

# “Snowmelt Sign” and “Corkscrew Microvessels” Predicting Epithelium Regeneration After Acute Rejection of Small-Bowel Transplantation: A Case Report

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## ABSTRACT

Intestinal failure characterized by inadequate maintenance of nutrition via normal intestinal function comprises a group of disorders with many different causes. If parenteral nutrition dependency develops, which is associated with higher mortality and complications, it is considered for intestine transplantation. However, the graft failure rate is not low, and acute cellular rejection is one of the most important reasons for graft failure. As a result, early identification of rejection and timely modification of anti-rejection medications have been considered to be associated with better graft and patient survival rates. The diagnostic gold standard for rejection is mainly based on histology, but hours of delay by pathology may occur. Some researchers investigated the association of endoscopic images with graft rejection to provide timely diagnosis. In this study, we present the first case report with characteristic features under magnifying endoscopy with a narrow-band imaging system to predict epithelial regeneration and improvement of graft rejection in a patient with small-bowel transplantation.

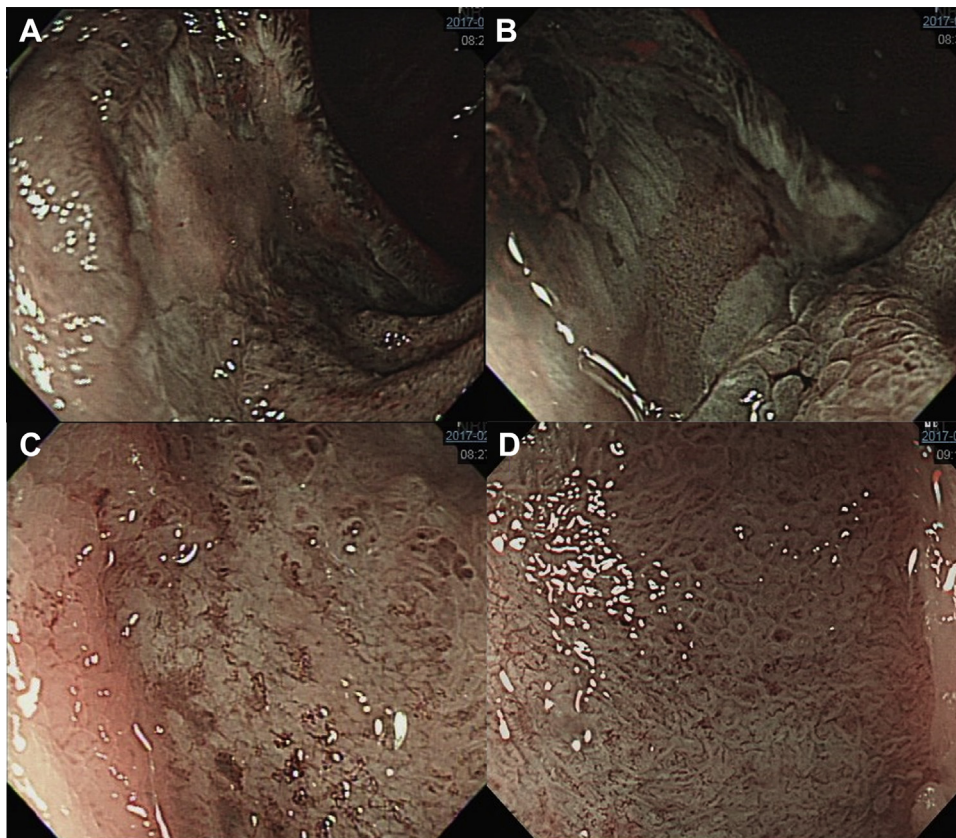
A 31-YEAR-OLD, female heavy cigarette smoker had development of acute thrombosis of the portal vein and superior mesenteric vein; she received wide resection of the ischemic bowel with the residual 30-cm small intestine. Because of short-bowel syndrome, she underwent small-bowel transplantation. Unfortunately, acute cellular rejection (ACR) was found 3 weeks after transplantation. Through surveillance with the use of magnifying endoscopy (ME) under narrow-band imaging (NBI) (Evis Lucera CLV-260NBI, GIF-H260Z endoscopy, Olympus Medical Systems Corp) via chimney ileostomy, exfoliation with denuded mucosa was observed (Fig 1A). After administration of high-dose steroids and immunosuppressants, surveillance endoscopy showed whitish exudates (“snowmelt sign”) crawling from peripheral normal-appearing mucosa to the exfoliating base and increasing density of black dots on the base (Fig 1B). ME-NBI of the black dots showed “corkscrew microvessels” (Fig 1C). Two months later, epithelium regeneration with dome to tongue-like villi was found (Fig 1D), and histopathological examination showed improvement of ACR.

## DISCUSSION

Intestinal transplantation (IT) is one of the treatment strategies for severe intestinal failure patients with parenteral nutrition dependency [1]. According to an IT registry report that gathered information on 2887 transplants in 82 programs since 1985, survival rates were 76%, 56%, and 43% at 1, 5, and 10 years, respectively [2].

However, the outcomes of IT have only modestly improved over the past decades, and the rates of graft loss beyond 1 year have not improved [2]. The reasons for graft failure may be due to complications from IT, including graft rejection, infection, renal dysfunction, de novo malignancy (post-transplantation lymphoproliferative disorders), nutrition, and development impairment, in addition to limited

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**Fig 1.** Endoscopic findings during epithelial regeneration of acute rejection after small-bowel transplantation. (A) Denuded mucosa without microvessel on ulcer base. (B) Whitish exudates (“snowmelt sign”) crawling from peripheral normal mucosa to denuded area, accompanied by dark dot microvessels on the ulcer base. (C) Magnifying endoscopy under narrow-band imaging during improvement of acute rejection shows “corkscrew-like microvessels” on the regenerating mucosa. (D) Epithelial regeneration with dome to tongue-like villi.

experiences from low case volume at most centers [1,2]. Rejection is one of the most important complications among others, and nearly 50% of recipients develop at least 1 episode of rejection in the first year after IT [1,2]. Although medical care of rejection with the use of induction therapy, steroids, and immunosuppressants has markedly decreased the rate of early severe acute rejection, the consequences of severe rejection are considerably worse than that of other solid organs, that is, a 50% mortality rate [3]. As a result, early identification of ACR and timely modification of anti-rejection medications has been considered to be associated with better graft and patient survival rates.

Most of the clinical manifestations of graft rejection are non-specific, including abdominal pain/distension, nausea/vomiting, and fever. The diagnostic gold standard for ACR is mainly based on histology, and magnifying endoscopic findings could also be used to minimize the performance of biopsies in grafts to reflect the histologic severity of rejection [4–6]. However, there are no endoscopic features characteristic of improvement of ACR. Herein, we report a

first case report of characteristic endoscopic findings, including morphological changes of mucosa and vasculature, to predict epithelium regeneration after ACR. During endoscopy surveillance via chimney ileostomy, the margin of exfoliating parts were covered by gradually elongating whitish exudates (Fig 1A, B) with the appearance of corkscrew-like microvessels on the ulcer base under ME-NBI (Fig 1C).

Histologic examination of the endoscopic biopsy at the margin between normal appearance mucosa and whitish exudates showed improvement of ACR and a decreasing number of apoptotic bodies. Proliferation of villi (Fig 1D) was noted on the parts with those characteristic endoscopic features.

## CONCLUSIONS

We believe that improvement of ACR could be predicted by endoscopy surveillance, especially with the use of ME-NBI, and unnecessary biopsies or adjustment of immunosuppressant medications can be avoided by these characteristic

endoscopic presentations. More case studies are warranted to validate the result of this case report.

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