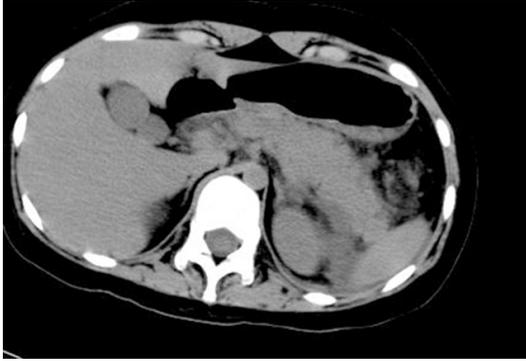
A young patient suffering from acute pancreatitis after allo-HSCT is reported. Also reported are the clinical characteristics, etiology analysis, relevant medicine, treatment and follow up. These data may contribute to better under-

standing and preventing this rare but severe complication after transplant.

### Case report

A 16-year-old Han ethnic female patient, who was diagnosed with acute B lymphoblastic leukemia (ALL-B), achieved continuously remission by multi-chemotherapy treatments for about three years. Three years later, she relapsed and received HLA-identical unrelated donor transplantation. She got hematopoietic reconstruction at 11 days after transplant, and no severe complications were found, including hepatic vein occlusive disease (HVOD), heart failure, engraft syndrome, and GVHD. But at 24 days after transplant, the patient suddenly developed nausea and severe abdominal pain, which was located initially around the umbilicus, accompanied by pressure pain, rebound pain and muscular tension. No cardiovascular disease, gallstones or biliary tract disease were found in her previous history. While laboratory

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**Figure 1.** Image of CT scan for the patient showed acute pancreatitis had occurred. On 24 days after transplantation, the abdominal CT scan showed that the pancreas enlarged accompanied by peripheral exudation and pancreatic swelling. The diagnosis of acute pancreatitis was confirmed (Grade D on the Balthazar score).

examination showed that the serum amylase concentration was 1007.4 IU/L (Normal range, 0-220 IU/L), and abdominal computed tomography (CT) showed that the pancreas was swelling and enlarged, which was surrounded by lots of peripheral exudation (**Figure 1**). The diagnosis of acute pancreatitis was confirmed, and the grading of pancreatic appearance was Grade D according to the computed tomography severity index (CTSI or Balthazar score) [6].

Urgent medical interference was performed for the treatment of acute pancreatitis, including abrosia, anti-infection, anti-acid, protecting gastric mucosa, and inhibiting trypsin secretion, according to the guideline of management of acute pancreatitis. [7-9] In order to exclude the medical causes contributing to the development of acute pancreatitis, concomitant medications were screened cyclosporin A (CsA) and tigacycline were found to have the high possibility to induce acute pancreatitis. The CsA concentration test showed 690.10 ng/ml when urgently investigated (**Figure 2**), and CsA was substituted by rapamycin for anti-GVHD, as well as the tigacycline was discontinued. But the patient's condition became worse and worse due to the reduplicated abdominal hemorrhage and hemorrhagic shock. Fortunately, she was gradually stabilized after timely anti-shock and pancreas protection treatment.

After puncture drainage of the pseudocyst around the pancreas, the drainage liquid decreased little by little and the drainage tube

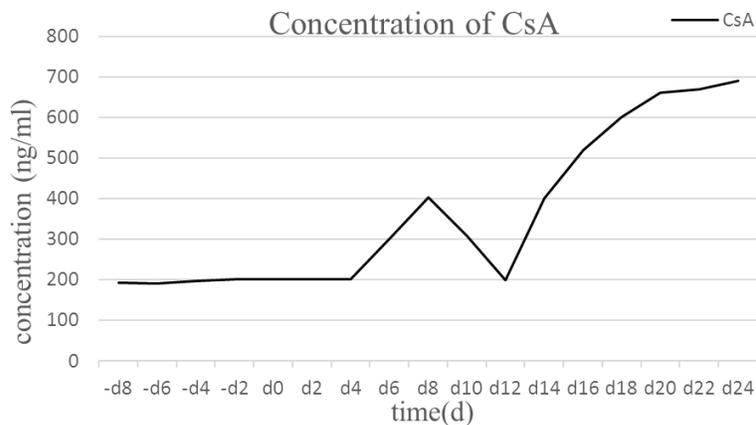
was removed at last, and the amylase concentration returned to the normal range accordingly. The patient was discharged from the hospital after improvement of symptoms and performance status. As the last followed up time, the disease free survival (DFS) was 13 months after transplant.

### Discussion

Acute pancreatitis is a common disease with high mortality and complex etiology, which is an inflammation of the glandular parenchyma of the retroperitoneal organ that leads to injury with or without subsequent destruction of the pancreatic acini. This inflammatory process can either result in a self-limited disease or involve life-threatening multi-organ complications. [10] However, post-transplantation pancreatitis has not been heavily studied, so it is crucial for both clinicians and research fellows to have a better understanding of the acute pancreatitis developed after allo-HSCT.

The relative reports of post-transplantation pancreatitis were first described in 1990, in which the incidence of acute pancreatitis in 202 children after transplantation was 3.5%. [11] It can be seen that the incidence was out of our imagination, but the relevant cases were not as much as reported. Then a retrospective study of Japan analyzed 57 cases of transplantation in 2002, enrolled from 1984 to 2000, with the conclusion that pancreatitis after allo-HSCT was not very rare and most of them had no corresponding clinical manifestations. Some were associated with severe GVHD, and some were attributed to viral infection. [12] Fernandes reported a case of spontaneous hepatitis and pancreatitis after transplantation. The results of laboratory examination indicated that hepatase, lipase and amylase were increased, and acute pancreatitis was diagnosed by ultrasonography. The patient's symptoms were improved significantly with immunosuppressive drugs. [13] DE Singly B reported a case of acute myelocytic leukemia (AML) with acute pancreatitis after allo-HSCT, who had no diarrhea, but the biopsy suggested pancreas GVHD and the symptoms were relieved after the use of corticosteroid. [14] Milica Stefanovic' analyzed the cause of acute pancreatitis as a complication of childhood cancer treatment; the result was multiple drugs or virus infection that could

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**Figure 2.** The vertical axis represented the concentration of CsA in the valley point. The horizontal axis represented the time from the day receiving allo-HSCT. The mark point was 24 days after transplantation when the patient developed acute pancreatitis. The concentration of CsA increased dramatically at the day of acute pancreatitis, far beyond the optimum serum drug level.

cause post-transplantation pancreatitis, such as immunosuppressants (CsA, tacrolimus), antiviral drugs (acyclovir, ganciclovir). Glucocorticoid could also induce post-transplantation pancreatitis, and while in virus infection cytomegalovirus infection might be the most common one. [15] No definitive explanation for the development of acute pancreatitis after transplantation has been documented according to the studies above, but our center speculated that the two main medicines applied might be the potential causes.

Tigecycline, the first of a new class of broad-spectrum antibiotics (the glycylicyclines), has been used for the parenteral treatment of adult patients with complicated intra-abdominal infections (cIAIs). [16] Marot reported two cases of mild tigecycline-induced pancreatitis. Tigecycline was given for soft-tissue infection in both cases. Pancreatic enzymes elevation occurred five to six days after initiation of treatment, and resolved within a week after drug-discontinuation. Diagnosis of mild pancreatitis was confirmed after performing CT scan of the abdomen in both cases. [17] A phase 3 and 4 comparative tigecycline studies of PC McGovern in 2013, which included 3788 subjects treated with tigecycline and 3646 subjects treated with a comparator. They concluded that pancreatitis was uncommon in subjects treated with tigecycline, accounting approximately for 1%. [18] Jinwen Lin reported a patient developed a

donor-derived infection after kidney transplantation, which was treated with tigecycline at the 8th post-transplant day combined with other antibiotics. After 15 days of tigecycline treatment, the patient was observed with recurrent fever and abdominal distension with a rise in pancreatic enzymes. After withdrawal of tigecycline, CT scans showed that exudation around the pancreas were relieved, and blood amylase returned to the normal range in a week. [19] Tigecycline should attract our more attentions, and the symptoms and blood amylase could return to the normal range in a short time (usually

one week) after the discontinuation of the drug. Hence concomitant medications known to cause acute pancreatitis should be cautious when administration of tigecycline.

Cyclosporin A (CsA) is a kind of immunosuppressants, which is widely used to prevent rejections after organ transplants. In 1998, Foitzik T conducted a comparative study in an improved animal model about the effect of different immunosuppressive agents on acute pancreatitis, the results suggested that azathioprine and high doses of CsA aggravate acute pancreatitis, which should be abandoned in case of suspecting post-transplantation pancreatitis. [20] Guo et al. analyzed a patient with AML-M2a who received allogeneic stem cell transplant, with the prophylaxis of GVHD by CsA. Clinical and laboratory signs of acute pancreatitis were found in the patient on day 20 after transplant, and the patient recovered with the reduction of CsA dosage. [21] Hackert T et al. studied the influence of immunosuppressants on graft pancreatitis, and they concluded that CsA was tending to aggravate tissue damage in ischemia reperfusion which might induce acute pancreatitis [22].

In conclusion, herein is described a case of acute pancreatitis after allo-HSCT, presented with vomiting and severe abdominal pain. Additional approach to prevent the post-transplantation pancreatitis is also needed. It is also

important to explore the potential mechanism in the immunologic predisposing factors as well as medicine application, such as CsA, tigecycline, which might increase the risk of acute pancreatitis.

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### Disclosure of conflict of interest

None.

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