

Superselective arterial embolization of the superior mesenteric artery for the treatment of gastrointestinal hemorrhage following allogeneic hematopoietic stem cell transplantation

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Abstract: Superselective arterial embolization is a common therapeutic procedure for cases of visceral hemorrhage. However, until now, it has not been applied in the treatment of gastrointestinal (GI) hemorrhage caused by acute graft-versus-host disease (GVHD) after allogeneic hematopoietic stem cell transplantation. We describe a case presenting with persistent GI bleeding associated with acute GVHD successfully treated by superselective arterial embolization of the superior mesenteric artery with gelatin sponge after noneffective conventional management. This case will help guide hematologists to deal with a similar situation in the future.

Keywords: gastrointestinal bleeding, acute graft-versus-host disease, allo-hematopoietic stem cell transplantation, arterial embolization

Background

Acute graft-versus-host disease (GVHD), the immunologic attack of transplanted donor T lymphocytes against foreign host tissues, is a major complication of allogeneic hematopoietic stem cell transplantation (HSCT). The skin, liver, and gastrointestinal (GI) tract are the main targets of acute GVHD.¹⁻⁴ GI tract involvement is less common compared with that of skin and liver¹ but is recognized as the most severe and difficult to treat, especially GI hemorrhage.² The incidence of GI hemorrhage following bone marrow transplants is approximately 10%,⁵ and its mortality can reach as high as 30%–60% in patients who experience acute GVHD.⁶ Though overt GI bleeding is uncommon, because of the frequent problem of severe thrombocytopenia, when it occurs, GI bleeding requires prolonged hospitalization and often results in mortality.

Routine therapy for GI bleeding is based on intensive supportive treatment, such as transfusion of blood cells, infusion of coagulation factors, and use of hemostatic agents,⁷ but their effect on controlling severe GI hemorrhage is limited. Where these conservative measures have failed, numerous therapeutic approaches, including endoscopy and surgery, have been tried with little success in patients with hematopoietic malignancies. Recently, a new technique named superselective arterial embolization (SAE) has been attempted in our hospital. SAE is a safe and minimally invasive method used as treatment for severe visceral bleeding and may be especially valuable to patients whose initial conservative therapy is ineffective, or after a failed primary endoscopic approach. However, to the best of our knowledge, there are no publications showing that SAE has been applied to treating GI bleeding caused by acute GVHD following HSCT. Herein, we report a case of a patient with severe GI hemorrhage

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after allogeneic HSCT successfully treated by means of SAE of the superior mesenteric artery.

Case presentation

A 51-year-old Chinese female presenting with general weakness and pancytopenia for half a year was admitted to our hospital. A complete blood cell count analysis showed mild anemia, with a hemoglobin level of 87 g/L, white blood cell (WBC) count of $2.35 \times 10^9/L$, and platelet count of $23 \times 10^9/L$. Myelodysplastic syndrome (refractory cytopenia with multilineage dysplasia) was diagnosed by bone marrow examination, and karyotyping revealed 20q-:29.2% (73/250). After being conditioned with fludarabine, busulfan, high-dose cyclophosphamide, and antithymocyte globulin as a preparative regimen, allogeneic peripheral blood stem cell transplantation from her human leukocyte antigen (HLA)-matched sibling was performed. Engraftment was apparent on day 16 after transplantation, with total leukocytes recovering, from less than $0.5 \times 10^9/L$ before transplantation to over $1 \times 10^9/L$. Prophylaxis for GVHD consisted of cyclosporin A, Mycophen, and high-dose dexamethasone. Despite these intensive efforts, by day 30, the patient had developed watery diarrhea, burst oral mucosa, skin rash, and abnormal liver function. Her alanine aminotransferase (ALT) and aspartate aminotransferase (AST) of serum were 301 IU/L and 106 IU/L, respectively, and her serum albumin was only 28 g/L, which was lower than the normal value. These symptoms and laboratory indexes strongly suggested the onset of acute GVHD, so the patient was additionally given supporting treatment, including magnesium isoglycyrrhizinate, omeprazole, berberine, and Smecta[®], to improve liver function, protect the stomach, and control the symptom of diarrhea.

Cytomegalovirus (CMV) infection was diagnosed at day 80 after transplantation, with the level more than 5×10^2 Copies/mL, so the patient was treated with ganciclovir. The patient started GI bleeding at day 90, accompanied with abdominal cramping and bloody diarrhea of total 400 to 500 mL approximately five times per day. Multiple transfusions of red blood cell (RBC) concentrates, platelet, fresh frozen plasma, high-dose prednisolone, broad-spectrum antibiotics, antiviral coverage, and even daily hemostatic agents were utilized. The patient received therapeutic doses of RBC concentrates and platelet transfusions for more than 20 consecutive days after the symptom of bloody diarrhea began. However, despite all these efforts, the bloody diarrhea could not be stopped.

Upper and lower endoscopies were performed, which revealed multiple superficial mucosal lesions of the

duodenum and active oozing of blood from the ileocecal junction (Figure 1), and the biopsy specimen revealed lymphocytic duodenitis, which was consistent with GVHD. The problem ahead of us was controlling the severe GI hemorrhage of a patient with RBC counts less than $3 \times 10^9/L$, hemoglobin level less than 60 g/L, and platelet counts less than $30 \times 10^9/L$, with a safe method. After careful consideration, we made a bold attempt to introduce the technique of SAE for the treatment of this patient.

The procedure was performed in an angiography room under fluoroscopic guidance. Using local anesthetics, a retrograde catheterization of the left femoral artery was carried out in order to perform digital angiography of the aortoiliac sector, by modified Seldinger's technique. Subsequently, selective catheterization of the celiac artery, with a standard angiographic catheter (Cobra 5F), was carried out to localize the bleeding vessels. Then, the catheter was guided into the superior mesenteric artery at the initial segment of the pancreaticoduodenal artery, where digital subtraction angiography (DSA) showed obvious signs of contrast extravasation, which was confirmed as the bleeding site (Figure 2A). A Progreat[®] microcatheter was guided into the bleeding branch, and DSA confirmed the previous finding again; then 700 to 1,000 μm gelatin sponge microparticles were used to occlude the bleeding branch of the pancreaticoduodenal artery until blood flow was ceased. Subsequently, a further angiography was performed to confirm the occlusion of the bleeding branches (Figure 2B). The catheter was removed after verifying that there were no other bleeding sites. Action of the unilateral lower limb was prohibited for over 12 hours after the angiography.

The patient's GI bleeding stopped following the arterial embolotherapy; there was no further bleeding at the site of embolism and also no clinically obvious bowel necrosis. Two days later, a fecal occult blood test was performed, and the result was negative. The counts of RBCs and hemoglobin also increased gradually, while bloody diarrhea and related symptoms had ceased after treatment and had no recurrence. Though GVHD still existed, the GI hemorrhage had been fully controlled.

Discussion

GI bleeding is a significant cause of morbidity and mortality of patients suffering from acute GVHD.⁸ Therapy for GI hemorrhage is usually conservative and is accompanied by supportive care, and surgical intervention is rarely needed and generally avoided given the rebleeding risks of the newly transplanted patients.⁹ After ineffective conservative management,

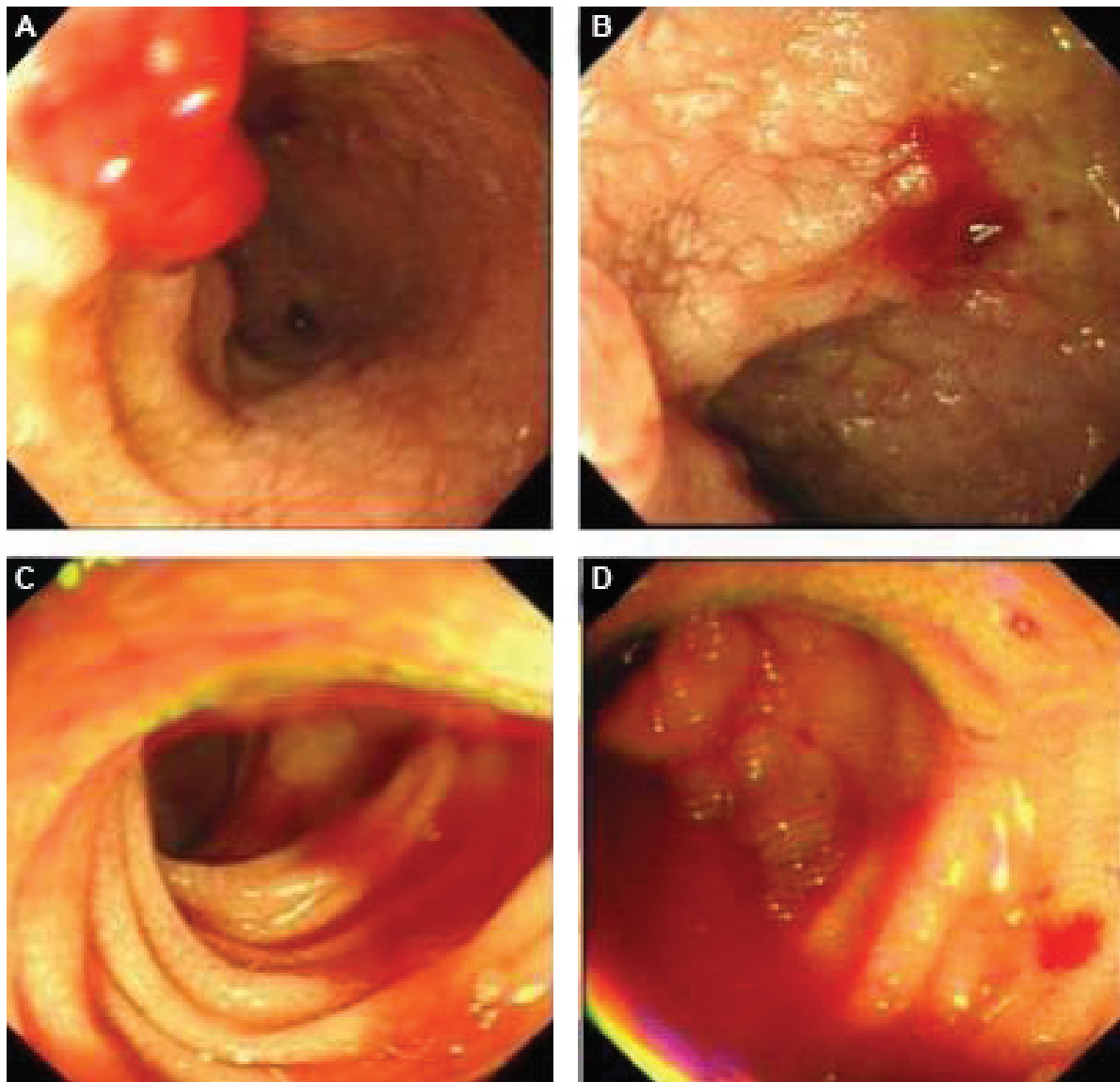


Figure 1 Endoscopic examinations.

Notes: Gastroscopy showed multiple superficial mucosal lesions of duodenum and diffuse mucosal bleeding (A and B), and colonoscopy indicated active oozing of blood from ileocecal junction (C and D).

we decided to utilize SAE as our treatment option. To our knowledge, this is the first reported case of the use of SAE for controlling GI bleeding secondary to acute GVHD.

These days, SAE plays an increasing role in hemorrhage therapy, and it is an accepted approach for intractable hemorrhage, offering the obvious advantage of a lower rate of morbidity.^{10,11} Several studies have confirmed the role of SAE in controlling GI bleeding.^{12–23} Though endoscopy could also be the choice to establish hemostasis,²⁴ this patient's low platelet count (less than $30 \times 10^9/L$) and extensive mucosal hemorrhage were the contraindications for endoscopy treatment. Hence, in this case, endoscopy was only used to initially evaluate and diagnose acute GI GVHD.

The reasons for our choices were as follows: firstly, conventional treatment was ineffective for this patient; secondly, the SAE technique is very mature to stop bleeding, in our hospital, for dealing with hemorrhage – though we knew that potential side effects of SAE might occur, the surgeons performing this procedure were all very experienced, having done more than 100 cases per month in our hospital; thirdly, gelatin sponges have been used extensively as an absorbable hemostatic agent with no toxic or antigenic effects on the body.

This case indicated that SAE offers an opportunity for both diagnostics and therapeutics in the management of acute GVHD complicated by GI hemorrhage. However, we should also be careful, throughout the embolization, to



Figure 2 Mesenteric arterial angiography.

Notes: Initial angiography (A) showed a hemorrhage spot in the initial branch of the superior mesenteric artery (indicated by arrow). Selective arterial embolization with gelatin sponge was performed and final angiography (B) demonstrated no signs of arterial bleeding (indicated by arrow).

prevent potential complications, such as fever, hematoma, buttock ischemia, vascular perforation, and infection. Before choosing the technique of SAE, hospital facilities and surgeons' experience should also be considered. What is more, for a better understanding of the therapeutic and adverse effects of SAE in controlling GI hemorrhage after HSCT, a large sample of clinical trial is needed in the future. After this first attempt, we confidently believe that this case will provide a good example and help guide hematologists to deal with a similar situation in the future.

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Disclosure

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