CASE REPORT

Persistent duodenal ulcers bleeding in postkidney transplant patient treated by infliximab

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SUMMARY

A 50-year-old woman with end-stage kidney disease was admitted for a living-donor kidney transplantation. On post-transplantation day 6, she developed antibody-mediated rejection and was treated with plasmapheresis, rituximab and intravenous immunoglobulin. 1 week later, she developed severe upper gastrointestinal bleeding from multiple duodenal ulcers along the bulb and the third part of the duodenum. She underwent 11 sessions of endoscopic and interventional therapies comprised with the combination of various techniques including bipolar coaptation, hemoclippping, band ligation and angiogram with coil embolisation of duodenal branch of gastroduodenal artery. Histopathology showed neither any organism nor any feature of graft-versus-host disease. However, empiric treatments with intravenous proton pump inhibitor and broad-spectrum antibiotics/antifungal were given but failed to heal the ulcer, and bleeding recurred from the new developed ulcers. Finally, a single dose of intravenous infliximab was administered to stop bleeding. The patient responded dramatically with rapid ulcers healing and there was no recurrent bleeding during a 3-month follow-up.

BACKGROUND

Although, gastrointestinal bleeding in solid organ-transplanted patients may be the presentation of ulcers developed from various aetiologies, the response to standard endoscopic therapies including endoscopic, medical and interventional is not different from peptic ulcer bleeding.¹ We report a post-kidney transplanted patient with bleeding duodenal ulcers that failed to respond to all-standard endoscopic and interventional therapies. Infliximab, a biological drug was used to enhance rapid ulcer healing and stop bleeding in this patient.

CASE PRESENTATION

A 50-year-old woman with end-stage kidney disease of unknown aetiology was admitted at the King Chulalongkorn Memorial Hospital for an elective operation for a living-donor kidney transplantation. She had been on regular haemodialysis twice a week via the arteriovenous fistula on the left arm for 1 year prior to the admission. Except for kidney disease, she had unremarkable medical history. Preoperatively, Cytomegalovirus (CMV) viral load was less than 20 copies/ml. Her stool exam was unremarkable. She never smoked. Basiliximab, methylprednisolone, tacrolimus and mycophenolate mofetil were preoperatively used for an induction of immunosuppression. The right

kidney from her spouse was successfully transplanted into her right iliac fossa without perioperative complication. On post-transplantation day 6, her serum creatine was elevated. Kidney biopsy showed antibody-mediated rejection of the transplanted kidney. She received multiple sessions of treatment with plasmapheresis and intravenous immunoglobulin (IVIG). A single dose of Rituximab was also given and later her serum creatine level and urine output were gradually improved after the treatment. She was also treated with intravenous meropenem plus cefoperazone/sulbactam plus colistin for *Acinetobacter baumannii* urinary tract infection at the same time of her graft rejection. Her oral medications were tacrolimus (Prograf) 0.2 mg/kg/day, enteric-coated mycophenolate sodium (Myfortic) 540 mg every 12 h and prednisolone 1 mg/kg/day. On post-transplantation day 14, she passed melena and became anaemic. She had normal platelet count and coagulogram. Over the 3-week course, she underwent 11 sessions of therapeutic upper endoscopy for duodenal ulcers that resulted in bleeding. Despite a high-dose intravenous infusion of proton pump inhibitor, the new bleeding sites were discovered from different ulcers. Oral prednisolone was rapidly tapered off. Oral mycophenolic acid (Myfortic) was discontinued on day 10 after the first bleeding episode.

INVESTIGATIONS

Oesophagogastroduodenoscopy showed linear, deep, irregular border duodenal ulcers with yellowish exudates on top extending from the bulb to the third part of the duodenum. There were more than one visible bleeding vessels. (figure 1) Biopsy was performed from the border and crater of ulcers. Histopathology showed an acute ulcer without organism or inclusion body and there was no evidence of graft-versus-host disease. Tissue PCR for tuberculosis and immunohistochemistry stain for Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) were negative. *Helicobacter pylori* antibody was positive. Colonoscopy and double balloon enteroscopy were performed to exclude other small bowel and colonic bleeding lesions. Blood cultures for bacteria, mycobacteria and fungus showed no growth. Serum CMV viral load was <20 copies/ml and EBV viral load was <600 copies/ml. Serum PCR for BK virus were negative. Serum *Aspergillus galactomannan* antigen was unremarkable (0.68). Stool examination and agar plate culture for *Strongyloides* result were negative.

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Figure 1 Three types of duodenal ulcers in this patient. Left: Linear, deep, irregular border duodenal ulcers with yellowish exudates on top extending from the bulb to the third part of the duodenum. Middle: the bleeding visible vessel from duodenal ulcer in the second part of the duodenum. Right: blood spurting out from the duodenal ulcer in the bulb of the duodenum.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis includes opportunistic infection-induced ulcers, acid-related ulcers, ulcers related to medications and idiopathic duodenal ulcers.¹

TREATMENT

The bleeding was stopped during each endoscopic session with a combination of two or three standard haemostatic endoscopic procedures including adrenalin injection, haemostatic clips, argon plasma coagulation, bipolar coaptation and band ligation. A few sessions required histoacryl injection to control visible vessel bleeding. Angiogram with superselective coil embolisation of the duodenal branch of gastroduodenal artery was also performed. Intravenous pantoprazole was infused continuously at the rate 8 mg/h. Meropenem and sulperazon were administered for the treatment of *Acinetobacter baumannii* urinary tract infection. Intravenous gancyclovir 5 mg/kg every 12 h and intravenous voriconazole had been prescribed empirically. However, the recurrent visible bleeding vessels kept appearing one after another. At the 11th episode of recurrent bleeding on post-transplantation day 35, a single-dose intravenous infliximab 5 mg/kg was administered. The patient dramatically responded to infliximab by showing rapidly healed ulcers (figure 2) and there was no recurrent upper gastrointestinal bleeding. Triple therapy including oral pantoprazole, metronidazole and amoxicillin for 14 days was given as the treatment of *H pylori* infection during non-bleeding days. Oral enteric-coated mycophenolate sodium 360 mg every 12 h and prophylactic oral acyclovir 400 mg every 12 h were also prescribed. She was discharged on post-transplantation day 56. Thirty-nine units of packed red cells were given throughout her admission. Her

serum creatine before discharge was 1.52 mg/dl. Urea breath test confirmed the successful eradication of *H pylori* infection.

OUTCOME AND FOLLOW-UP

Follow-up endoscopy was carried out 20 days after intravenous infliximab. All duodenal ulcers healed and the patient had no recurrent gastrointestinal bleeding at the 3-month follow-up.

DISCUSSION

We reported an interesting case of persistent bleeding duodenal ulcers with visible vessels in the setting of postkidney transplantation. Histological, virological and serological tests showed no evidence of opportunistic infection. The ulcers did not respond to intravenous proton pump inhibitor, empiric antibacterial, antiviral and antifungal agents. In fact, intravenous proton pump inhibitor was administered continuously from the first day of bleeding but it failed to promote ulcers' healing. All potential causative medications including prednisolone and mycophenolic acid were stopped. Amazingly, new ulcers causing bleeding kept on developing one after another. Other possible cause of duodenal ulcers in this patient after excluding many common causes is an inflammatory ulcer secondary to the derangement of the immune system that was aggravated by immune-modulators administered during the postoperative period. The pathogenesis of this ulcer may resemble those in inflammatory bowel disease which some of the episodes of severe bleeding can dramatically respond to a single dose of intravenous infliximab.² It has been reported that an intravenous infliximab can rapidly stop severe bleeding from isolated small bowel ulcers in Crohn's disease in a series of seven patients.² A similar case of post-transplant-related gastrointestinal ulcer was a large idiopathic oesophageal ulcer in a middle-aged man who had a living-related kidney transplantation 4 months prior to the onset of bleeding. The ulcer bleeding responded to an oral prednisolone.³ To our knowledge, this is the first case of duodenal ulcer bleeding in postkidney transplanted patient that dramatically responded to the treatment with a biological agent.

Figure 2 On day 20, all duodenal ulcers dramatically healed after a single dose of intravenous infliximab.

Learning points

- Inflammatory gastrointestinal tract ulcer is a rare cause of bleeding ulcer in solid organ transplant patients and should be diagnosed only after excluding other aetiologies. Opportunistic infections are more common aetiologies of ulcer in solid organ transplant. Perhaps empiric treatment of other more common causes may be required before entertaining the diagnosis.
- Treatment with infliximab for inflammatory gastrointestinal ulcer in solid organ transplant patients with persistent rebleeding may be a lifesaving measure and can avoid unnecessary surgery.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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