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# Anastomotic ulcers in short bowel syndrome: New suggestions from a multidisciplinary approach☆,☆☆

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ABSTRACT

*Background and aims:* Anastomotic ulceration (AU) is a rare potential life-threatening complication that may occur after intestinal resection. The diagnosis is often delayed after a long-lasting history of refractory anemia. The pathogenesis remains unknown and there are no established therapies. The aim of the study was to analyze the medical history of children with short bowel syndrome (SBS) who were experiencing AU.
*Methods:* Records of SBS children were retrospectively reviewed. Demographics, baseline characteristics, presentation, diagnosis and treatment of AU cases were analyzed.
*Results:* Eight out of 114 children with SBS were identified as having AU. Mean gestational age was 32.5 weeks. Underlying diseases were: 5 necrotising enterocolitis, 2 gastroschisis and 1 multiple intestinal atresia. The mean age at AU diagnosis was 6.5 years (diagnosis delay of 35 months). All but 2 patients had AU persistency after medical treatment. Endoscopic treatment (2 argon plasma coagulation; 1 platelet-rich fibrin instillation; 2 endoscopic hydrostatic dilations) was effective in 3 out of 5 children. Surgery was required in 3 patients.
*Conclusions:* Severe bowel ischemic injury, especially in preterm infant, could predispose to AU development. Medical treatment showed discouraging results. We firstly described that different endoscopic treatment could be attempted before resorting to further surgery.
*Level of Evidence:* IV.



Short bowel syndrome (SBS) is the most common cause of intestinal failure in childhood. It is a malbsorptive condition following extensive surgical resection of the small bowel causing inability of the gastrointestinal tract to sustain nutrient and hydratation status requiring total or partial parenteral nutrition (PN), to maintain health and/or growth [1]. In the majority of cases, SBS originates during the neonatal period (80% of SBS patients) and its incidence varies from 0.02–0.1% among the all live births, to 0.7% among very low birth weight neonates [2–4]. The leading causes of SBS are necrotising enterocolitis (NEC), intestinal atresia, gastroschisis, and extensive intestinal aganglionosis [5]. Advances in neonatal intensive care, nutrition support and innovative surgical techniques coordinated in a multidisciplinary setting have improved the outcome of children affected by SBS [6,7]. Mortality rates falling from 20 to 40% to 10% in more recent studies [6,7]. Mortality and outcomes are historically linked to the length of residual bowel, the absence of the ileocecal valve, the inability to achieve enteral autonomy and complication related to long-term PN such as sepsis and chronic liver disease [5–8]. Anastomotic ulceration (AU) is a rare and potential life-threatening complication in patients affected by SBS, which may occur insidiously as a chronic anemia or as severe bleeding even after several years of intestinal resection and anastomosis [9,10].

Limited data have been published on AU and there are no definitive therapeutic indications for its management. Both medical and surgical therapeutic strategies have been attempted, but variable and often discouraging results were obtained [9–19].

We describe a series of children with neonatal SBS who have experienced AU. The aim of this case series was to critically analyze our experience in order to provide new possible steps toward understanding, diagnosis and treatment of this rare condition.

## 1. Patients and methods

Medical records of 114 children with SBS referred between 1995 and 2015 to the Intestinal Failure Rehabilitation Groups at Bambino Gesù

*Abbreviations:* APC, argon plasma coagulation; AU, anastomotic ulceration; EGF, epidermal growth factor; EHD, endoscopic hydrostatic dilations; ICV, ileocecal valve; LILT, longitudinal intestinal lengthening and tailoring; NEC, necrotising enterocolitis; PN, parenteral nutrition; PPI, proton pump; PRF, platelet-rich fibrin; pt, patient; SBS, short bowel syndrome; SIBO, small intestinal bacterial overgrowth; WCE, wireless capsule endoscopy.

☆ Case Series With no Comparison Group IV.

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Children's Hospital in Rome, Italy and to the Pediatric Department at Saint Luc Hospital, Université Catholique De Louvain in Brussels, Belgium were reviewed. The study was conducted under the approval of the institutional review board (IRB number 201503 × 003572) at the Bambino Gesù Children's Hospital of Rome.

Detailed data of patients (pts) with SBS experiencing AU were collected: demographics and baseline disease characteristics as well as clinical presentation, diagnosis, treatment of AU cases and their outcome were carefully analyzed.

Patients were defined as having SBS when intestinal failure resulted from surgical bowel resection leading to loss of intestinal length below the minimal amount necessary for the absorption of nutrients to maintain a normal nutritional status. Children included in our study underwent resection of ≥50% small bowel length according to age-adjusted reference value, or showed ≥60 days of PN dependence with history of intestinal resection.

All AU cases were detected endoscopically during the SBS children's workup for chronic or acute anemia. Endoscopic assessments were performed under deep sedation or general anesthesia according to the standard hospital procedures. Endoscopic equipment were: Olympus GIF Q165 or 160, PCF 160 or 180, SIF Q 140 (Olympus, Tokyo, Japan). Wireless Capsule Endoscopy (WCE; SB2 PillCam, Given Imaging, Yoqneam, Israel) and advance delivery capsule device (US Endoscopy, Mentor, Ohio, USA) were used according to the manufacturers' instructions.

In case of active AU bleeding a therapeutic endoscopy approach with argon plasma coagulation (APC; ERBE APC System, Marietta, Ga, USA) or autologous platelet-rich fibrin (PRF) instillation (Vivostat PRF®, Borupvang, Alleroed, Denmark) was used.

Endoscopic hydrostatic dilations (EHD; G-Flex, 12–15 mm, Atlanta, Ga, USA) were performed in presence of narrow stricture at the anastomotic site.

Surgery was reserved in case of medical and endoscopic treatment failure.

Positive outcomes were defined as a stable increase in hemoglobin levels with fecal occult blood disappearance and no further need of blood transfusions or iron replacement during the follow-up.

## 2. Results

Of 114 patients affected by SBS, 8 children (7%) were identified as having AU. Demographic and baseline disease characteristics are summarized in Table 1, while clinical presentation, diagnosis, treatment and outcome are detailed in Table 2.

### 2.1. Demographics and baseline disease characteristics

Five out of 8 children were male. Mean gestational age was 32.5 weeks (range 30–38 weeks) and median birth weight was 1988.7 g (range: 1500–3650 g). All but one patients were preterm (<37 weeks), two of them were very preterm (<32 weeks).

Causes leading to SBS were: five necrotizing enterocolitis (NEC; pts. 2, 3, 4, 5 and 8), two gastroschisis complicated by bowel ischemia (midgut volvulus of gastroschisis: pt. 1; vanishing gastroschisis: pt. 6) and one multiple intestinal atresia complicated by volvulus (pt 7). The median age at first resective surgery was 10.3 days of life (range 1–40 days). All anastomosis were end-to-end type and they were made by interrupted absorbable sutures (5 ileocolonic, 2 ileoileal and 1 colo-colonic). The mean residual intestinal length was 58.4 cm (range 27–120 cm). Ileocecal valve was preserved in 3 patients. Mean residual colon length was 87.5% (range 50%–100%).

Three patients underwent further surgical procedures because of severe bowel dilatation proximally to AU site: one underwent longitudinal intestinal lengthening and tapering (LILT) procedure (pt 6), one had simple tapering (pt 4), and the last one had partial resection (pt 3).

All patients required PN for a median time of 21.3 months (range: 2–51 months). At the time of the data collection, 2 patients were still on PN (pts 5 and 6).

### 2.2. Revealing symptoms and signs of AU

Clinical history of seven out of 8 children showed a chronic iron-deficiency anemia refractory to oral iron supplement. Four of them presented a chronic occult gastrointestinal bleeding revealed by a positive fecal occult blood test while the other 3 children experienced also a sentinel episode of acute gastrointestinal bleeding (1 melena, 2 rectal bleeding) leading to hemodynamic instability. One patient had a sudden onset life-threatening intestinal bleeding episode requiring emergency treatment. All patients received at least one blood transfusion (1 to 3).

The median age at AU diagnosis was 6.5 years (range 12 months–18 years). The median delay between symptoms onset and AU diagnosis was 35 months (range 2–156 months).

### 2.3. AU diagnosis

In all cases, AU was identified by endoscopy: 3 ileocolonoscopy (pts 2, 3 and 8) (Fig. 1), 3 deep enteroscopy (pts 4, 5 and 7), and 2 small bowel wireless capsule endoscopy (WCE; pts. 1 and 6) (Fig. 2). The mean number of endoscopic procedures was 4.3 (range 3–6).

Similar endoscopic appearance of AU was observed in all cases: single round or oval well-delineated lesion (1 to 3 cm) surrounded by healthy mucosa localized within a few centimeters from anastomotic site (Figs. 1 and 2). Histological evaluation from endoscopic biopsies (6 patients) and surgical specimens (3 patients) showed features of non-specific inflammation characterized by polymorphous lymphocytic infiltrate.

Tagged red blood cell scintigraphy was performed in 3 children with positive fecal occult blood test (pts 4, 5 and 8); only in one case (pt 5), the scan showed an abnormal focus of increasing activity in the right iliac region evocative of a gastrointestinal bleeding. Afterward, in this patient, a WCE confirmed AU diagnosis. In two of these patients (pts 4 and 8), selective angiography was also performed, but failed to localize any source of bleeding.

**Table 1**
Demographics and disease characteristics.

| Patients | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|
| Gestational age | 33 | 30 | 32 | 31 | 32 | 34 | 38 | 33 |
| Gender | M | F | M | F | M | M | M | F |
| Birth Weight (gr) | 1830 | 1600 | 2080 | 1500 | 1500 | 2150 | 3650 | 1600 |
| Underlying condition | Midgut volvulus of gastroschisis | NEC | NEC | NEC | NEC | Vanishing gastroschisis | Intestinal atresia | NEC |
| Age at surgery (days) | 1 | 10 | 18 | 9 | 40 | 1 | 2 | 2 |
| Anastomosis sites | I-C | C-C | I-C | I-C | I-I | I-C | I-C | I-I |
| Length of remnant bowel (cm) | 60 | 100 | 27 | 35 | 30 | 35 | 120 | 60 |
| Presence of ICV | No | Yes | No | No | Yes | No | No | Yes |
| Residual colon length (%) | 70% | 100% | 90% | 90% | 100% | 50% | 100% | 100% |
| Need for PN (months) | 22 | 14 | 51 | 12 | 18 (Still on PN) | 49 (Still on PN) | 2 | 5 |
| Further surgical procedures | / | / | resection | tapering | / | LILT | / | / |

C-C, colo–colic; I-C, ileocolic; I-I, ileoileal; ICV, ileocecal valve; LILT, longitudinal intestinal lengthening and tapering; NEC, necrotizing enterocolitis; PN parenteral nutrition.