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Intestinal twin-to-twin transplant for short gut: Review of the literature and discussion of a complex case

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Abstract

Paediatric Intestinal Transplantation (IT) presents the highest mortality on the waiting-list due to anatomical disproportion. Living-Donor IT (LDIT) offers the best advantages and when performed among identical monozygotic twins, it also benefits from unique immunology. According to MEDLINE/Pubmed, twin-to-twin LDIT has been performed in seven cases (6:7 males, median age of 32 years). None of the patients received immunosuppression postoperatively. Only one paediatric twin-to-twin LDIT was carried out with a 160-cm mid-ileum tract: an interposed 4/5-cm arterial graft was required to ensure a tension-free anastomosis to the anterior wall of the infra-renal abdominal aorta. In contrast, venous anastomosis was done directly to the inferior cava vein. We present a case for debate of a 13-month-old SBS patient where a twin-LDIT was discussed with parents, who decided to wait after careful analysis and ethical considerations.

Introduction

The treatment of Short Bowel Syndrome (SBS) has developed significantly over the past 40 years. However, metabolic and surgical complications are still challenging for intestinal rehabilitation teams.[1–4] Bowel lengthening procedures have increasingly been proposed and, in selected groups of patients, Intestinal Transplantation (IT) can also be an option.[4–9] Intestinal grafts are most commonly cadaver-derived, but Living-Donor Intestinal Transplantation (LDIT) is now feasible and similar to patient and graft survival rates.[5,7,8] It provides unique advantages such as reduced waiting and ischemia time and better tissue compatibility, and it allows for adequately treating the recipient and optimizing medical conditions pre-operatively as it is a planned surgery. Unfortunately, in pediatrics, IT presents the highest mortality rate on the waiting-list because of anatomical disproportion between available organs and recipients.[5] Moreover, complications such as rejection and immunosuppression-related morbidity in pediatric age are significant because of the longer life expectancy and peculiar immune physiology. An exciting and promising field of study is identical monozygotic twin-to-twin LDIT with its unique immunological advantages.[5] We present a literature review on twin-to-twin LDIT, and we describe a complex SBS case managed by non-transplant surgery for which twin-to-twin LDIT had been considered.

Systematic Review

A systematic MEDLINE/PubMed search has been conducted (and updated to March 2022) looking for: "Twin" AND ("Bowel" OR "Intestine") AND "Transplant". A total number of 31 abstracts were retrieved and, after duplicates removal, they were screened by inclusion criteria ("English language", "twin-to-twin bowel transplantation case description") and exclusion criteria ("ex vivo, non-human or preclinical studies", "other solid organs transplantation except bowel"). Eight full-text articles were selected[10–17] and another two papers meeting inclusion and exclusion criteria were found as cited from other articles and thus included in the review.[18,19] The entire process is displayed in Figure 1. A total number of 10 articles were selected, and seven cases of twin-to-twin LDIT have been identified worldwide within the literature (Table 1).[10–19] Among the described patients, six out of seven were males, and the median age was 32 years (range 13–45). The underlying diagnosis was abdominal desmoid tumor (n=1), post-traumatic Superior Mesenteric Vein (SMV) thrombosis (n=1), midgut volvulus (n=1), "unspecified" trauma (n=1), Churg-Strauss syndrome (CSS) (n=1), acute Superior Mesenteric Artery (SMA) thrombosis (n=1), and SMA/SMV thrombosis after gunshot wounds (n=1). All seven patients (100%) received no immunosuppression postoperatively, except for immediate prophylaxis in the CSS case. All patients underwent HLA testing to confirm the zygosity. Although the patients had variable lengths of lost bowel, all the grafts were between 110 and 200 cm, irrespectively of the age of the patient. The choice of the type of bowel and vascular anastomoses appears to be based on the specific recipient and the donor bowel segment taken. The feeding regimen was patient-tailored, although, surprisingly, Morel *et al.* did report starting enteral nutrition within the first 24 hours to promote early mucosal regeneration, while others preferred initial TPN until adequate calorie intake can be achieved orally. Schena *et al.* reported a regular diet being tolerated by Post-Operative Day (POD) 10 and Morris *et al.* described a soft diet not tolerated until POD 31.[16,17] No serious complications were noted within the described follow-up, even if both postoperative ileus and diarrhea might be expected. Moreover, good results were reported following surgery for recipients and donors, despite occurrence of the same desmoid tumor of the twin in the donor one year after IT. Only one pediatric twin-to-twin LDIT was carried out with a 160-cm mid-ileum tract:[11–13] an interposed 4/5 cm arterial graft of the recipient's right superficial femoral artery was required to ensure a tension-free anastomosis to the anterior wall of the infra-renal abdominal aorta. The venous anastomosis was done directly to the inferior cava vein. The bowel graft was proximal to the third portion of the duodenum and distally to the transverse colon. No immunosuppression was administered, and the patient was discharged on the POD 53 on a regular diet. He was also followed-up for five years following the operation.[11]

Case Report

We present a case for debate of a 13-month-old SBS patient in whom twin-LDIT was an option in light of these previously reported cases.

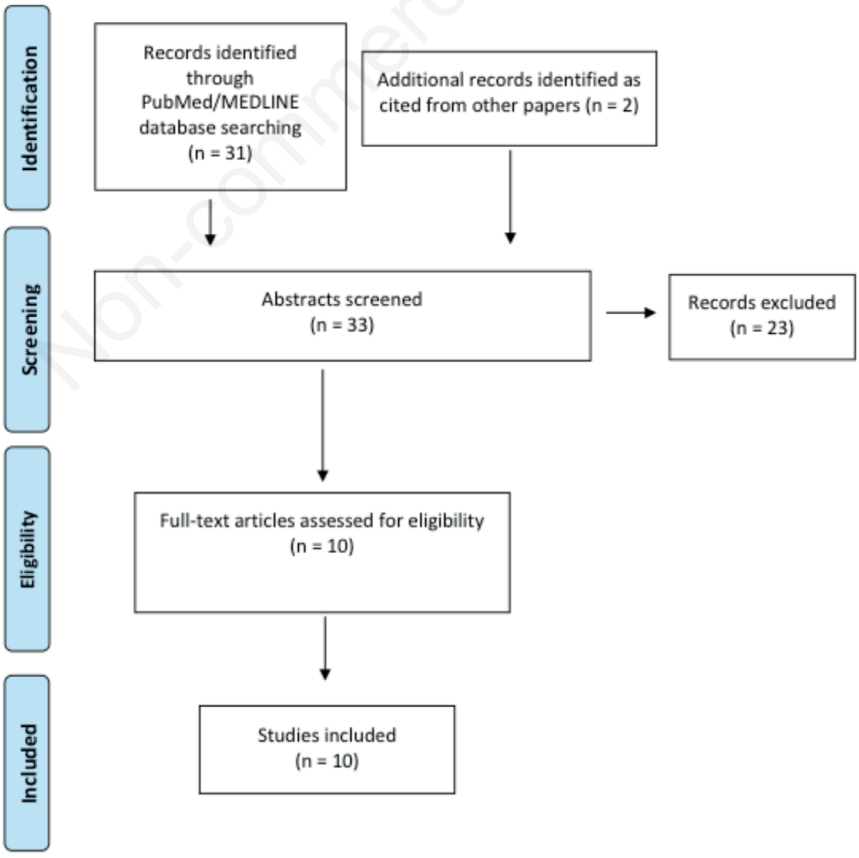

Figure 1. Flow chart showing the systematic review process: 10 full-text articles have been included.

Table 1. Previously published cases of twin-to-twin living-donor intestinal transplants have been identified within the Pubmed literature. Abbreviations: CSS: Churg-Strauss Syndrome, ICV: inferior cava vein, SBS: short bowel syndrome; SMA: superior mesenteric artery, SMV: superior mesenteric vein, TPN: total parenteral nutrition, PN: parenteral nutrition, PO: per os, POD: postoperative day.

	1995, Morris[17] 1999, Busch[10]	1997, Calne[19]	2000, Morel[13] 2003, Genton[12] 2004, Berney[11]	2001, Cicalese[18]	2006, Schena[16]	2018, Wu[14]	2018, Gheza[15]
Country	Stanford California (USA)	Cambridge (UK)	Geneva (Switzerland)	Chicago Illinois (USA)	Chicago Illinois (USA)	Xi'an (China)	Chicago Illinois (USA)
Recipient Age (years/sex)	31/male	40/male	13/male	27/male	33/male	45/female	32/male
Donor	Twin brother/Monozygotic	One identical triplets	Twin brother/Monozygotic	Twin sister/6 antigens HLA matching	Twin brother/Monozygotic	Twin sister/monozygosity	Twin brother/Monozygotic
Cause of SBS	Mesenteric desmoid tumour	SMV thrombosis post tibia	Appendectomy fracture complicated by midgut volvus	Trauma	CSS	Acute SMA thrombosis	SMA/SMV thrombosis following gushot
Viable recipient bowel	Duodenum and descending colon	60 cm of jejunum and colon	Duodenum, transverse descending colon		5 cm proximal jejunum, 10 cm terminal ileum, colon	15 cm jejunum, transverse and left colon	Duodenum and colon
Graft	106 cm, distal ileum with ileocecal valve	150 cm, distal ileum	160 cm, midileum	200 cm, distal ileum	200 cm, distal ileum	155 cm, distal ileum	200 cm, distal ileum
Vascular anastomoses	Venous end-to-end and arterial end-to-side anastomoses (ileocolic vessels and superior mesenteric vessels)	Mesenteric vessels to aorta and ICV with interposition of 7-cm saphenous vein graft	Mesenteric vessels to ICV and infrarenal aorta with interposition of 5-cm of the right femoral artery graft			End-to-side distal SMA and SMV to aorta and ICV	Mesenteric vessels (extended by deceased donor iliac artery graft) to right common iliac artery and ICV
Bowel anastomoses	End-to-side ileum and caecum to native duodenum and descending colon	Ileum to duodenum and ascending colon	Ileum to third portion of duodenum and transverse colon			Ileum to the jejunum (side-to-side) and to transverse colon (end-to-side)	
Additional intraoperative details	Gastrostomy	Ileostomy	No ileostomy			Ileostomy	
Post-transplant	POD 31: soft diet tolerated POD 58: discharged	Started to eat normally after 3 weeks	POD 15: enteral nutrition started POD 21: eating PO POD 53: dicharged on a regular diet		Uneventful; POD 10: regular diet tolerated	Uneventful POD 12: eating normally and off-PN	POD 7: regular diet tolerated
Complications	POD 4: Culture-negative sepsis-like syndrome. Bowel frequency and perianal skin irritation. Nausea and bloating	No bowel function for 3 weeks	POD 34: SAureus right jugular septic thrombophlebitis POD 36: Thrombectomy	CMV gastritis			
Immunosuppression	None	None	None	FK506, ATG, Steroids	Recurrent CSS prophylaxis (Prednisone + Cyclophosphamide)	None	None
TPN discontinuation	Few weeks after discharge		POD 34	"Weaned"		"Weaned"	
Donor conditions	POD 5: discharged In 1996: diagnosed with an abdominal desmoid tumour	"Recovered"	"No complications"		POD 3: discharged Well at 27-month follow-up	POD 4: discharged	POD 12: discharged
Follow-up	3 years: TPN free. No recurrence of the desmoid tumour		5 years: caught up with brother's height and fat free mass, though lower body fat mass and femoral bone mineral densities	36 months: TPN free	27 months: unrestricted diet	5 years: TPN free	9 months: "regular lifestyle"

She was born at 36 weeks gestational age, and her birth weight was 2380 gr. Her past clinical history included an emergency laparotomy for midgut volvulus at seven days of life with total slight bowel loss from the duodenum (D3) to the mid-transverse colon, which was noted at emergency laparotomy. At that time, proximal and distal tube stomas have been placed to allow recycling of the stoma in the attempt of stimulating mucosal absorption. The length of the viable bowel was limited to 2/3 of the colon. At 7 months of age, the patient underwent a second procedure with anastomosis between the duodenum (D3) and proximal transverse colon. A tube stoma was performed to both prevent skin damage from the duodenal secretions and hopefully allow eventual further management. The postoperative period was complicated by perforation of the anterior wall of the proximal stoma and subsequent dehiscence requiring suturing. After three months, controlled tissue expansion was deemed unsuccessful, the stomas were closed and a reversed sigma segment was interposed At laparotomy, the proximal transverse colonic tract was found to have a "jejunal-like" macroscopic appearance, indicating that it acquired features allowing nutritional absorption. Unfortunately, no further clinical improvement was noted, and the patient remained on 7/7 nights TPN. Given that the patient had a monozygotic twin sister, a twin-to-twin LDIT was considered and discussed with the parents. After careful analysis and ethical considerations, the parents decided to postpone as they were not ready for the decision.

Discussion

SBS survival has increased significantly over the last decade thanks to multidisciplinary Intestinal Rehabilitation Programs (IRP).[1] Long-term TPN may lead to complications such as Intestinal Failure-Associated Liver Disease (IFALD) or central venous access loss for patients who fail to improve intestinal function. To restore an adequate intestinal length and achieve enteral autonomy, many surgical lengthening techniques are available based on the anatomical status of the patient.[1]

The twin-to-twin LDIT is an interesting and promising option carrying significant advantages. The most notable is avoiding immunosuppression therapy and its associated side effects. Moreover, living-donor transplants allow the operation to be performed at the optimal time for both recipient and donor.

According to the authors, reported concerns are those related to the living-donor associated morbidity and mortality since the healthy twin may run into trouble later. Morris reported the donor himself being diagnosed with an abdominal desmoid tumor later in life. This highlights the uncertainty of long-term outcomes for the donor and the family. Furthermore, LDIT intraoperative technical peculiarity is ensuring that the donor bowel has adequate vessels to perform an anastomosis and, at the same time, maintaining a good donor blood supply. According to the reports, this might be overcome by using a third-generation branch of the superior mesenteric vessels.

Among twin-LDIT published cases, only one was in pediatric age: a 13-year-old male with history of midgut volvulus complicating an appendectomy. A 5-year follow-up has reported an impressive outcome (Table 1). We believe that in cases like the one we are facing, an early twin LDIT, with no immunosuppression, may carry significant advantages such as preventing morbidity and mortality associated to TPN and recurrent line infections, thus reducing the risk of sepsis and abolishing the need of a future liver transplant. Since the patient is in stable conditions, parents' choice was that one of delaying the transplant option to the future. Otherwise, we would have been required to harvest a 50-80 cm distal ileum which, according to our experience, would have allowed enteral autonomy and weaning off TPN. The main issue we encountered was that, from an ethical point of view, parents and physicians must face the eventuality of risking the donor child health. In fact, it has been debated that the recipient child might be given other treatments while siblings get older before undertaking the operation. Though, this risks the complications of long term TPN, such as the need for a combined liver/bowel transplant. In conclusion, early twin LDIT is an interesting and promising option to achieve enteral autonomy and lower SBS morbidity, without the immunosuppression adverse events. While the available literature on seven cases provides some guidance, the best method of treating SBS children not amenable of non-transplant surgery will only be determined after trialing treatments. Ethical issues must be discussed with the family, but the decision ultimately lies with the parents within the legal limitations of the country concerned.

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