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Inflammatory bowel disease after kidney transplantation-two case reports

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INTRODUCTION

- Inflammatory bowel disease (IBD) arises from abnormalities in the barrier function of the intestinal epithelium and immune responses. Recent studies have highlighted the relationship between dysbiosis, a disruption in the gut microbiota, and the decline in mucosal barrier function and immune response abnormalities.
- Dysbiosis induced by environmental factors (such as medications, infections, diet, and lifestyle) and genetic predispositions (such as susceptibility genes) is involved in the pathogenesis of IBD through its interplay with immune dysfunction.
- These pathological mechanisms have been elucidated in IBD model experimental animals. (Ungaro R.Lancet ; 2017;389;1756-70)

CASE1

Patient Information:

•53 years　Male
•Dialysis History: Peritoneal dialysis for 5 years, hemodialysis for 1 year (Underlying disease: Unknown)
•Blood Type: AB, Rh positive
•Donor: Mother,Blood Type:,A, Rh positive
•HLA: One haplotype identical
•Diagnosed with ulcerative colitis (pancolitis) at age 20

Post-Transplant Course:

•Immunosuppressive Therapy: Tacrolimus + MMF + BXM + PSL
•Post-Transplant: No rejection episodes; Infection: CMV infection
•Tacrolimus trough levels: 2.3–3.8 ng/dL
•Serum creatinine levels: 1.5–1.7 mg/dL

7 Years Post-Transplant:

•Chief Complaints: Fever and diarrhea, indicative of a relapse of ulcerative colitis.
•Treatment: Remission achieved with 5-ASA and a reduction in tacrolimus dosage (from 5 mg to 3.5 mg).

CASE1

14 Years Post-Transplant；［Figure1・2］

・Chief Complaints: Hematochezia and diarrhea, indicative of a relapse of ulcerative colitis

Initial Treatment:

•Initiated Budesonide in the outpatient setting.

•No improvement in symptoms noted.

Treatment Adjustment:

•Reduced Tacrolimus dosage.

•Increased steroid dosage, leading to symptomatic improvement.

Subsequent Complications:

•12 days later, the patient presented with hematochezia.

•Admitted for hospitalization and underwent repeat endoscopy.

Endoscopic Findings:

•Improvement in endoscopic findings observed.

Management:

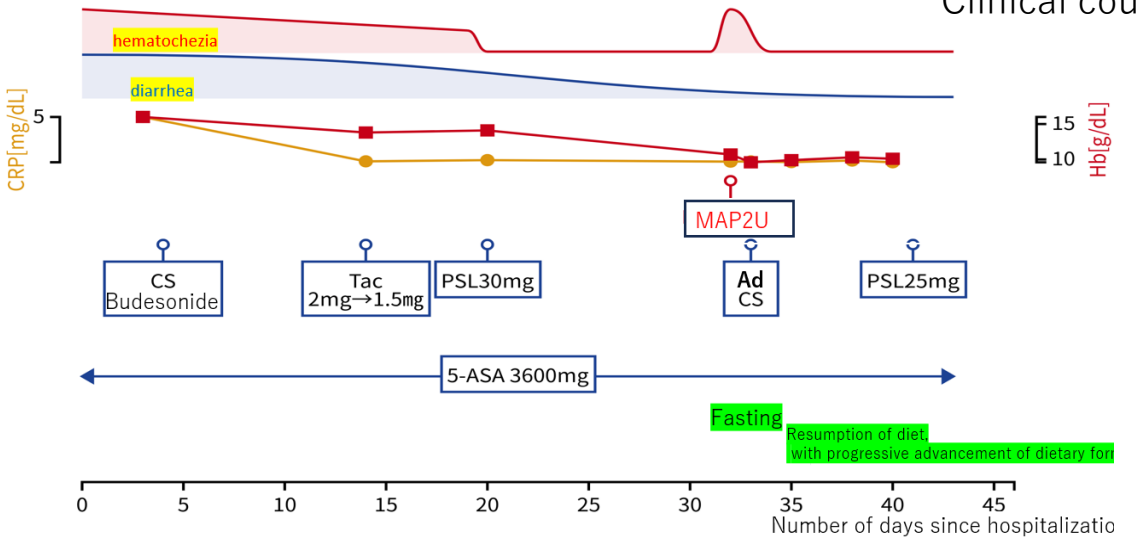
•Patient was placed on fasting and showed symptom improvement.

•Gradual reintroduction of diet.

•Tapered steroid dosage.

•Discharged from the hospital.

Figure1
Clinical course



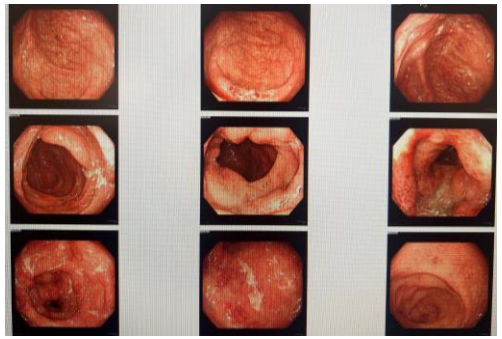


Figure2
erosions and ulcers throughout the entire colon

16 Years Post-Transplant: ［**Figure3**］

- Chief Complaints: Hematochezia and fever
- Despite an increase in budesonide dosage, colonoscopy revealed a trend towards worsening of ulcerative colitis.

Action Taken: Vedolizumab introduced in the outpatient setting

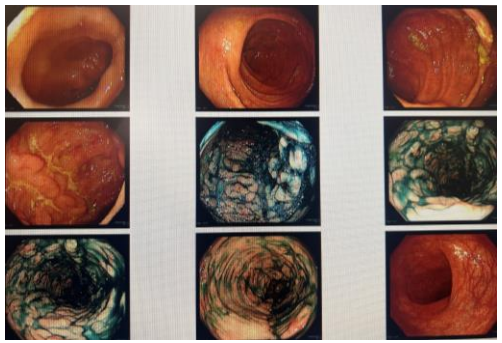


Figure3
Longitudinal Ulcers and Mosaic Pattern Mucosa

CASE2

Patient Information:

- 54 years Female
- Dialysis History: 7 years (Underlying disease: Pregnancy-induced nephropathy)
- Blood Type: A, Rh positive
- Donor: Father, Blood Type A, Rh positive
- HLA: One haplotype identical

Post-Transplant Course:

- Immunosuppressive Therapy: Tacrolimus + MZR + PSL
- Post-Transplant: No infections or rejection episodes
- Tacrolimus Trough Levels: 6–8 ng/dL
- Serum Creatinine Levels: 1.7–2.3 mg/dL

Development of Crohn's disease［Figure1］

- Chief Complaints: Fever and diarrhea
- 22 Years Post-Transplant: Diagnosed with Crohn's disease via colonoscopy and nodular erythema

Post-Hospitalization Course:［Figure2・3］

- **Initial Treatment:** Blood in stool and diarrhea improved with fasting management. An endoscopy conducted after admission showed a trend toward improvement, leading to the initiation of Elental . However, blood in stool and diarrhea reappeared.
- **Treatment Adjustment:** Increased steroid dosage with continued fasting was implemented. Subsequently, symptoms improved, Elental was resumed, and regular meals were reintroduced. The patient was discharged with a judgment of remission.
- **Recurrence Post-Discharge:** 12 days after discharge, blood in stool and diarrhea recurred. Vedolizumab was introduced, but symptoms did not improve. An endoscopy was showed, revealing scar tissue from ulcers in the colon, but persistent bleeding from the small intestine was observed.
- **Treatment Change:** Infliximab was introduced, and steroids were discontinued. Symptoms improved thereafter, and the patient was discharged without further relapse following reintroduction of meals.
- **Current Status:** The patient is maintaining remission with Infliximab administration every 8 weeks.

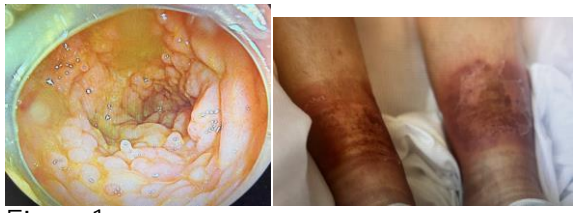


Figure1
Longitudinal ulcers; cobblestone mucosa
Extraintestinal complications;nodular erythema

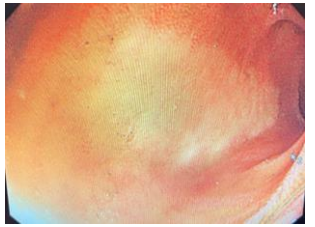


Figure2
Scar formation in colonic ulcers

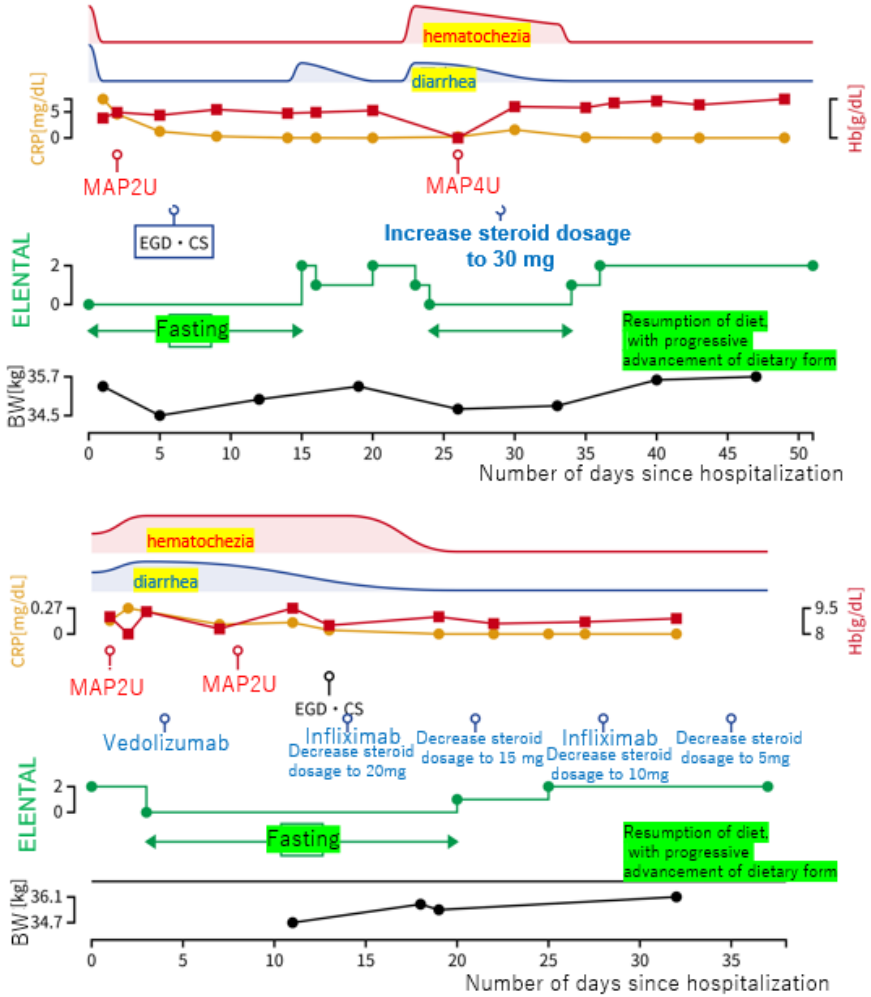


Figure3 Clinical course

DISCUSSION

・Gastrointestinal adverse events are commonly observed after kidney transplantation, with an incidence rate of 20-50% among kidney transplant recipients (Kurnatowska I. Transpl Int. 2010;23(5):553-8).

・The incidence of inflammatory bowel disease (IBD) following solid organ transplantation is approximately ten times higher compared to the general population, particularly in liver transplant patients. However, reports of IBD occurrence after kidney transplantation are limited, accounting for about 5% of IBD cases following solid organ transplants (Pittman ME. Am J Surg Pathol. 2017;41:1666-1674; Indriolo A. World J Gastroenterol. 2014;20:3525-3533).

・Calcineurin inhibitors (CNI) suppress IL-2 secretion from $CD4^+$ T cells. IL-2 is involved in the differentiation and proliferation of regulatory T cells (Treg), which play a suppressive role in immune responses. The suppression of IL-2 may disrupt mucosal immune regulation, potentially contributing to the development of IBD.

・Experimental studies have reported that IL-2 deficient mice raised with a normal intestinal microbiota spontaneously develop ulcerative colitis (UC)-like colitis (Sadlack B. Cell. 1993;75:253-61).

・Reports indicate that MMF can cause mucosal abnormalities and UC-like colitis (Farooqi R. Cureus. 2020;12).

・Generally, 5-ASA is the first-line treatment for IBD, with oral steroids considered for patients who do not respond adequately to 5-ASA. For steroid-dependent patients, treatments may include azathioprine, 6-mercaptopurine, TNF inhibitors, or vedolizumab (Burri E. Digestion. 2020;101:2-15).

・ There is no established standard treatment for IBD post-kidney transplantation due to concerns about the interactions between IBD medications and immunosuppressants.

Case 1: Achieved remission with increased steroid dosage but experienced a relapse. Vedolizumab was initiated, resulting in remission without significant adverse events.

Case 2: Initially achieved remission with increased steroid dosage but experienced a relapse. Vedolizumab was introduced, but symptoms did not improve. Infliximab was subsequently administered, resulting in remission without significant adverse events.

CONCLUSION

•**Case 1** achieved remission with vedolizumab.

•**Case 2** was resistant to treatment but ultimately achieved remission with infliximab.

•The safety of infliximab for IBD patients post-kidney transplantation is not well-established. However, in this case, remission was achieved without deterioration of kidney function.