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Treatment of Complex Desmoid Tumors in Familial Adenomatous Polyposis Syndrome by Intestinal Transplantation

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Background. Desmoid tumors are fibroblastic lesions which often have an unpredictable and variable clinical course. In the context of familial adenomatous polyposis (FAP), these frequently occur intra-abdominally, especially in the small-bowel mesentery resulting in sepsis, fistulation, and invasion of the abdominal wall and retroperitoneum. In selected cases where other modalities have failed, the most radical option is to perform a total enterectomy and intestinal transplantation (ITx).In this study, we present our center's experience of ITx for desmoid in patients with FAP. **Methods.** We performed a retrospective review of our prospectively collected database between 2007 and 2022. All patients undergoing ITx for FAP-related desmoid were included. **Results.** Between October 2007 and September 2023, 144 ITx were performed on 130 patients at our center. Of these, 15 patients (9%) were for desmoid associated with FAP (7 modified multivisceral transplants, 6 isolated ITx, and 2 liver-containing grafts).The median follow-up was 57 mo (8–119); 5-y patient survival was 82%, all with functioning grafts without local desmoid recurrence.These patients presented us with several complex surgical issues, such as loss of abdominal domain, retroperitoneal/abdominal wall involvement, ileoanal pouch–related issues, and the need for foregut resection because of adenomatous disease. **Conclusions.** ITx is a viable treatment in selected patients with FAP and extensive desmoid disease. The decision to refer for ITx can be challenging, particularly the timing and sequence of treatment (simultaneous versus sequential exenteration). Delays can result in additional disease burden, such as secondary liver disease or invasion of adjacent structures.

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Desmoid tumors are rare fibroblastic lesions that can occur anywhere in the body. Although they do not metastasize, they can be locally aggressive and can invade and damage surrounding tissues.[1,2] Most desmoids (85%–95%) occur sporadically, whereas the remaining 5% to 15% develop within the context of familial adenomatous polyposis (FAP).[3,4] In the latter group, desmoid formation is strongly associated with particular genotypes, family history, and surgical trauma.[5]

There are significant differences between sporadic and FAP-associated desmoids, but many publications often combine them. The desmoids that occur in FAP tend to be larger and more frequently occur intra-abdominally,[4] particularly in the small-bowel mesentery, where small areas of fibromatosis can progress, thickening and puckering the mesentery and, in some cases, progressing to form a large mass.[6] Since the advent of prophylactic colectomy, ameliorating the risk of colorectal cancer, intra-abdominal desmoid disease is, along with duodenal malignancy, one of the leading disease-related causes of death in FAP.[7,8] It is also relevant that gastric adenoma and carcinoma seem to be increasing in FAP.[9]

These tumors, which predominantly arise in the small-bowel mesentery, often cause ureteric or intestinal obstruction. Central necrosis can lead to fistulation and sepsis, and infiltration of the mesentery can render surgery (eg, completion proctectomy or duodenectomy) impossible. Patients can often present with intestinal failure and

require parenteral nutrition as a consequence. As a result, despite the histologically benign nature of the tumor, the overall disease-specific mortality can be as high as 11%.[4] The Church staging system has been described that stratifies desmoids based on size of the tumor, growth rate, and associated symptoms.[10]

The majority of desmoids cease growing or even regress spontaneously, so many patients can be managed conservatively with close follow-up.[11] Treatment of growing desmoids lacks a sound evidence base, with a reported series mixing FAP-associated and sporadic desmoids, lacking controls, and not taking into account the variable natural history. A variety of agents, including non–steroidal anti-inflammatory drugs, antiestrogens, and cytotoxic chemotherapy, are used, along with radiotherapy,[12] although the use of the latter within the abdomen is limited by the proximity of radiosensitive organs. Potential advances with tyrosine kinase and γ-secretase inhibitors have yielded promising results in selected cases with advanced disease.[13,14] Despite this, some patients may require surgical excision because of the size, symptoms, and/or location of the desmoid disease.[15,16] However, surgery in desmoids is controversial because of high recurrence rate, even if wide negative margins are achieved.[17] This may be due to "new" desmoid forming because of the surgical trauma of excision, rather than true "tumor recurrence."[18] Furthermore, surgery is often very challenging because of the presence of adhesions, fistulae, and involvement of critical structures such as major vessels, ureters, bladder, or abdominal wall.[19] In addition, achieving a complete excision in this population may be impossible without a (near) total enterectomy and, thus, irreversible intestinal failure.

To address this, some centers have proposed performing an intestinal transplant (ITx) in selected cases.[20-24] The potential advantage is that this allows for a radical resection without compromising intestinal function. However, this introduces additional challenges, such as finding suitable donor organs, opportunistic infections, rejection, and the need for life-long immunosuppression. Many patients have advanced disease with infiltration of vital structures meaning that tailored surgical strategies must be implemented to allow successful resection and transplantation.

The aim of this retrospective study was to review the transplant experience in FAP patients with extensive desmoid disease at a large-volume adult ITx center with specific reference to surgical techniques to facilitate successful resections.

MATERIALS AND METHODS

We performed a retrospective review of our prospectively collected database between 2007 and 2022. All patients receiving an ITx for desmoid disease with underlying FAP were identified. Any additional required information was retrieved from electronic medical records of patients. Data missing from the electronic record were recovered from external centers or scanned documents. The stage of desmoid disease was defined according to the Church Desmoid Staging System, ranging from stage I (asymptomatic, <10 cm maximum diameter, not growing) to stage IV (severely symptomatic, septic complications, or >20 cm or rapidly growing).[10] The diagnosis of FAP was made at the referring centers based on clinical/endoscopic findings supplemented with genetic testing when applicable.[25]

The patient demographics included in the study were age, weight, gender, cause of intestinal failure (if present), parenteral nutrition, previous treatments, indication for transplantation, graft type, rejection type and treatments, and cause of death. All donors were deceased after certified brain death at the time of retrieval. Posttransplant, all patients underwent continued joint follow-up at Cambridge and their referral center.

Graft types were divided according to the most recent classification into multivisceral grafts (multivisceral transplantation [MVT]—stomach, duodenum, pancreas, liver, small bowel ± colon), modified multivisceral (modified MVT—MVT without a liver), and isolated ITx (duodenum, pancreas, small bowel ± colon).[26]

Patients' treatments were categorized into (1) simultaneous (undergoing resection followed by transplantation during the same operation) or (2) sequential (undergoing resection before transplantation).

Immunosuppression

This is described in detail previously.[27] Briefly, all patients received induction immunosuppression (alemtuzemab 30 mg and intravenous methylprednisone). A second dose of alemtuzemab was given on day 4 if there was no elevated risk of sepsis (collections, fistulas, or abdominal sepsis). For maintenance therapy, tacrolimus was started on day 2, aiming for trough levels of 8 to 12 ng/mL, which is progressively weaned down to 5 to 7 ng/mL in the next year. Additionally, methylprednisolone and either mycophenolate mofetil (500 mg twice per day) or azathioprine (1 mg/kg/d) are used.

Ethics Declaration

All patients signed informed consent forms for their data to be anonymously used for retrospective research at the time of their listing for transplantation.

RESULTS

Between October 2007 and December 2022, 144 ITx in 130 patients were performed at Addenbrooke's Hospital, Cambridge, United Kingdom. Of these, 15 (9%) were for desmoid disease associated with FAP. The median age at the time of transplant was 35 y (range, 29–52); 9 of the patients were women (Table 1). All 15 patients were diagnosed with FAP previously and 9 patients had advanced desmoid disease at the time of transplantation (Church grade 4). The remaining patients had previously undergone extensive resections because of desmoid disease. Most patients underwent preemptive pan-proctocolectomy (14/15 patients) and/or extensive enterectomy.

Ongoing Abdominal Sepsis and Loss of Abdominal Domain

Three patients were transferred to our center with active sepsis because of extensive fistulation with drains in place or a laparostomy (Figure 1). Some of them required additional percutaneous drainage and antimicrobial treatment before being eligible for transplantation.

Loss of abdominal domain/abdominal wall involvement was present in 10 of 15 patients because of extensive desmoid disease and/or previous intestinal resection. To achieve closure, these patients received nonvascularized rectus fascia in

TABLE 1.

Preoperative data

Patient number	Age	Gender	Indication for transplant	Church grade (at time of transplant)	Previous colectomy	Previous other surgeries	Ureteric involvement	Extra-abdominal involvement	On parenteral nutrition
1	37	F	Extensive desmoid disease requiring resection due to vascular compromise, large growing duodenal polyp	4	No	No	Y—left ureter (nephrectomy)	None	No
2	35	F	Extensive desmoid disease requiring resection due to ureteric compromise	4	Yes	High-defunctioning jejunostomy due to recurrence	Y—left ureter (nephrectomy)	None	Yes
3	28	M	IFALD due to SBS after resection	1	Yes	Subtotal enterectomy due to mesenteric recurrence	None	None	Yes
4	44	F	Ultrashort bowel after extensive resection	1	Yes	Subtotal enterectomy due to mesenteric recurrence	None	Chest wall	Yes
5	34	F	Extensive desmoid disease requiring resection due to symptoms, left ultrashort	1	Yes	Subtotal enterectomy due to mesenteric recurrence	None	None	Yes
6	38	F	IFALD + extensive desmoid disease requiring resection, ultrashort	1	Yes	Subtotal enterectomy due to mesenteric recurrence	None	None	Yes
7	34	F	IFALD + extensive desmoid with abdominal wall compromise and ureteric obstruction	4	Yes	Partial gastrectomy and roux-en-y reconstruction	Y—right autotransplant	Chest and abdominal wall	Yes
8	34	M	Fistulating desmoid disease with ureteric obstruction	4	Yes	Previous J-pouch reconstruction	Y—right autotransplant	Abdominal wall	No
9	37	M	Fistulating desmoid disease	4	Yes	Previous J-pouch, abscess drainage, laparostomy	None	None	Yes
10	52	F	IFALD due to SBS after resection	1	Yes	Subtotal enterectomy	None	None	Yes
11	30	F	Extensive fistulating desmoid disease requiring resection with ureteric compromise	4	Yes	Previous J-pouch, drain placement due to fistulating disease	Y—encasing the left ureter	None	No
12	34	M	IFALD due to SBS after resection	2	Yes	Subtotal enterectomy	None	None	Yes
13	35	F	Fistulating desmoid disease—abdominal wall compromised	4	Yes	No	None	None	Yes
14	35	M	Extensive desmoid disease requiring resection — abdominal wall compromised	4	Yes	No	None	None	No
15	50	M	Extensive desmoid disease requiring resection — abdominal wall compromised	4	Yes	No	None	None	No

F, female; FAP, familial adenomatous polyposis; IFALD, intestinal failure–associated liver disease; M, male; SBS, small-bowel syndrome.

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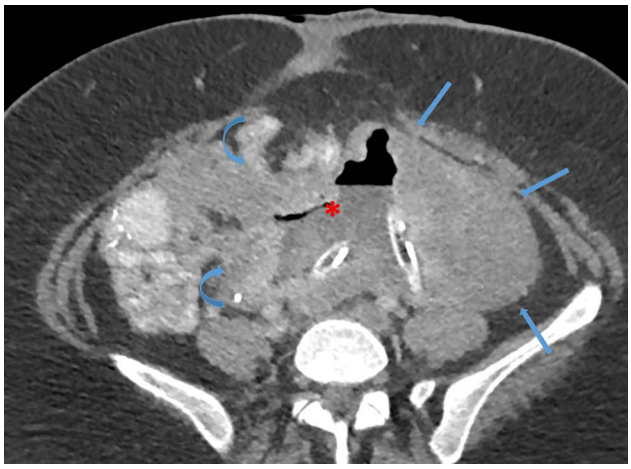

FIGURE 1. Active infection/abdominal sepsis in desmoid patient. Axial CT image demonstrating the desmoid lesion (arrows) with encasement of small bowel loops (curved arrows) and fistulation. Small-bowel content and gas centrally within the desmoid mass (asterisk). Two surgical drains within the cavity. CT, computed tomography.

8 cases, biological mesh in one, and a pedicled muscle flap in another (Figure 2).

Retroperitoneal Involvement

Eight patients had extensive desmoid disease involving the retroperitoneal structures, such as the major vessels and ureters. Depending on the level and degree of encasement of the ureters (present in 5 patients), several resection strategies were used. This ranged from extensive dissection to free the ureter from the desmoid, partial ureteric resection with ureteroureteral reanastomosis, renal autotransplantation, and native nephrectomy with allotransplantation (Figure 3).

One patient required an iliac artery and vein resection and subsequent reconstruction with donor vessels because of desmoid incasement. In another case, the desmoid mass had to be dissected off the inferior vena cava (IVC; Figure 4).

Ileoanal Pouch Issues

Three patients had desmoid disease after a prophylactic restorative proctocolectomy with ileoanal J-pouch reconstruction. This presented an additional technical problem as the native enterectomy would compromise the vascularity of the pouch, and there was often desmoid disease in the pelvis. In all 3 cases, the pouch was transected leaving a segment of the small bowel that was not perfused by the superior mesenteric artery (divided as part of the enterectomy to allow small-bowel transplantation). Furthermore, given the complexities and length of the procedure, any remnant of desmoid disease in the pelvis was left behind. Only 1 patient developed a postoperative ischemic pouch, which was treated conservatively by external drainage and antimicrobial therapy (Figure 5).

Graft Type Selection

The graft types used in our series were 7 modified MVT, 6 ITx, and 2 liver-including grafts (2 MVT; Table 2). One patient also received a renal graft from the same donor. The selection of graft type was influenced by the state of the foregut (see Figure 6). If the patient had a high adenoma polyp burden in the stomach or duodenum (as measured by the Spigelman

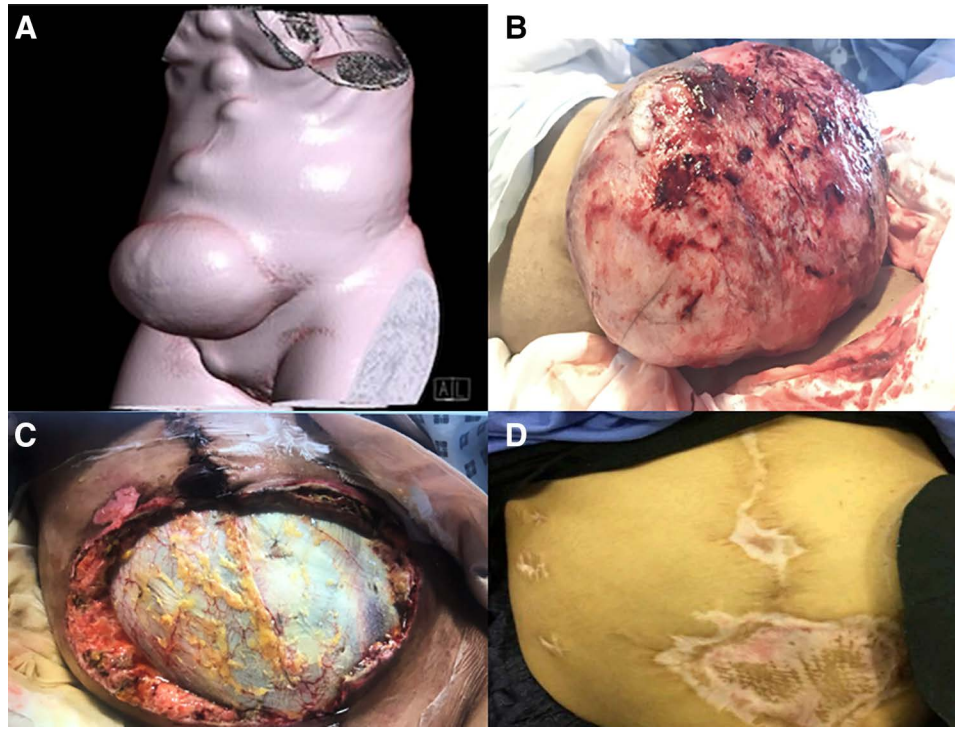

FIGURE 2. Patient presenting with an extensive desmoid disease that infiltrated the abdominal wall. The patient underwent an extensive abdominal wall/intestinal resection and received a fascia and intestinal graft: (A) extensive disease on CT reconstruction, (B) intraoperative image, (C) immediate postoperative situation, (D) status after 3 mo of vacuum-assisted closure therapy with skin graft.

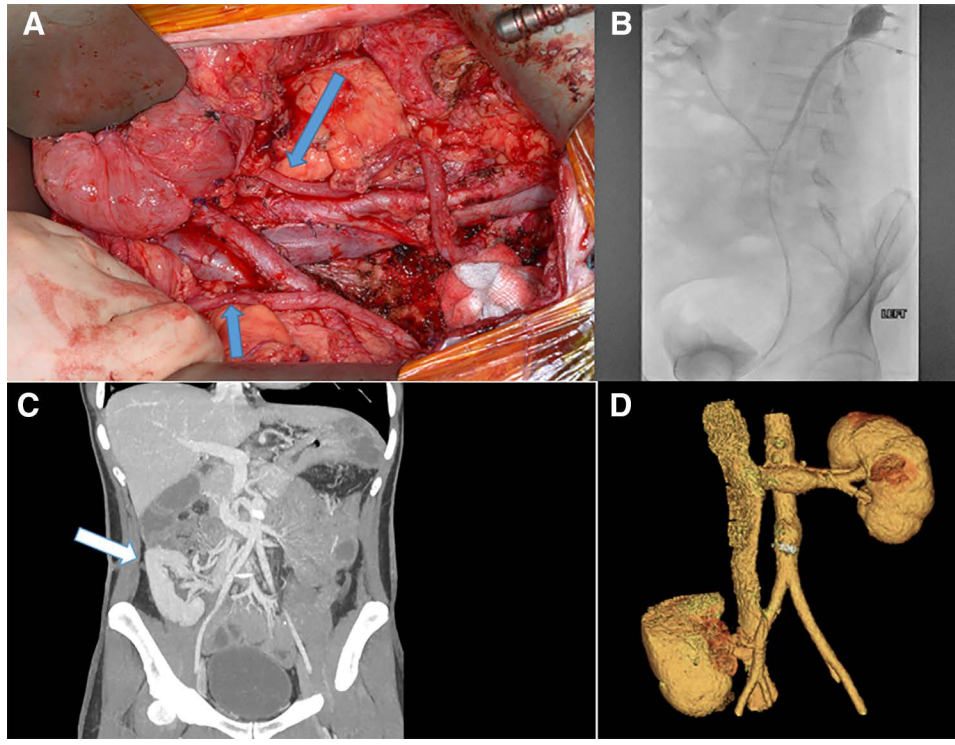

FIGURE 3. Surgical options when faced with ureteric encroachment in desmoid disease. A, Extensive dissection of the desmoid disease off the ureters (blue arrows). B, Antegrade pyelogram showing a status after a distal right ureteric resection and uretero-ureteral anastomosis due to encasement in the desmoid disease. Note the bilateral DJ stent placement. C, Right renal autotransplant in a case where remnant ureter reimplantation was not possible. D, CT reconstruction of the autotransplant case.

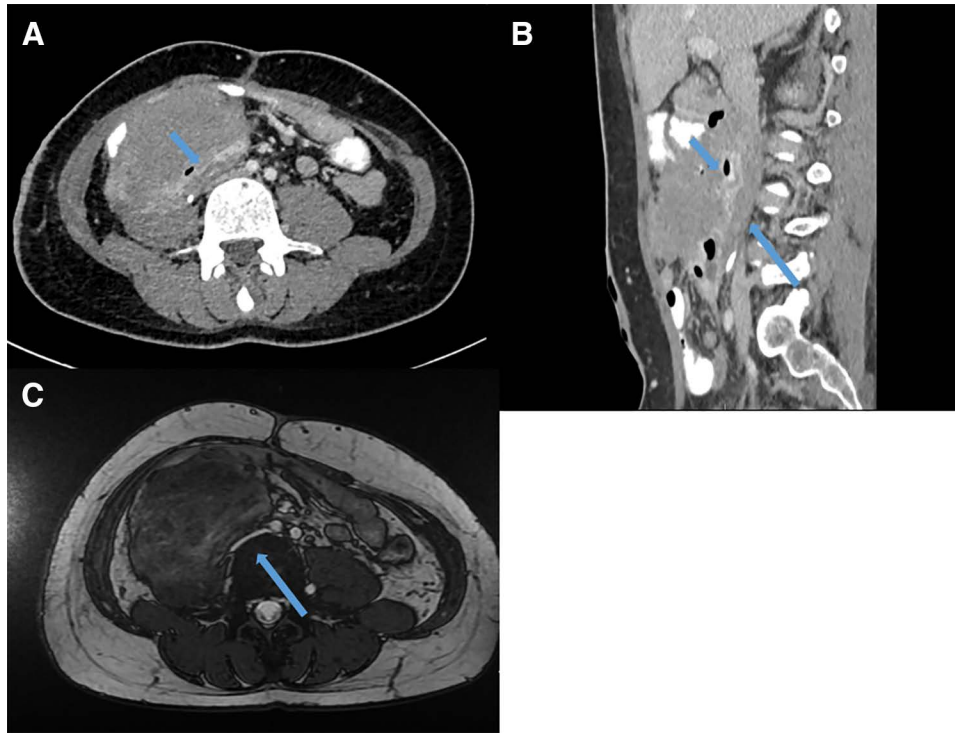

FIGURE 4. Desmoid tumor encroachment on critical structures. Axial (A) and sagittal CT (B) images as well as axial T2-weighted MRI image (C) demonstrating a desmoid mass encasing duodenum (short arrow) and abutting cava (long arrow).

score[28]), then a foregut resection with modified MVT was undertaken. Conversely, if the potential risk of development of foregut malignancy was perceived to be relatively low, the patient received an isolated ITx (with life-long endoscopic screening every 6 mo). One patient (patient 5) developed metastatic gastric adenocarcinoma 6 y after isolated ITx,

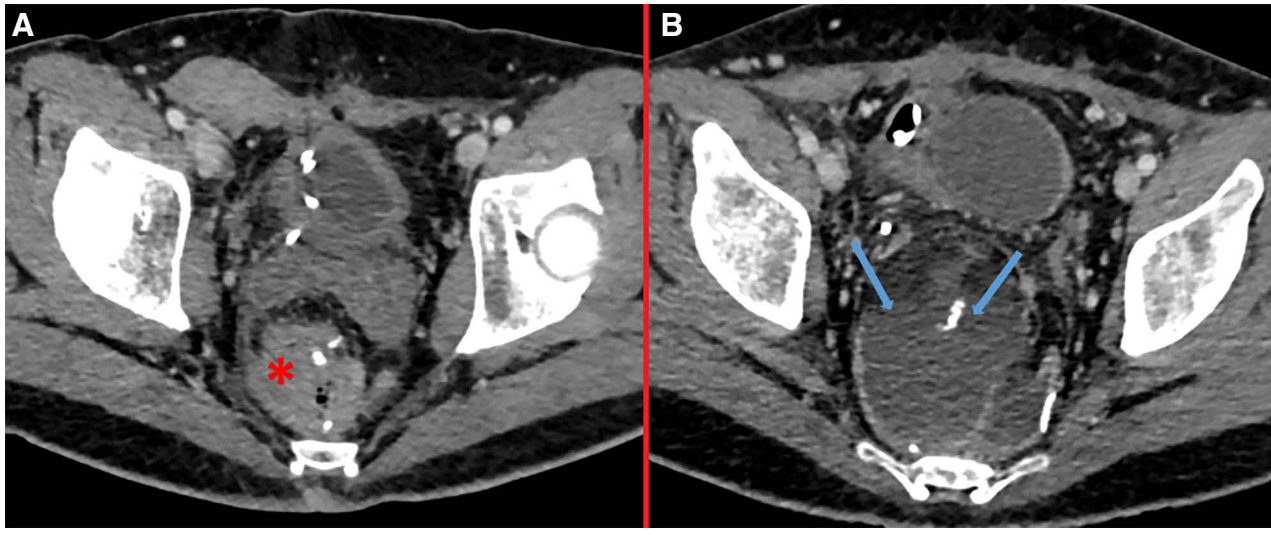

FIGURE 5. Ischemic remnant rectal J-pouch after intestinal transplantation. A, Preoperative image demonstrating the ileoanal pouch (asterisk). B, Postoperative image demonstrating poor enhancement of the anterior wall of the pouch (arrows) consistent with ischemia.

presenting as intra-abdominal adenopathy. Despite palliative chemotherapy, the disease rapidly progressed, and the patient died 3 mo after the diagnosis.

Regarding the liver, most patients had no or minimal liver disease despite some being on long-term parenteral nutrition. Hence, a liver graft was included only twice in our series. In the first case, a full MVT was performed for technical reasons to avoid the hilar dissection required in a modified MVT (patient 1). In a second case (patient 6), a full MVT was performed because of IFALD-induced grade III liver fibrosis on a pretransplant biopsy. In some patients, the desmoid encroached on the liver, but at transplant, it was successfully dissected from the surrounding desmoid disease (Figure 7).

Simultaneous Versus Sequential Transplantation

In our cohort, 5 patients underwent a sequential procedure compared with 10 patients with simultaneous resection and ITx. The sequential cases had no or low desmoid burdens at the time of ITx and underwent isolated ITx in all but 1 case (required modified MVT due to high-risk gastric polyp disease). In contrast, the simultaneous cases often had abdominal wall, retroperitoneal involvement, or uncontrollable collections at the time of ITx (Table 1). No differences were seen in patient survival between the 2 groups (Figure 8).

Desmoid Recurrence

There were no instances of desmoid recurrence intra-abdominally, either within the graft or the native gut. Three patients developed desmoids elsewhere, of which 2 required surgical resection (1 in the thoracic wall and 1 in the abdominal wall). These patients remained alive and well at the time of writing.

Overall Outcomes

The median follow-up was 57 mo (8–119). The 5-y patient survival was 82% (Figure 8). Ten of 15 patients were alive at the time of writing (67%), all with a functional graft. Five patients died since their transplantation: 1 patient from abdominal compartment syndrome many years after transplant, leading to perforation and sepsis. The other deaths were not transplant related (Table 3).

Four patients developed acute cellular rejection, 1 of which was exfoliative requiring antithymocyte globulin (patient 2). The remaining patients were treated using pulsed dose steroids.

DISCUSSION

This series represents the experience from an adult large-volume center where ITx is used as a treatment modality in selected cases of advanced desmoid disease.

The patients referred to us for ITx had significant disease burden, often presenting with fistulation and infiltration in the abdomen and/or the retroperitoneum. The majority had intestinal failure at the time of transplantation, which has been shown to be an important predictor of poor outcomes.[10] In their series, the Cleveland Clinic demonstrated that conventionally treated patients with the highest disease burden (Church grade 4) had a 70% 5-y survival and a 60% 10-y survival.[29] This is worse than the outcome in our ITx cohort (82%), whereas the latter patients are also nutritionally autonomous and free from significant desmoid disease. Furthermore, it could be argued that these patients form an advanced disease subset with an even higher risk. Indeed, our cohort was either referred to with extensive disease where conventional treatment was impossible or had undergone extensive resections previously and were now developing intestinal failure-related complications.

A major challenge of surgical resection in desmoid disease is the high rate of local recurrence, even in those cases with negative resection margins. It should be noted that there is significant debate whether most "local recurrences" are actually new-onset diseases in high-risk patients induced by surgical trauma. Regardless of nomenclature, several series have demonstrated recurrence rates up to 50%, even after achieving resection with widely negative margins.[30-32] The role of achieving total clearance remains controversial because some series have shown no impact on the recurrence rate.[33,34] As a result

TABLE 2.

Intraoperative data

Patient number	Graft type	Desmoid present at time of transplant	Sequential/simultaneous resection implant	Ureteric reconstruction	Vascular reconstruction	Abdominal closure
1	MVT	Extensive desmoid disease enveloping iliac vessels	Simultaneous	Not required	Aortic jump graft, cavo-caval anastomosis	Primary closure
2	Modified MVT + kidney	Large desmoid in the mesentery and envelopment of native ureters	Simultaneous	Bilateral native nephrectomy	Aortic jump graft, PV to PV	Primary closure
3	Modified MVT	None, extensive bowel resections prior	Sequential	Not required	Aortic jump graft, PV to PV	Primary closure
4	Isolated ITx	None, extensive bowel resections prior	Sequential	Not required	SMA to aorta, PV to IVC	Pedicled ALT flap
5	Isolated ITx	Colonic adenoma, no desmoids	Sequential	Not required	SMA to aorta, PV to IVC	NVRF
6	MVT	Extensive adenomas in the duodenum; desmoid in small bowel mesentery	Sequential	Recurrent left ureteric stenosis requiring stenting—left native nephrectomy at later stage because of recurring urosepsis	Aortic jump graft, cavo-caval anastomosis	NVRF
7	Isolated ITx + renal autotransplant	Massive desmoid growth into abdominal wall	Simultaneous	Encasement right ureter—>autotransplant	Y graft (SMA, splenic artery) to aorta, PV to PV	NVRF
8	Modified MVT + renal autotransplant	Large desmoid in root of mesentery/abdominal wall/IVC—required sharp dissection/right ureter encased	Simultaneous	Encasement right ureter—>autotransplant, recurrent left ureteric stenosis—> stenting	Aortic jump graft, PV to PV	Biological mesh
9	Modified MVT	Very extensive intra-abdominal and abdominal wall with fistulae	Simultaneous	Not required	Aortic jump graft, PV to PV	NVRF
10	Isolated ITx	Desmoid in the previous midline incision and tip of native rectal stump	Sequential	Not required	Carrel patch (celiac, SMA) to direct to aorta, PV to SMV	NVRF
11	Modified MVT	Large desmoid mass involving pelvis and right ureter	Simultaneous	Right ureter dissected free from desmoid mass and closed on DJ stent, left ureter to right ureter anastomosis, numerous stent changes—finally removed	Aortic jump graft, PV to PV	NVRF
12	Isolated ITx	Desmoid in jejunal mesentery	Sequential	Not required	Carrel patch (celiac, SMA) to direct to aorta, PV to SMV	Primary closure
13	Modified MVT	Extensive desmoid disease in anterior abdominal wall, affecting entire small bowel, pancreas, and abutting but not the liver	Simultaneous	Not required	Aortic jump graft, PV to PV	NVRF
14	Isolated ITx	Large desmoid in the small-bowel mesentery	Simultaneous	Not required	Aortic jump graft, PV to SMV	NVRF
15	Modified MVT	Desmoid dissected from anterior abdominal wall and right lobe of liver	Simultaneous	Not required	Aortic jump graft, PV to PV	Primary closure

ALT, anterolateral thigh; DJ, Double J; ITx, intestinal transplant; IVC, inferior vena cava; MVT, multivisceral transplant; NVRF, nonvascularized rectus fascia; PV, portal vein; SMA, superior mesenteric artery; SMV, superior mesenteric vein.

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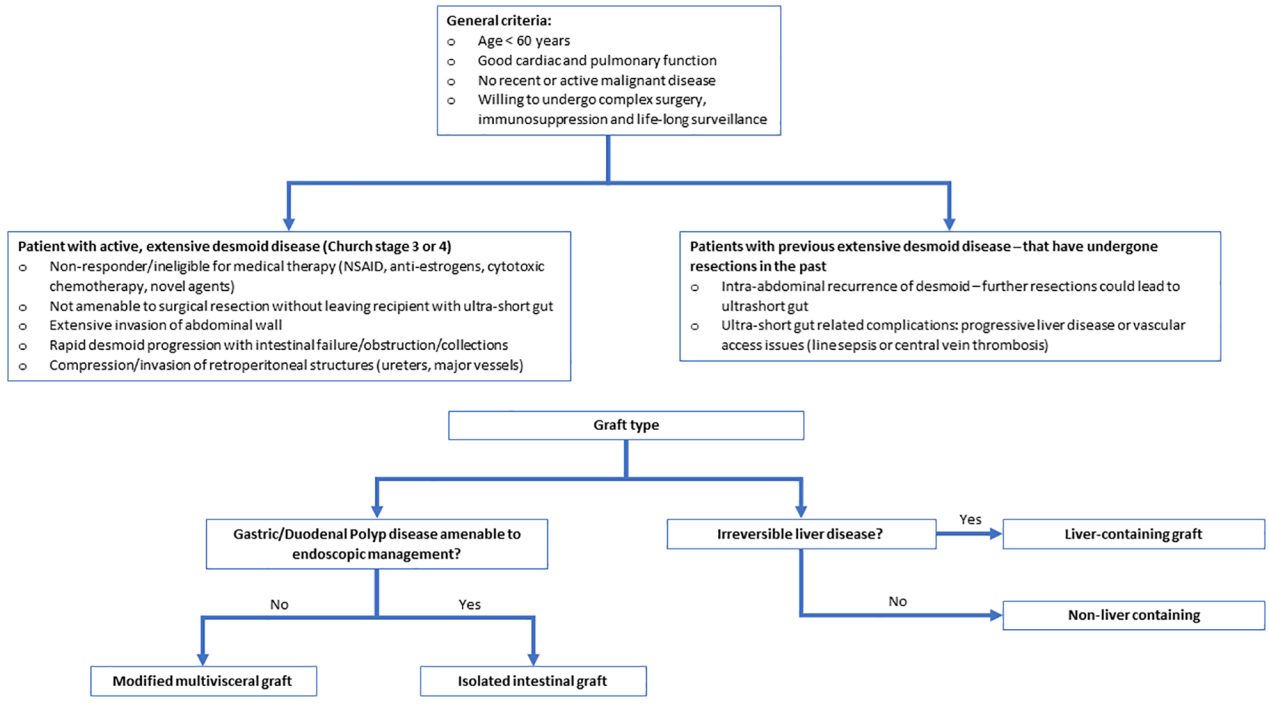

FIGURE 6. Proposed flowchart to identify potential candidates for ITx referral. ITx, intestinal transplantation.

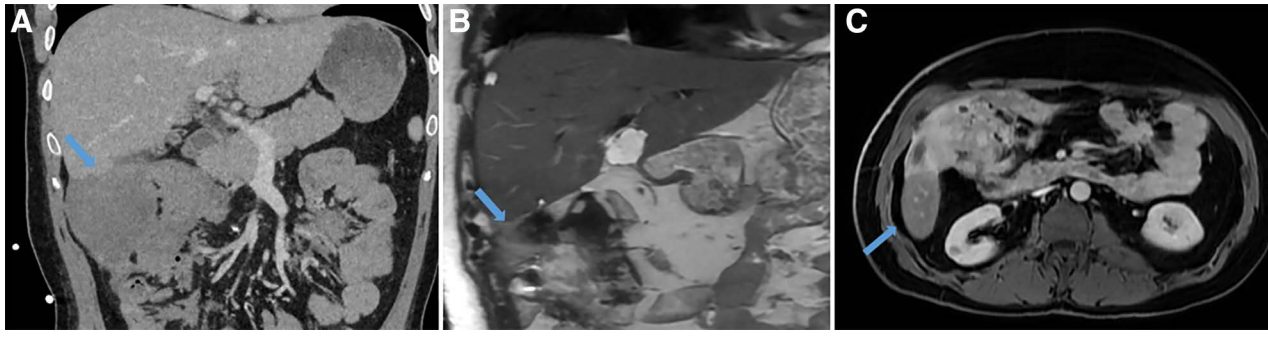

FIGURE 7. Desmoid encroachment on the liver. A, Coronal CT image. B, T2-weighted coronal MRI image. C, Axial MRI image following intravenous gadolinium demonstrating a desmoid mass abutting the capsule of segment 5/6 of the liver. This tumor was carefully resected off the liver to preserve it. CT, computed tomography.

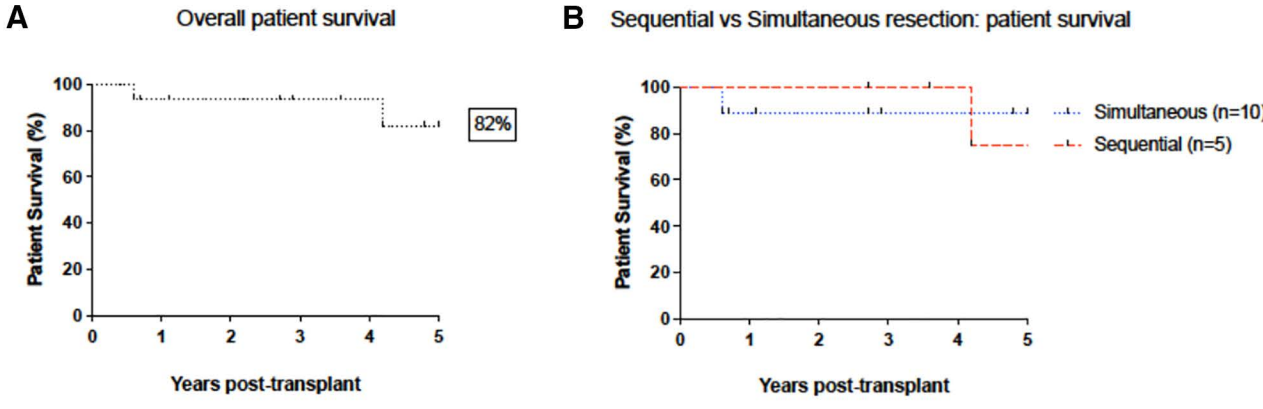

FIGURE 8. Kaplan-Meier survival curve. A, Overall patient survival. B, Sequential vs simultaneous resections.

of this, in advanced cases, a balance must be found between achieving "total" clearance versus the risk of significant morbidity. In some extensive cases where conventional therapy has failed, ITx can thus offer a rescue option by allowing for extensive intra-abdominal resection without compromising intestinal function.

TABLE 3.
Outcomes

Patient number	Patient survival (y)	Graft survival (y)	Retransplantation	Rejection	Rejection treatment	Alive	Cause of death
1	8.7	0.6	Yes—second graft survival 8.7 y	No	NA	No	Abdominal compartment syndrome—perforation and sepsis
2	5.3	5.3	No	Yes—grade III	Steroids/ATG	No	Chest sepsis
3	6.3	6.3	No	Yes—grade I		No	Hyperkalemia-induced circulatory arrest because of AKI
4	9.9	9.9	No	No	NA	Yes	Alive
5	6.3	6.3	No	No	NA	No	Metastatic gastric cancer
6	4.2	4.2	No	Yes—grade II	Steroids	No	Urosepsis
7	5.4	5.4	No	Yes—grade II	Steroids	Yes	Alive
8	5.0	5.0	No	No	NA	Yes	Alive
9	4.8	4.8	No	No	NA	Yes	Alive
10	3.6	3.6	No	No	NA	Yes	Alive
11	2.9	2.9	No	No	NA	Yes	Alive
12	2.7	2.7	No	No	NA	Yes	Alive
13	2.7	2.7	No	No	NA	Yes	Alive
14	1.1	1.1	No	No	NA	Yes	Alive
15	0.7	0.7	No	No	NA	Yes	Alive

AKI, acute kidney injury; ATG, antithymocyte globulin; NA, not available.

Interestingly, there was no intra-abdominal recurrence in our ITx cohort, in contrast to the conventional surgical literature. Three patients did have extra-abdominal desmoid occur elsewhere, with 2 patients requiring resection. This phenomenon has also been seen in most other series, with no intra-abdominal recurrences being reported.[21-24,35] The only exception was one report by the Miami group where a desmoid did recur in the abdomen but did not affect the transplanted intestine.[36] Although the exact reasons are unclear, the replacement with non-FAP genotype carrying transplant viscera, the ability to achieve radical disease clearance, and potential growth inhibition by some of the immunosuppressive agents may be contributing factors. For example, sirolimus (a mammalian target of rapamycin inhibitor) has been shown to slow desmoid development in FAP animal models and has been evaluated for this use in pediatric desmoid cases.[37] We did not start sirolimus for this specific reason in our series although 4 patients were started on it for renal protection.

Despite the capacity to achieve total clearance of intra-abdominal desmoid with ITx, the retroperitoneum is often involved. Ureteric obstruction is a frequent problem; in a large series of 107 patients, 28% had evidence of obstruction on imaging, of which 60% required at least retrograde stenting.[38] In our series, the ureter(s) were involved in 5 patients. Surgical strategies depended on the level of involvement. If possible, dissection of the ureter from the tumor was undertaken, facilitated by preoperatively placed stents for guidance. If surrounded, the ureter required partial resection followed by a uretero-ureteric anastomosis. In the most extensive cases (with complete encasement of the distal ureter), a renal autotransplantation was performed. This has been described previously in both transplant and nontransplant settings and allows for the maximum preservation of renal function.[35,38] One patient (patient 2) in our series had renal failure with bilateral ureteric desmoid involvement and recurrent urosepsis. As a result, she underwent bilateral native nephrectomy with renal allotransplantation, in addition to a modified MVT. Similarly, involvement of the iliac vessels (patient 1) was tackled by resection and reconstruction with the donor iliac vessels.

External compression of the IVC by desmoid disease can also be present, although direct invasion is rare.[39] In our series, 1 patient required sharp dissection of the desmoid off the IVC (patient 8). If needed, an IVC resection and reconstruction could be undertaken, as seen in other soft-tissue tumors such as sarcomas.[40] In the context of ITx, the use of donor vessels for vascular reconstruction is a substantial advantage.

The abdominal domain is often severely restricted due to large desmoid masses and previous extensive intestinal resection. The abdominal wall is frequently involved, directly by desmoid disease or enterocutaneous fistulae. This makes exenteration and subsequent abdominal closure very challenging. As in any ITx, achieving primary closure is vital to prevent morbidity and mortality.[41] Various techniques have been described including biological meshes, nonvascularized rectus fascia, and vascularized abdominal wall transplantation.[42,43] Our center now uses nonvascularized rectus fascia as a default due to the ease of procurement and implantation, together with low failure rates. It is very useful in large fistulating desmoid cases, as large fascia defects can be bridged comfortably and can be used despite heavy bacterial contamination.

Selecting the appropriate ITx graft to use is equally important, and decisions are driven largely by the extent of the disease. The burden and nature of gastric and duodenal polyps will dictate the need for foregut resection, whereas the degree of liver disease will dictate the need for liver transplantation (Figure 6). Our preference is to perform isolated ITx if deemed appropriate because the outcomes are superior compared with more complex grafts, and this strategy also optimizes organ utilization. However, the incidence of gastric/duodenal adenomas is high in patients with FAP.[44] This requires rigorous endoscopic screening and assessment in a high-volume center because "carpeting" polyps are very challenging to detect.[45] The various scoring systems, including the Spigelman classification, have not been validated in the context of ITx, and therefore, decisions regarding foregut resection (and therefore, modified MVT) should be made on a case-by-case basis. In patients with FAP, our team tends to have a low threshold to include a foregut resection with modified MVT if gastric or duodenal polyps are at all concerning (due to size, histological signs of dysplasia, and number) given the very poor prognosis of subsequent cancers arising from them.[46] These challenges are highlighted by patient 5 in our series. This individual had duodenal polyps but with a low Spigelman score (5 points, stage II) at the time of listing and, therefore, underwent an isolated ITx. Despite rigorous follow-up endoscopies, they developed metastatic gastric cancer 6 y after ITx and died several months later.

Splenic preservation has been described by the Pittsburgh group in 4 of 10 modified MVT for desmoid disease.[24] Although technically more challenging, the aim was reducing the risk of graft-versus-host disease, a known complication linked to an asplenic state after transplantation.[47] However, this technique is not always possible if the desmoid has infiltrated the splenic region and increases the total ischemia time because of the complex dissection. To date, we have not seen any graft-versus-host disease in our desmoid cohort.

Liver inclusion was avoided if possible and was only performed in 2 cases. The first patient in our series underwent a full MVT (despite not having significant liver disease) to avoid a hilar dissection and biliary anastomosis. With increased experience, this is no longer practiced at our center. In the second case, the underlying IFALD-associated liver disease required a liver graft (patient 6). In all other patients, the native liver function was sufficiently preserved, and the desmoid disease was successfully dissected from it. Modified MVT appears to be the preferred technique in all other reported ITx literature, with the intent to preserve a liver graft for another patient.[21-24] If the liver function is borderline or it is unclear if a modified MVT will be technically achievable, our center will list the patient for an MVT and start the operation. If not required, the liver can be dissected off and fast-tracked to another center.

Another significant challenge in desmoid disease is the complex resection of the native gut.[20,33] Combining this with ITx results in prolonged surgery time that can reach extreme lengths (up to 20 h in our series). Various options could be considered to ameliorate this, such as rotating the team (one for the resection and one for the ITx), although this would affect the patient. Alternatively, the explant could be commenced the identification of an appropriate donor and delay the organ retrieval process by 24 to 48 h. The drawback is that the retrieval surgeon would not have inspected the organs before commencing the recipient resection, although this risk could be partially mitigated by donor computed tomography imaging.[48] Finally, another strategy would be to perform the resection electively and then list for ITx. However, this interval to transplant is uncertain, with the current median waiting time for a non–liver-containing graft being 100 d in the United Kingdom.[49] Although separating the exenteration and Itx procedures is an attractive proposition, it may not be possible if the former requires significant bdominall wall resection, ureteric reconstruction, renal autotransplant, or vascular reconstruction with donor vessels. In addition, the potential for the development of antibodies as a result of blood transfusions may further limit the potential donor options. Despite this, on balance, we prefer the 2-stage technique whenever technically possible, and ideally, the discussion to consider ITx is done before performing the first stage. This allows the transplant assessment and listing process to occur beforehand so that patients can be activated rapidly afterward.

An interesting surgical alternative to ITx is autotransplantation with back-table resection in the cold. The first description in desmoid disease was made by Moon et al[21] documenting 6 patients. This is especially useful in patients with large tumors in the root of the mesentery without involvement of the intestines themselves. By removing the intestines and performing ex situ resection on the back table, visibility can be significantly improved while reducing the impact of ischemia (due to cold preservation). After vascular reconstruction, the graft can be reimplanted without the need for any immunosuppression.

Despite this study providing valuable insight into this rare disease, we have to acknowledge some limitations. First, due to the retrospective nature, some data may not have been included or lost. However, it should be noted that no patients were lost to follow-up. Second, there is likely to be significant referral bias because only those patients considered eligible for ITx (relatively young patients with no other known comorbidities) would be considered for this pathway. We do not have exact figures on how many patients were considered but eventually declined referral. However, in the United Kingdom, given the strongly existing centralized pathwayto identify and treat hereditary colorectal cancer/polyposis disease, these data could help create more evidence-based referral guidelines.

CONCLUSION

ITx is a viable treatment option in selected patients with extensive desmoid disease in which all other treatment options have been exhausted. Deciding which patients would benefit from ITx is important to ensure timely referral. Delays in this process can result in additional disease burden, such as secondary liver disease, loss of vascular access, or invasion of adjacent structures, requiring additional resections and reconstructions. In the future, prediction models based on clinical presentation, histological appearance, and genetic and familial risk factors should be devised to aid clinicians with appropriate referrals.

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