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Limited surgical resection for graft salvage following recovery from complicated exfoliative rejection in pediatric intestinal recipients

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Abstract

Complications of ER contribute significantly to morbidity and mortality following intestinal transplantation. The surgical management of three pediatric patients who experienced complications of late ER after composite LSB transplantation is described, highlighting the potential for allograft salvage after limited surgical resection. A retrospective case series was compiled. Data collected included time to ER from transplant, medical management of ER, complications, and surgical management of ER complications. All patients had undergone composite LSB transplantation between one and two yr of age. Time to ER after transplantation was 9.5–26.5 months. ER complications included ileal allograft stricture, intramural hematoma with perforation of jejunal allograft, and massive GI hemorrhage secondary to focal ulceration and pseudopolyp formation. With evidence of mucosal regeneration, all three patients underwent limited segmental allograft resection. Two patients continue to maintain satisfactory allograft function 39–44 months following operation. The third patient retained adequate allograft function until he developed PTLN, subsequently dying from disseminated Adenovirus infection 51 months after resection. Severe disruption of intestinal allograft integrity in ER can lend itself to medically refractory complications. Prompt recognition and surgical correction of complications can play a crucial role in allograft salvage and patient survival after ER.

Keywords

pediatric transplantation; liver/intestine transplant; allograft; complications; graft rejection

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Conflict of interest

None.

Intestinal transplantation is now a well-established treatment option for intestinal failure patients with life-threatening complications related to long-term parenteral nutrition. Recent clinical and surgical advances have improved outcomes in intestinal transplant recipients, with both pediatric patient and allograft survival increasing to over 75% at one yr post-transplantation (1–3). Although significant immunologic challenges following intestinal transplantation remain, there has been a decrease in the rates of ACR in the first 90 days post-transplantation from 70–90% to 33–50% (2). Despite the progress in clinical and surgical management of intestinal transplant recipients as well as a greater understanding of the profound immunogenicity of the transplanted intestine (2, 3), ER remains a significant challenge, occurring during the post-transplantation course of up to 15% of recipients (4). The complications associated with ER contribute significantly to morbidity and mortality following transplantation. We report the surgical management of three pediatric patients who experienced complications of late-onset (greater than six months following transplantation) ER after composite LSB transplantation, highlighting the potential for patient and allograft salvage with limited surgical resection.

Methods

We performed a retrospective review of the medical records of three pediatric recipients who underwent composite LSB transplantation and developed late-onset ER. Data collected included time to ER after transplantation, medical management of ER episodes, complications, surgical management of complications of ER, and patient outcomes. ATG and methylprednisolone were used as induction therapy at transplantation as follows: ATG 3 mg/kg plus methylprednisolone 10 mg/kg in the pre-operative phase, ATG 2 mg/kg plus methylprednisolone 5 mg/kg just prior to revascularization of the allograft, and either ATG 1 mg/kg plus methylprednisolone 5 mg/kg or methylprednisolone 10 mg/kg alone on POD 1. Post-operative maintenance immunosuppression consisted of methylprednisolone and tacrolimus. Methylprednisolone was dosed at 8 mg/kg/day on POD 2 and tapered by 2 mg/kg/day until POD 5. Methylprednisolone was then gradually tapered by 25% from 1 mg/kg/day on POD 6 to off by week 6 after transplantation. Target tacrolimus trough levels were 12–18 ng/mL through post-operative week 8, after which the trough target was reduced to 10–15 ng/mL through post-operative week 16 and 5–8 ng/mL beyond week 16. Ileoscopy with mucosal biopsy was performed via a Mikulicz double-barreled ileostomy as surveillance twice weekly during the first two months post-transplantation, then weekly for six wk, then every other week for four wk, and then whenever clinically indicated thereafter. Because all three patients presented >6 months after transplant on stable immunosuppression, endoscopies and biopsies were only on an *ad hoc* basis according to our protocol. Symptoms of diarrhea and intestinal bleeding prompted endoscopic procedures in all three. The standard treatment protocol for Grade 1–2 ACR included intensified immunosuppression with a burst of methylprednisolone at 10 mg/kg/day for three days and increased tacrolimus trough goals of 12–18 ng/mL. Following the therapeutic burst, methylprednisolone was dosed at 2 mg/kg/day for seven days, after which it was tapered by 10% of the starting dose per week. Histologic evidence of refractory rejection despite intensified immunosuppression or the presence of severe rejection on initial surveillance ileoscopy warranted escalation of treatment with ATG or OKT3, as described below.

Exfoliative rejection was diagnosed by nearly complete mucosal exfoliation of the intestinal allograft and confirmed by histological evaluation of mucosal biopsies. The standardized grading scheme for ACR in small bowel transplantation was used for histological diagnosis (5). Institutional review board approval was obtained to perform this review.

Results

All three patients had undergone composite liver-small bowel transplantation for intestinal failure with complications of parenteral nutrition-associated liver disease between 2009 and 2011. One patient (patient C) had previously undergone isolated intestinal transplantation, which failed due to acute ischemic enteropathy requiring removal of the allograft three days after transplantation. At the time of LSB transplantation, B- and T-cell FXMC results were negative for two patients (patients B and C), whereas one patient (patient A) had a positive T-cell FXMC and a negative B-cell FXMC. All three patients were receiving tacrolimus monotherapy, and had attained 100% enteral autonomy by the time of onset of ER.

Patient A underwent LSB-colon composite transplantation at 20 months of age for parenteral nutrition-associated liver disease and intestinal failure secondary to megacystis-micro-colon-intestinal hypoperistalsis syndrome. Prior to the development of ER, she experienced two separate episodes of Grade 1–2 ACR at weeks 2 and 31 after transplantation, respectively, both of which responded to increased immunosuppression with increased target tacrolimus troughs (12–18 ng/mL) and methylprednisolone burst. At approximately nine and a half months after transplantation, she presented with ER in the setting of fever, bloody stoma output, and decompensated septic shock with associated *Staphylococcus aureus* blood stream infection and Norovirus enteritis. Endoscopic inspection of approximately 20 cm of the proximal limb of the allograft ileum revealed diffusely necrotic debris, ulceration, and pseudomembrane formation. Histological evaluation of allograft ileal biopsies mirrored the gross ileoscopic examination, demonstrating diffuse mucosal necrosis with marked crypt dropout as well as focal abundance of epithelial and lamina propria apoptosis. With histological evidence of ER, immunosuppression was intensified with methylprednisolone burst and ATG 1.5 mg/kg/day for 14 days in conjunction with increased tacrolimus trough goals of 12–18 ng/mL. Response to intensified immunosuppression was monitored by serial surveillance endoscopies with biopsies, which showed gradual regeneration of allograft mucosa. Her course was subsequently complicated by intermittent, persistent paroxysms of abdominal pain and distention on goal enteral feeds. Contrast stomagram performed two and a half months after ER diagnosis revealed an allograft stricture located approximately 15 cm proximal to the ileostomy. Endoscopic stricture dilation was not attempted because of peristicture bowel inflammation and potential for perforation. Due to persistent clinical small bowel obstructive symptoms, she underwent exploratory laparotomy with resection of a 9-cm segment of the allograft ileum proximal to the stoma with end-to-end anastomosis. The stoma was not closed at this time because we elected to perform routine surveillance ileoscopy for several weeks thereafter. Histopathology demonstrated stricture with mucosal denudation and ulceration with evidence of ischemic change. She recovered without complication, and continues to thrive with complete enteral autonomy on maintenance

immunosuppression of tacrolimus (target trough level of 5–8 ng/mL) and azathioprine 1 mg/kg/day 39 months following segmental ileal resection.

Patient B underwent LSB transplantation at one yr of age for parenteral nutrition-associated liver disease and short bowel syndrome secondary to extensive resection for meconium peritonitis. She presented at approximately 26.5 months after transplantation with her first episode of ACR (Grade 2) in the setting of fever and bloody diarrhea with associated *Escherichia coli* urinary tract infection and Norovirus enteritis. Despite intensified immunosuppression with a burst of methylprednisolone and increased tacrolimus trough goals of 12–18 ng/mL, ER developed within one wk of initial ACR episode, as evidenced by repeat endoscopy (Fig. 1) and biopsy (Fig. 2). A 14-day course of ATG 1.5 mg/kg/dose, every 24 h was initiated. Response to ATG was monitored by surveillance endoscopy with biopsies on days 6, 13, 20, 27, and 34 after ER diagnosis, demonstrating slowly progressive regeneration of allograft mucosa. Despite effective response to therapy, GI bleeding developed on day 26 after ER diagnosis, evolving into a large intramural hematoma with perforation of proximal allograft jejunum by day 37. It is unclear whether the hematoma occurred at the site of prior jejunal biopsy. Exploratory laparotomy was performed with evacuation of intra-abdominal hematoma and drainage of perforated viscus with placement of two Jackson-Pratt drains. Persistent, profuse GI bleeding, however, mandated a repeat exploratory laparotomy on day 48 after ER diagnosis, at which time a repair of the perforation at the anastomosis between native duodenum and allograft jejunum was performed. This repair proved to be futile, as continued bleeding prompted repeat exploratory laparotomy with intra-operative endoscopy on day 71 after ER diagnosis. Endoscopy revealed severe denudation and granulation limited to the site of the previous repair in addition to significant ulceration of the first 25 cm of the efferent limb of the allograft jejunum. This appearance was not amenable to endoscopic therapy. Segmental resection of this contiguous region of allograft jejunum was performed. Intestinal continuity was re-established with end-to-end anastomosis of allograft duodenum to allograft jejunum and end-to-side anastomosis of native duodenum to allograft jejunum. Histopathology of the resected allograft jejunum revealed ischemic enteritis with prominent hyperplastic mucosal regeneration (Fig. 3). Patient B subsequently recovered and was discharged on day 112 after ER diagnosis. She is currently alive with partial enteral autonomy and intermittent intravenous fluid supplementation on maintenance immunosuppression with tacrolimus alone (target trough level of 7–12 ng/mL) 44 months following this operation. Azathioprine was not started due to hypersplenism with associated cytopenias secondary to persistent post-transplant splenomegaly. Sirolimus was trialed, but subsequent, discrete mucosal ulceration necessitated its discontinuation.

Patient C underwent LSB transplantation at two yr of age for parenteral nutrition-associated liver disease and intestinal failure secondary to ultra-long-segment Hirschsprung's disease after failed isolated intestinal transplantation. Prior to development of ER, he experienced one episode of steroid-responsive ACR at day 17 after transplantation. At 11 months after transplantation, he presented with histological evidence of ER in the setting of fever and non-bloody stoma output with associated adenoviral and enteroviral enteritides. Endoscopic evaluation showed diffuse friability of the proximal limb of the allograft ileum with hyperemia, edema, exudate, and villous effacement. Histopathology was consistent with the

endoscopic diagnosis, revealing segments of inflamed lamina propria and granulation tissue virtually devoid of surface epithelium, crypts, and villi. Immunosuppression was intensified with OKT3 at 2.5 mg once daily for four days followed by 5 mg once daily for 10 days. Of note, OKT3 was commercially available at this time and was preferred over ATG due to the possibility that the efficacy of ATG may have been compromised by previous exposure during induction. Immunosuppression was further maximized with methylprednisolone burst and taper, as well as increased tacrolimus trough goals of 12–18 ng/mL. Twice weekly ileoscopies demonstrated gradual regeneration of allograft mucosa. However, intraluminal GI hemorrhage ensued within one month of ER diagnosis. Ileoscopy revealed chronic ulceration and pseudopolyp formation at a former biopsy site approximately 12 cm proximal to the ileostomy. Attempts to control bleeding both medically and endoscopically proved futile. Exploratory laparotomy was performed with an 18-cm resection of diseased allograft ileum and re-maturation of an end ileostomy. Histopathology of the resected allograft segment demonstrated focal mucosal ulceration with some areas showing persistent epithelial loss and other areas showing regenerative epithelial changes. Patient C's post-operative course was complicated by a hollow viscus perforation with pneumoperitoneum and intra-abdominal abscess formation approximately two months after ileal resection, necessitating exploratory laparotomy for washout and drainage of abscesses. Due to the presence of significant intra-abdominal adhesions and inflammation, the site of the hollow viscus perforation could not be definitively identified. The remainder of his course was uncomplicated, and he recovered fully. He retained good allograft function with full enteral autonomy on maintenance immunosuppression of tacrolimus (target trough level of 5–8 ng/mL) and azathioprine 1 mg/kg/day. Care was transferred to another transplantation center where he developed PTLN 50 months after segmental allograft resection. He subsequently expired from disseminated Adenovirus infection 51 months after segmental allograft resection.

Discussion

Pediatric intestinal transplant recipients have benefited from innovative changes in immunosuppression protocols, surgical advances, improved post-operative care, and accumulated experience over the last 15–20 yr (1–3). Patient and allograft survival curves one yr after transplantation have improved, and the rates of ACR within the first three months after transplantation have declined (1–3). However, even with current preconditioning immunosuppression strategies, ACR still occurs in up to 50% of patients (2). Failure to diagnose ACR at early stages can be detrimental to allograft and patient survival, particularly as the immunologic and inflammatory cascade gains full momentum.

While mild-to-moderate ACR is often controlled with intensified immunosuppression, delayed diagnosis, immunologic phenotype or risk (2), or the influence of a secondary inflammatory mechanism associated with concomitant infection can perpetuate the hyperactive immunologic cascade. Allograft rejection in the face of infection is certainly a clinical challenge. Numerous studies have investigated the relationship between solid organ transplant rejection and infections such as cytomegalovirus, adenovirus, and herpes simplex virus (6–9). While the mechanisms of cellular immunity that precipitate rejection during a period of infection are highly complex and incompletely understood, provocation of T-cell

immunity, particularly by viruses trophic to the GI tract, cannot be argued. Ultimately, as the inflammatory attack on the allograft progresses, ER can develop with almost complete sloughing of intestinal mucosa. All three patients in this series presented with ER in the setting of viral enteritides, further highlighting the link between rejection and infection in the post-transplant period.

The clinical presentation of ER can vary. For example, ER can develop from a mild-to-moderate ACR episode, as seen in patient B, in whom ER was diagnosed during repeat endoscopy for surveillance of response to treatment of ACR. Exfoliative rejection can also present abruptly with fever, abdominal distention, and/or increased stool output in the face of infectious enteritides or serious bacterial infections, as seen in patients A and C. Despite variations in the clinical presentation of ER, its endoscopic and histopathologic features are unmistakable. ER is marked by endoscopic evidence of complete loss of morphological architecture with mucosal sloughing of the allograft bowel (5, 10). Histologically, the mucosa appears severely inflamed and denuded with early formation of granulation tissue devoid of surface epithelium, crypts, or villi (5, 10). While mucosal exfoliation is obvious, it is important to examine the appearance of the native stomach or bowel, noting that some enteritides can mimic ER (10). Involvement of both the native and allograft GI tract often suggests an infectious etiology of exfoliation, whereas sparing of the native organ raises the likelihood of ER.

Hypervigilance to the unpredictable nature of ER is essential throughout all stages of the post-transplantation course, with a 15% incidence after intestinal transplantation (4). In our own series of 45 intestinal transplants, we have seen five episodes of early ER (11.1%) and four of late ER (8.9%), of which three are reported here. Aside from these three patients, only one other ER patient is currently alive. Three of the other five underwent nearly complete graftectomy because of failure of graft regeneration. Despite graftectomy, one of those died of progressive pulmonary insufficiency and two of disseminated Adenovirus infection. The other two deaths occurred without graftectomy. One of those patients also had disseminated Adenovirus infection, and the other died of acute kidney injury in the absence of adequate vascular access.

Serial endoscopic surveillance with random biopsies is routine in the early post-transplantation period (<6 months after transplantation) during immunologic reconstitution of the transplanted bowel. As ER can occur at various periods after transplantation, however, a low threshold for endoscopic evaluation should be maintained even in the late post-transplantation period (>6 months after transplantation) (4, 10). In an analysis of 92 pediatric intestinal transplant recipients, Ishii et al. (4) reported that 27% of ER episodes occurred in the late post-transplantation period, presumably precipitated by intentional or unintentional decreases in immunosuppression (10). Despite its indeterminable course, ER in the late post-transplantation period has been associated with better response to therapy (4, 10). Kato and Ruiz (10) reported a 40% allograft loss rate in the late post-transplantation period, in contrast to a 100% allograft loss rate in the early post-transplantation period when the immunologic reconstitution of the allograft is at its peak. This observation is consistent with our case series, as all three patients presented with late-onset ER and responded to intensified immunosuppression with mucosal regeneration. At the time of their presentation,

we did not measure DSA or perform C4d staining of biopsies on any of our patients, so we are uncertain whether a humoral component contributed to their rejection episodes. Our screening protocols have since changed such that DSA is measured routinely and C4d staining is performed on all biopsies.

Without other biochemical markers of allograft rejection or recovery, repeat endoscopic surveillance is essential after ER is diagnosed. Due to the significant risk of complication with perforation, hematoma formation, and ulceration (as seen with patient C) of a severely damaged mucosa, it is imperative to consider both the frequency of endoscopic surveillance and the number of biopsies obtained for adequate histologic diagnosis. At our institution, we repeat endoscopy every 3–4 days after initiation of lymphocyte depleting therapy and aim to obtain only one biopsy with each endoscopic evaluation.

Following recovery, maintenance immunosuppression was also intensified in two of the patients (patients A and C) with the addition of azathioprine to tacrolimus. It was also attempted in patient B, but drug-associated complications prevented its implementation. Following their resections, all three patients experienced a long rejection-free period. With endoscopic and histological demonstration of allograft recovery, surgical management of the complications of ER was more likely to have a favorable outcome, and because of our experience, we have modified our maintenance immunosuppression protocol to employ dual therapy with tacrolimus and either sirolimus or azathioprine.

Unfortunately, evidence of regenerating mucosa does not ensure allograft survival, noting an 86% incidence of allograft loss despite initial histological recovery (4). The complications associated with ER are possibly to blame. While total graftectomy and subsequent re-transplantation may be necessary in the absence of response of ER to immunosuppressive therapy, removal of the allograft may also be precipitated by the occurrence of PTLT, the development of serious bacterial, viral, or opportunistic infections, severe GI hemorrhage, chronic rejection, intestinal obstruction, or sclerosing peritonitis (4, 10–12). None of the patients in this series had histological evidence for chronic rejection.

The medically refractory complications of ER, as described in this case series, warrant a high level of clinical suspicion and prompt recognition. The immunologic attack on the allograft in ER renders the mucosal layer severely damaged. The extensive destruction of intestinal mucosa results in an interruption in mesenteric microcirculation by nature of mucosal exfoliation and loss of bowel morphological architecture, including embedded blood vessels. Regeneration and reconstitution of the allograft mucosa with treatment is gradual and typically non-uniform, and regions of severe ischemic injury can ultimately result in stricture formation (13), as seen in patient A. Additionally, areas of granulation tissue, pseudopolyps, and chronic ulceration remain fragile during intestinal healing, and they can become a nidus for intramural hematomas, persistent GI bleeding, and perforation. Thus, while endoscopy and histological evaluation may demonstrate mucosal recovery in the regions examined, other regions remain at risk for the consequences of compromised vascular, digestive, and barrier function of the allograft intestine.

Prior studies reporting very low rates of allograft salvage in the setting of ER highlight the importance of early graftectomy if it is evident that severe allograft damage and rejection are ongoing despite intensification of immunosuppression. This approach is critical to ensuring patient survival by avoiding the development of complications of intensified immunosuppression, such as opportunistic infections, when no improvement in ER is evident. However, a role exists for segmental resections in the setting of regeneration. The three patients in our series demonstrated endoscopic and histologic evidence of regeneration of allograft mucosa following intensification of immunosuppression regimens while avoiding the development of severe infections. Therefore, early graftectomy was not necessary. However, all three patients developed medically refractory complications associated with the management of their late-onset ER, including allograft stricture with obstruction, intramural hematoma with perforation, and massive GI bleeding. Combined laparotomy and endoscopy were especially valuable in mapping the extent of persistent allograft denudation in patient B. Endoscopy and histological evidence of allograft recovery also confirmed that persistent abnormalities of the other two allografts (patients A and C) were focal. Therefore, limited surgical resection of the diseased allograft segment could be accomplished instead of complete graftectomy. It is important to note, however, that histological evidence of allograft recovery was the sine qua non to contemplation and pursuit of this directed surgical approach. Without early response to intensified immunosuppressive therapy, graftectomy would have likely been performed early in the course of management of their ER episodes. Nevertheless, our approach of limited surgical resection of the intestinal allograft played a crucial role in allograft salvage and patient survival in the management of ER complications following intestinal transplantation. While recurrence of ER has been previously described (4), ER has not recurred in any of the patients reported in this series. In conclusion, limited surgical resection of the allograft in the setting of gradual histological recovery can play a critical role in both patient survival and allograft salvage, can improve outcomes following ER in pediatric intestinal transplant recipients, and is preferable to total graftectomy.

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Abbreviations:

ACR	acute cellular rejection
ATG	anti-thymocyte globulin
DSA	donor-specific antibodies
ER	exfoliative rejection
FXMC	flow crossmatch
GI	gastrointestinal

LSB	liver-small bowel
POD	postoperative day
PTLD	post-transplant lymphoproliferative disease

References

1. Abu-elmagd KM, Costa G, Bond GJ, et al. Five hundred intestinal and multivisceral transplantations at a single center: Major advances with new challenges. *Ann Surg* 2009; 250: 567–581. [PubMed: 19730240]
2. Fishbein TM. Intestinal transplantation. *N Engl J Med* 2009; 361: 998–1008. [PubMed: 19726774]
3. Garg M, Jones RM, Vaughan RB, et al. Intestinal transplantation: Current status and future directions. *J Gastroenterol Hepatol* 2011; 26: 1221–1228. [PubMed: 21595748]
4. Ishii T, Mazariegos GV, Bueno J, et al. Exfoliative rejection after intestinal transplantation in children. *Pediatr Transplant* 2003; 7: 185–191. [PubMed: 12756042]
5. Ruiz P, Bagni A, Brown R, et al. Histological criteria for the identification of acute cellular rejection in human small bowel allografts: Results of the pathology workshop at the VIII International Small Bowel Transplant Symposium. *Transplant Proc* 2004; 36: 335–337. [PubMed: 15050150]
6. Stern M, Hirsch H, Cusini A, et al. Cytomegalovirus serology and replication remain associated with solid organ graft rejection and graft loss in the era of prophylactic treatment. *Transplantation* 2014; 98: 1013–1018. [PubMed: 24837540]
7. Cainelli F, Vento S. Infections and solid organ transplant rejection: A cause-and-effect relationship? *Lancet Infect Dis* 2002; 2: 539–549. [PubMed: 12206970]
8. Couzi L, Pitard V, Moreau JF, et al. Direct and indirect effects of cytomegalovirus-induced gammadelta T cells after kidney transplantation. *Front Immunol* 2015; 6: 3. [PubMed: 25653652]
9. Hoffman JA. Adenovirus infections in solid organ transplant recipients. *Curr Opin Organ Transplant* 2009; 14: 625–633. [PubMed: 19741532]
10. Kato T, Ruiz P, Tzakis A. Exfoliative bowel rejection—a dangerous loss of integrity. *Pediatr Transplant* 2004; 8: 426–427. [PubMed: 15367275]
11. Yandza T, Schneider SM, Nishida S, et al. Outcome of exfoliative rejection after isolated intestinal transplantation in an adult: Case report. *Transplant Proc* 2010; 42: 100–102. [PubMed: 20172289]
12. Ramos E, Molina M, Sarria J, et al. Chronic rejection with sclerosing peritonitis following pediatric intestinal transplantation. *Pediatr Transplant* 2007; 11: 937–941. [PubMed: 17976132]
13. Iinuma Y, Hirayama Y, Yokoyama N, et al. Intraoperative near-infrared indocyanine green fluorescence angiography (NIR-ICG AG) can predict delayed small bowel stricture after ischemic intestinal injury: Report of a case. *J Pediatr Surg* 2013; 48: 1123–1128. [PubMed: 23701792]

Fig. 1.
Endoscopic image of allograft jejunum at time of ER. The allograft mucosa is completely denuded, and only granulation tissue remains.

Fig. 2. Histology of the allograft ileal biopsy at time of ER. (a) Severe rejection. The mucosa is virtually devoid of crypts and surface epithelium (H&E, 4X). (b) Higher power magnification of the lamina propria with granulation tissue and admixed acute and chronic inflammation (H&E, 20X).

Fig. 3.

Pathology of the allograft jejunum. (a) Gross photograph of the resected allograft shows a hemorrhagic serosal surface with multiple areas of serosal adhesions and adherent exudate. (b, c) Hematoxylin and eosin-stained sections reveal patchy areas of ulceration with complete denudation of the mucosa (B, H&E, 4X) as well as more preserved areas with villous hemorrhage/congestion and regenerative epithelial changes (C, H&E, 2X). This figure demonstrates nicely how some areas of allograft may almost completely regenerate (c) while others may show no regeneration whatsoever (b).