Nasointestinal tube feeding of platelet-rich plasma cured obscure gastrointestinal bleeding

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To the Editor: Obscure gastrointestinal bleeding (OGIB) has been defined as bleeding of unknown origin that recurs or persists after gastroscopy, colonoscopy, enteroscopy, and radiographic testing, and occurs in approximately 5% of patients presenting with all gastrointestinal hemorrhages.[1] The usual course of treatment includes transfusion support, hemostatic medication, endoscopic therapy, vascular embolization, and surgery. Patients with unstable hemodynamics, persistent bleeding, advanced age, increased complications, chronic renal failure, and severe anemia have a poorer prognosis.[2] Platelet-rich plasma (PRP) contains growth factors and bioactive proteins that promote the healing of cutaneous and mucosal damage.[3] Here, we report a case of incurable OGIB treated with nasointestinal tube feeding of PRP in a renal transplant patient with chronic graft failure.

A 24-year-old man with a history of renal transplantation and long-term oral administration of prednisone, cyclosporine, and mycophen presented with hematemesis and hematochezia for 2 weeks and fever for 9 days. His symptoms were accompanied by paroxysmal abdominal pain, without cough, chest distress, unconsciousness, and so on. He also had bloody stools of 400 to 500 mL/day and hemoglobin level as low as 62 g/L. In the other hospital, he received octreotide, hemostatic drugs, blood transfusion, proton pump inhibitors, and continuous renal replacement therapy (CRRT) by regional citrate anticoagulation; however, the bleeding did not stop. On the second day after he was transferred to our renal intensive care unit, he experienced hematemesis twice and hematochezia once, accompanied by dizziness and heart palpitations. His blood pressure fell to 60/35 mmHg, hemoglobin was 52 g/L, platelets were 82×10^9/L, and fibrino gen was 1.33 g/L. The patient was treated with fasting, CRRT, nasal feeding of norepinephrine with ice saline, thrombin powder, Yunnan Baiyao, intravenous pumping of octreotide, terlipressin, intravenous drip of tranexamic, esomeprazole, and continued blood transfusion. We performed selective mesenteric artery digital subtraction angiography (DSA), and no arterial bleeding was observed in the celiac artery, superior mesenteric artery, or inferior mesenteric artery. Gastroscopy revealed diffuse congestion and erosion in the greater curvature of the stomach and the duodenal mucosa without ulcers [Figure 1A]. Colonoscopy revealed dark red bloody fluid in the terminal ileum [Figure 1B], patchy hyperemia in the mucosa of the right colon [Figure 1C], massive blood clot retention in the left colon, dark red bloody fluid in the rectum, but no obvious active bleeding. During treatment, hemoglobin level decreased to 31 g/L, and dark red blood stools were still intermittent. A second mesenteric artery DSA on the sixth day after admission was normal. The symptoms of hematochezia did not improve. On the 15th day, the enteroscopy showed segmental patchy erosion of the small intestinal mucosa, edema of the small intestinal mucosa, easy bleeding by probe contact, and no obvious active bleeding [Figure 1D]. On the 27th day, DSA of the third mesenteric artery still showed no active bleeding. On the 31st day, capsule endoscopy revealed multiple small foci of erosion, ulcers and bleeding lesions in the empty ileum, and diffuse bleeding in the intestine was considered. The patient experienced repeated episodes of blood pressure drop, heart rate increase, restlessness, and sweating after each massive episode of hematochezia. A total of 147 U of red blood cells (RBCs) was transfused. On the 36th day, the patient began to receive nasointestinal tube feeding with 50 mL of PRP twice daily.

For the preparation of PRP, apheresis platelets from healthy donors were collected from the Jiangsu Province Blood Center, and the patient's blood was cross-matched with donor blood. The platelet count was 800 to 1000 $\times$ 10^9/L and contained approximately 30 mL acid citrate dextrose solution for each unit. The volume of one unit was 250 to 300 mL, and then each unit was divided into 50 mL per portion with a sterile tube welder (BMS,

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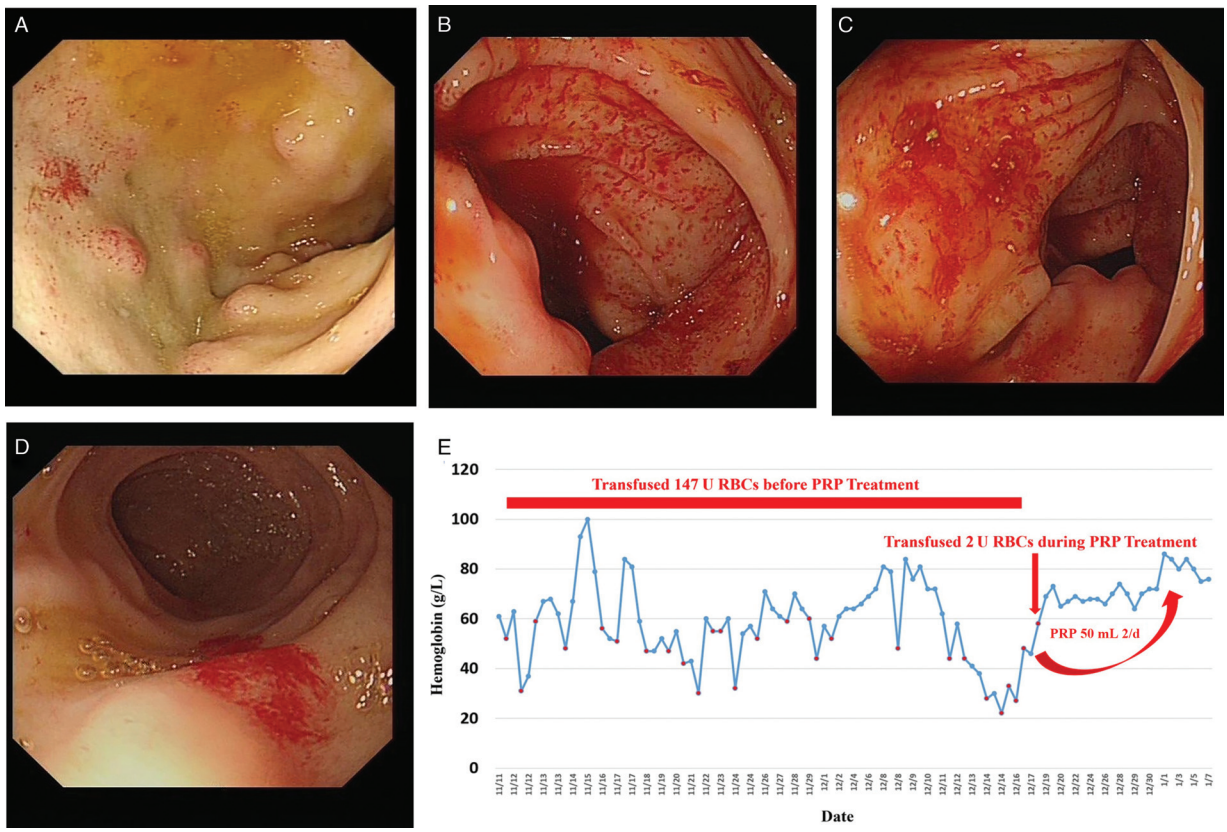

Figure 1: Gastroscopy revealed diffuse congestion and erosion in the greater curvature of the stomach and the duodenal mucosa without ulcers (A). Colonoscopy revealed dark red bloody fluid in the terminal ileum (B), patchy hyperemia in the mucosa of the right colon (C). Enteroscopy showed segmental patchy erosion of the small intestinal mucosa, edema of the small intestinal mucosa (D). Graphic illustration of hemoglobin during the patient's hospitalization. The red points indicate that the patient received a blood transfusion on that day (E). PRP: Platelet-rich plasma; RBC: Red blood cells.

Wuhan, China) and using a four-bag system (Fresenius Kabi, Guangzhou, China). The aliquots of PRP were frozen in a −80°C mechanical freezer in the transfusion medicine department until use. To obtain the platelet gel units, a frozen PRP aliquot was thawed at 37° for 15 min and activated by 10% calcium gluconate 10 mL. After 2 days of PRP treatment, dark green loose stools began to be discharged, and yellow loose stools were discharged after 3 days of PRP treatment. On the 43rd day, the patient gradually began nasointestinal tube feeding with enteral nutrient solution and continued to discharge yellow soft stools, and the fecal occult blood test was negative. PRP treatment was completed on the 51st day after admission, lasting 15 days in total, and only 2 U RBCs were infused during PRP treatment. On the 57th day, he was discharged with hemoglobin of 76 g/L [Figure 1E]. Up to now, the patient has been discharged for 20 months and returned to the local hospital for regular dialysis treatment, and no bloody stools occurred again.

Although various diagnostic methods are available to reveal the cause of OGIB, the origins of bleeding within the small intestine can be identified in only 41% to 75% of patients with OGIB, and therefore remains a therapeutic challenge because of the difficulty in performing prompt and accurate treatments.[1] In this case, the patient had been using steroids for a long time, and there was diffuse intestinal damage. It was difficult to identify active bleeding of the intestinal tract, which made treatment difficult. We performed nasointestinal tube feeding of PRP on the patient in an extreme condition where other treatments failed and intestinal bleeding continued to increase to the point of hypotensive shock. Surprisingly, the intestinal bleeding of the patient quickly improved, with stabilized vital signs, no need for further blood transfusion, gradual recovery of enteral nutrition, and no recurrence of bleeding.

PRP is a plasma product with a higher platelet concentration than whole blood and has been widely used in sports, spine, and musculoskeletal medicine for its potential to augment the repair of tissues with low healing ability. It contains a large number of bioactive factors, such as platelet-derived growth factor, transforming growth factor-β, vascular endothelial growth factor, and epidermal growth factor, which regulate basic aspects of wound healing.[4] There is one case in which PRP successfully treated a patient with extensive diabetic foot ulcers, non-responsive to other treatment modalities.[5] The first clinical trial on the use of PRP in human reproduction technologies was reported by a Chinese group to promote endometrial growth and to improve pregnancy outcomes of patients undergoing in *vitro* fertilization treatment.[6] Presently, clinical studies have investigated PRP for muscle, ligament, tendon, and cartilage repair, yielding limited level I evidence supporting use for knee osteoarthritis and lateral epicondylitis.[3] It is not well known whether PRP promotes

intestinal mucosal repair. Perotti[7] reported a case of postradiation proctitis successfully treated with a PRP enema, suggesting the possibility of PRP in the repair of rectal mucosal injury. To our knowledge, this is the first case reported in the literature for the treatment of OGIB with PRP, providing a method that can be tried for patients with incurable OGIB.

We are aware that our case report may have some limitations. We did not reperform gastrointestinal endoscopy in this patient to compare bowel changes before and after PRP treatment. The dose, frequency, and duration of PRP in the treatment of OGIB and whether it will lead to intestinal adhesions need to be further explored in subsequent studies. The spread of infectious diseases and allergic reactions during the use of PRP are also treatment risks that require attention.

In conclusion, we believe that nasointestinal tube feeding of PRP is an effective treatment method for patients with OGIB and can be tried when other treatment methods are ineffective.

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Conflicts of interest

None.

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