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Gastrointestinal Bleeding as a Complication of Serial Transverse Enteroplasty

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Abstract

Purpose—Serial transverse enteroplasty (STEP) lengthens and tapers bowel in patients with intestinal failure and has a generally low complication profile. Evaluation and treatment of serious gastrointestinal bleeding (GIB) in three STEP patients is described.

Methods—Records of patients participating in an interdisciplinary intestinal rehabilitation program were reviewed to identify those who underwent STEP and had GIB necessitating red blood cell transfusion.

Results—Of 296 patients, 23 underwent STEP and 3 (13%) had subsequent GIB requiring transfusion. Underlying diagnoses were multiple atresias/intrauterine volvulus, gastroschisis, and gastroschisis with volvulus. STEP was performed at ages ranging from 3–5 months, using 3–8 stapler firings with an increase in mean bowel length from 23 to 45 cm. GIB was noted at 10–33 months post-op and resulted in 2–7 transfusions per patient over a period of 3–16 months. Gastrointestinal endoscopic evaluation demonstrated ulcers adjacent to the staple lines in two patients. Both had improvement of GIB with enteral antibiotics, sulfasalazine, topical enteral steroids and, ultimately, a period of bowel rest. The third patient had histological evidence of eosinophilic enteritis and was treated sequentially with antibiotics, sulfasalazine, enteral steroids, and an elemental diet. In all three, hemoglobin levels improved despite persistent occult bleeding.

Conclusions—Significant GIB is a potential late complication of STEP. Endoscopy identified the underlying source of GIB in all three patients. A combination of enteral antibiotics, anti-inflammatory medications, and bowel rest was effective in the treatment of post-STEP GIB, without the need for additional bowel resection.

Keywords

Short bowel syndrome; Intestinal failure; Serial transverse enteroplasty (STEP); Autologous intestinal reconstruction surgery (AIRS); gastrointestinal hemorrhage

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Level of Evidence: 4

Autologous intestinal reconstructive surgery (AIRS) has been employed for patients with short bowel syndrome (SBS) who have significant bowel dilation and fail to wean from parenteral nutrition (PN). Serial transverse enteroplasty (STEP), first described in 2003^{1,2}, is now performed internationally^{3–5} and is the most commonly utilized operation for intestinal reconstruction.⁶ Forty-seven percent of patients achieve enteral autonomy after STEP.^{6,7} If needed, a second STEP is technically feasible and may be of benefit for some patients.^{4,8–11} STEP has also been successfully used in adults with SBS.¹²

Complications of STEP include staple-line leak, stricture, functional or adhesive bowel obstruction, and intra-abdominal abscess.^{6,13} Re-dilation of small intestine after STEP portends a lower rate of progression to enteral autonomy and higher rate of transplantation.^{14,15} Overall, mortality after STEP has been reported as 6–11% and progression to intestinal transplantation occurs in 5–6% of patients.^{6,7} Though published data are limited, gastrointestinal bleeding has been described in individual patients after STEP.^{5,16–19} Some patients have been successfully treated with conservative measures alone, one required angiography¹⁹ and another underwent laparotomy with intestinal resection.¹⁸ This work describes a series of three patients with gastrointestinal bleeding requiring transfusion months to years after STEP.

1. Methods

Following Institutional Review Board approval, the records of 296 patients followed by an interdisciplinary intestinal rehabilitation program at a single medical center (Center for Advanced Intestinal Rehabilitation [CAIR], Boston Children's Hospital) were reviewed. Twenty-three patients underwent STEP operations at the same institution. Of these, 3 (13%) had gastrointestinal hemorrhage requiring transfusion of packed red blood cells. Patient presentations are summarized in Table 1.

2. Cases

2.1 Case 1

Patient 1 was a female born by spontaneous vaginal delivery at 36 weeks gestation with vanishing gastroschisis and secondary jejunal atresia. She had an intact, distended abdomen at delivery. On her first day of life, she underwent tapering enteroplasty of an 8 cm segment of small bowel and primary anastomosis of jejunum to mid-transverse colon. Her residual small bowel measured 30 cm from the pylorus at her initial operation. Her course was complicated by fungal meningitis, and intestinal failure associated liver disease (IFALD) for which she received parenteral omega-3 fatty acids with subsequent biochemical resolution of cholestasis. She had intermittent occult fecal bleeding and 2 packed red blood cell transfusions prior to her STEP operation.

She underwent STEP at 4.5 months for poor enteral feeding tolerance with dilated small bowel proximal to the jejunocolic anastomosis. Fifteen endo-GIA staple firings lengthened her small bowel from 44 cm to 89 cm and decreased the caliber from 5 cm to 1.5 cm. The apex of each staple line was reinforced in a figure-of-eight fashion with an absorbable monofilament suture.

Her enteral feeds were gradually advanced and her PN was discontinued at 13 months when she was receiving 80 kcal/kg/day enterally (solid food and an elemental formula). Three weeks later she was admitted with anemia (hemoglobin 7.4g/dL), hypoalbuminemia (2.7g/dL), and electrolyte abnormalities. In this context, PN was restarted and empiric antibiotics for small bowel bacterial overgrowth (SBBO) were initiated (first with metronidazole, and then later ciprofloxacin). Esophagogastroduodenoscopy (EGD) and colonoscopy at that time did not identify the anastomosis or suture lines, but showed patchy, mild colonic erythema. Biopsy revealed chronic inactive gastritis and normal colonic mucosa.

Over the next year, patient 1 continued on a combination of enteral nutrition and PN. At age 27 months she presented with new-onset hematochezia, hypoalbuminemia (2.3g/dL), and symptomatic anemia (hemoglobin 7.3g/dL) requiring transfusion. EGD and colonoscopy were notable for mildly active enteritis, and multiple ulcerations that appeared to be along staple lines with minimal luminal narrowing in the small bowel. Workup revealed no stool pathogens, no coagulopathy, and no evidence of portal hypertension on ultrasound. Over the next 2 months she had persistent hypoalbuminemia and 3 more episodes of acute hematochezia, eventually requiring blood transfusion when hemoglobin reached 6.3g/dL. During this time she was treated with the maximum dose of sulfasalazine, rotating courses of antibiotics for SBBO (duodenal aspirate cultures grew greater than 10^{10} *Citrobacter* species and 10^6 *Klebsiella pneumoniae* sensitive to gentamicin and metronidazole), and luminal steroids (budesonide 1 mg mixed as slurry and given via G-tube once daily). Her hematochezia persisted despite these interventions, prompting a 3-month trial of bowel rest (clear liquids only) and full PN support. During this period, she had occult but not gross fecal blood, her hemoglobin improved from 9.0 to 11.2 g/dL, and her albumin increased from 3.4 to 4.2g/dL. Her hemoglobin has remained stable after the re-incorporation of bland solid foods.

2.2 Case 2

Patient 2 was a female born by cesarean section at 34 weeks gestation following preterm labor and concern for bowel obstruction on prenatal ultrasound. On her first day of life, she was found to have malrotation and jejunal atresia and underwent primary anastomosis of 10 cm of proximal jejunum to a microcolon. She had intermittent fecal occult blood and anemia, but no blood transfusions prior to her STEP operation.

She underwent STEP and stricturoplasty at 5 months of age for poor enteral feeding tolerance and dilated small bowel proximal to her jejunocolic anastomosis. Five staple firings of a 3.5 mm GIA stapler lengthened her small bowel from 24.5 cm to 35.5 cm as measured from the pylorus and decreased the caliber from 3.5 cm to 1.5 cm. The apex of each staple line was reinforced in a figure-of-eight fashion with an absorbable monofilament suture.

Over the following 6 months, enteral feeds were gradually advanced using a combination of elemental formula and solid foods, though she remained PN dependent. At age 10 months she was receiving 44 kcal/kg/day enterally (solid food and an elemental formula) and 65 kcal/kg/day parenterally when she developed anemia (hemoglobin 6.3g/dL) requiring transfusion. She had occult but not gross fecal blood. Workup showed no coagulopathy and

a negative Meckel's scan. EGD and colonoscopy were unrevealing. One month later she had recurrent anemia requiring blood transfusion and was empirically started on sulfasalazine (30 mg/kg/day daily divided in three doses) and antibiotics (metronidazole) for SBBO.

After a 7-month period of stability with increasing enteral intake, her formula was advanced from elemental to semi-elemental and sulfasalazine was discontinued. Shortly thereafter, worsening anemia (hemoglobin 6.6g/dL) and hypoalbuminemia (2.6g/dL) were noted, prompting a return to elemental formula and repeat endoscopy. Colonoscopy was grossly negative including a normal appearing anastomosis. Biopsies revealed focal acute inflammation in the ascending colon. Gentamicin replaced metronidazole for SBBO in response to culture and sensitivities of duodenal aspirates (10^7 *Citrobacter* species and *Klebsiella pneumoniae*). She again stabilized for a few months only to relapse with anemia, hypoalbuminemia, fecal occult blood, and one episode of gross blood per gastrostomy. This prompted re-initiation of sulfasalazine and eventually, 5 transfusions of packed red blood cells over 3 months (age 27–30 months, 22–25 months after STEP). Repeat endoscopy showed a non-bleeding gastric ulcer, localized congested mucosa in the duodenum and 2–3 anastomotic ulcers along presumed STEP staple lines (Figure 1). Her ultimate management included rotating courses of antibiotics for SBBO treatment (metronidazole and gentamicin, then later ciprofloxacin and sulfamethoxazole based on duodenal aspirate culture growing 10^9 *Klebsiella pneumoniae* and *E. coli*), mesalamine, acid suppression therapy, and luminal steroids (budesonide). She underwent endoscopic clipping of 2 identified ulcers in the small bowel. Despite these interventions, she continued to require blood transfusions and was therefore prescribed partial bowel rest (cessation of formula by mouth and gastrostomy with continued intake of oral solid foods) and full PN support at age 31 months. Despite continued occult fecal blood, she has had a stable anemia (hemoglobin 9.6–11.1 g/dL) without need for further transfusion.

2.3 Case 3

Patient 3 was a female born following induction at 35 weeks gestation given prenatally diagnosed gastroschisis. At birth she was found to have a scaphoid abdomen with necrotic bowel loops emanating from a pinpoint umbilical defect. She underwent immediate exploratory laparotomy with resection of nonviable intestine and primary enterocolostomy with 14 cm small bowel remaining measured from the pylorus. Her course was complicated by IFALD for which she received parenteral omega-3 fatty acids.

She underwent STEP at 3 months of age for failure to progress beyond trophic enteral feeds and presence of a dysmotile, significantly dilated small bowel. Eight GIA staple-firings increased her intestinal length from 48 cm to 60 cm with a 2 cm luminal channel. The apex of each staple line was reinforced in a figure-of-eight fashion with an absorbable monofilament suture.

Over the next 2.5 years, she remained PN dependent but was able to tolerate jejunostomy tube feeds and some oral intake with 66 kcal/kg/day as enteral nutrition and 50 kcal/kg/day as PN.

At 33 months, she presented with bloody stools and a down-trending hemoglobin to a nadir of 6.2g/dL prompting transfusion of packed red blood cells and ultimately 3 hospital admissions. Persistent hypoalbuminemia was also noted (low of 2.2g/dL). Workup revealed no stool pathogens, no coagulopathy, and no evidence of portal hypertension on ultrasound. EGD and colonoscopy revealed chronic duodenitis and diffuse moderate inflammation in the distal small bowel and proximal colon. No ulcers were noted in the examined bowel. Eosinophilic infiltration was seen in duodenal and cecal biopsy specimens. Peripheral eosinophilia was also noted, with up to 21% eosinophils on differential blood count. Skin prick tests to casein and milk were negative.

Initial therapy consisted of a sulfasalazine and empiric antibiotics for SBBO (enteral vancomycin 1 week/month). In response to culture and sensitivities of duodenal aspirate, which grew greater than 10^5 E. coli and Klebsiella pneumoniae, the antibiotic was changed to enteral gentamycin. Despite continued loss of gross blood with each stool after these interventions, her hemoglobin remained stable and no further transfusions were required. Enteral budesonide (1mg slurry daily via gastrostomy) was initiated followed 3 weeks later by resolution of gross bleeding. After 6 months on this regimen without blood loss, budesonide was stopped without relapse of hemorrhage. During this period, her oral and enteral feeds continued to advance.

2. Discussion

In this series, 3 patients underwent STEP for poor enteral tolerance with a dilated small bowel and developed gastrointestinal hemorrhage requiring transfusion between 5 and 30 months postoperatively (Table 1). In two patients, endoscopy showed STEP staple line ulcers, though multiple endoscopies were required to make the diagnosis. The third had eosinophilic enterocolitis without clear evidence of staple line ulcers. All patients were treated with antibiotics for SBBO, a 5-aminosalicylic acid (5-ASA) agent (sulfasalazine or mesalamine), and luminal steroids, but those with bleeding from staple line ulcers resolved only after periods of bowel rest. These patients represent 13% (3/23) of children undergoing STEP at this institution.

GI bleeding after STEP has been described in three patients in the literature and details were provided for two.^{5,17-19} One report described a 14 year old patient who developed gastrointestinal hemorrhage 8 months after STEP that was refractory to medical therapy including 5-ASA, antibiotics, and luminal and systemic steroids. Colonoscopy and capsule endoscopy showed ulcers along the lengthened segment. This patient required laparotomy with push enteroscopic assistance and each of the 7 ulcers along the staple lines was locally excised and the defects were repaired primarily.¹⁸

A 10 month old boy from the same institution had gastrointestinal bleeding after STEP that required transcatheter embolization. He had a history of gastroschisis and intestinal atresia and underwent STEP for malabsorption, PN dependence, and SBBO. Six months later, he presented with sudden onset of gross blood from his gastrostomy and sigmoid colostomy. At the time he was tolerating 60% of his calories enterally and was on parenteral omega-3 fatty acids for IFALD. His hemorrhage was unresponsive to intravenous pantoprazole and

octreotide, prompting urgent upper endoscopy and colonoscopy, which revealed only gross blood throughout the gastrointestinal tract without a clear source. Angiography localized intraluminal extravasation within the lengthened segment of small intestine. The vessel was selectively embolized successfully without need for further treatment.¹⁹

In the 2 previously reported patients and 2 of 3 presented here, the source of hemorrhage was identified as ulceration along the lengthened (STEP) segment. Bleeding in all 4 occurred months after surgery. All remained on PN, but had significant enteral intake at the time of their presentation. Though anastomotic ulcers are classically thought to result from ischemia,²⁰ the specific etiology in these cases is unclear. Tissue was available only from the patient in the previous case report who required resection. In that case, histology revealed no specific etiology (no ischemia, vasculitis, infection, inflammatory bowel disease, or malignancy).¹⁸ In the current series, all patients had duodenal aspirate culture data that supported a diagnosis of SBBO. However, treatment of this factor alone did not ameliorate the hemorrhage. Anti-inflammatory treatment (5-ASA and luminal steroids) may have reduced blood loss. Bleeding resolved only after the cessation of enteral feeding, suggesting that mechanical sheer forces or food allergy could have contributed. While relative ischemia along the staple lines may be an underlying factor, the specific etiology of such hemorrhage remains unclear and is likely multifactorial.

In case 3, eosinophilic enterocolitis, rather than staple line ulceration, appeared to cause her hemorrhage. Clinically, patients with this disease may have a history of atopy manifested as seasonal allergies, food sensitivities, eczema, or asthma. The mucosal form of the disease is the most common and results in symptoms such as vomiting, abdominal pain, diarrhea, fecal blood loss, anemia, protein losing enteropathy resulting in hypoalbuminemia and weight loss. Diagnosis is made by a combination of clinical factors and the presence of increased eosinophils on endoscopic mucosal biopsy. Treatment of eosinophilic enterocolitis involves removal of the offending agents if possible, with provision of an elemental diet to limit allergen exposure for some patients. Topical (luminal) glucocorticoid therapy may be needed, followed by systemic steroids if necessary.²¹ This alternative cause of gastrointestinal bleeding highlights the importance of having a wide differential diagnosis and completing a thorough investigation for hemorrhage in patients with intestinal failure.

Since evidence regarding the workup of a post-STEP patient with gastrointestinal bleeding is limited, the authors recommend a similar algorithm used for otherwise healthy children or those with intestinal failure and no history of STEP. In the setting of occult or gross blood loss and hemodynamic stability, evaluation should include a careful history and physical examination, complete blood count with differential, coagulation panel, and stool studies for infectious etiologies. Endoscopy is essential along with biopsies and duodenal aspiration for culture. It should be noted that multiple repeat endoscopies were required to make a diagnosis in the patients presented. In those with a history of liver disease, ultrasound to evaluate for portal hypertension may be helpful. Allergy testing may be of benefit for a subset of patients.

For stable patients with staple line ulceration after STEP, a trial of outpatient medical therapy is appropriate. The authors recommend empiric treatment for SBBO and

inflammation with antibiotics and a 5-ASA agent, use of which can be tailored based on specific endoscopic findings and culture data. Luminal or systemic steroids have been used in cases of severe inflammation,^{22,23} though the effect of these in the setting of staple line ulceration is less clear. Ultimately, a period of enteral feeding suspension may be required. Continued dependence on transfusions after these therapies may be an indication for surgery.

Gross bleeding with hemodynamic instability or rapid transfusion dependence warrants urgent intervention. If endoscopy cannot visualize or control the source, angiography and/or operative intervention may be required. Laparotomy with the assistance of push enteroscopy has been effective in stemming hemorrhage without substantial resection.¹⁸ Alternatively, angiography may allow localization and embolization without tissue disruption.¹⁹

Since the process leading to hemorrhage is poorly understood in these patients, predicting which patients will have this problem is difficult. In reviewing these patients, no specific technical factors regarding STEP appeared to set them apart from other children undergoing the operation. Thus no changes or specific caveats regarding operative technique can be recommended.

3. Conclusion

In this series, gastrointestinal hemorrhage requiring transfusion was seen in 3 of 23 patients (13%) months to years after STEP. No technical factors at operation distinguished these patients. All were on partial enteral feeds at diagnosis. Workup with repeat endoscopy revealed staple line ulceration in 2 patients and eosinophilic enterocolitis in the other. All patients stabilized without operation: those with staple line ulceration required a period of bowel rest and the patient with eosinophilic enterocolitis appeared to respond to luminal steroids. Gastrointestinal bleeding after STEP in patients with intestinal failure may occur from a variety of etiologies and warrants a workup similar to other patients with some specific considerations. A trial of medical therapy is reasonable and may be helpful for those who remain clinically stable. Further study is needed to specifically delineate the etiology and optimal therapy for this complication.

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Figure 1.
Endoscopic images showing ulcers along lengthened (STEP) small intestinal segment in Case 2.

Table 1

Summary of patients.

	Case 1	Case 2	Case 3
SBS Diagnosis	Vanishing gastroschisis/atresia	Malrotation and atresia	Gastroschisis
Age at STEP (months)	4.5	5	3
Preoperative Small Intestinal Length (cm)	44	24.5	48
Postoperative Length (cm)	89	35.5	60
Number of Stapler Firing	15	5	8
Months between STEP and GI bleed	1, 22	5	30
Albumin nadir (g/dL)	2.6	2.3	2.2
Hemoglobin nadir (g/dL)	6.3	6.3	6.2
Transfusions (number)	2	7	1
Etiology	Ulcers along STEP staple line	Ulcers along STEP staple line	Eosinophilic enterocolitis
Treatment	Antibiotics 5-ASA Luminal steroids Bowel rest	Antibiotics 5-ASA Gastric acid suppression Luminal steroids Endoscopic clipping Bowel rest	Antibiotics 5-ASA Luminal steroids
Outcome	Stable hemoglobin without gross hemorrhage	Stable anemia without gross hemorrhage	Stable hemoglobin without gross hemorrhage