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ORIGINAL ARTICLE

Proximal and distal rectal cancers differ in curative resectability and local recurrence

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Abstract

AIM: To evaluate patients with proximal rectal cancer (PRC) (> 6 cm up to 12 cm) and distal rectal cancer (DRC) (0 to 6 cm from the anal verge).

METHODS: Two hundred and eighteen patients (120 male, 98 female, median age 58 years, range 19-88 years) comprised 100 with PRC and 118 with DRC. The proportion of T1, T2 *vs* T3, T4 stage cancers was similar in both groups (PRC: T1+T2 = 29%; T3+T4 = 71% and DRC: T1+T2 = -31%; T3+T4 = 69%). All patients had cancer confined to the rectum - those with synchronous distant metastasis were excluded. Surgical resection was with curative intent with or without pre-operative chemoradiation (c-RT). Follow-up was for a median of 35 mo (range: 12 to 126 mo). End points were: 30 d mortality, complications of operation, microscopic tumour- free margins, resection with a tumour-free circumferential margin (CRM) of 1 to 2 mm and > 2 mm, local recurrence, survival and the permanent stoma rate.

RESULTS: Overall 30-d mortality was 6% (12): PRC 7 % and DRC 4%. Postoperative complications occurred in 14% with PRC compared with 21.5% with DRC, urinary retention was the complication most frequently reported (PRC 2% *vs* DRC 9%, $P = 0.04$). Twelve percent with PRC compared with 37% with DRC were subjected to preoperative c-RT ($P = 0.03$). A tumour-free CRM of 1 to 2 mm and > 2 mm was reported in 93% and 82% with PRC and 88% and 75% with DRC respectively (PRC *vs* DRC, $P > 0.05$). However, local recurrence was 5% for PRC *vs* 11% for DRC ($P < 0.001$). Three and five years survival was 65.6% and 60.2% for PRC *vs* 67% and 64.3% for DRC respectively. No patient with PRC and 23 (20%) with DRC received an abdomino-perineal resection.

CONCLUSION: PRC and DRC differ in the rate of abdomino-perineal resection, post-operative urinary retention and local recurrence. Survival in both groups was similar.

Key words: Rectal cancer; Pre-operative chemoradiation; Inter-sphincteric resection; Local recurrence; Survival

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INTRODUCTION

The aims of treatment for rectal cancer are first, to achieve curative resection and second, to restore bowel continuity, thus avoiding a long term stoma. Compared with the developed world, in the developing world, most patients adjust less satisfactorily to an abdominal stoma because of socio-economic constraints and the lack of stoma care nurses in many parts[1]. Cancer of the left side of the colon and rectum constitutes the majority of large bowel cancer in Southern Asia. Of these, most cancers are to be found in the rectum, approximately 60% in the lower rectum between 0 and 6 cm from the anal verge[2].

Historically, surgical operation for cancer of the lower rectum has been abdomino-perineal excision of the rectum[3]. With development of stapling technology and reduction in the minimum safe distal resection margin to one centimetre in favourable tumours, the rate of restorative resection for distal rectal cancer (DRC) has increased[4,5]. More recent developments that have further enhanced the feasibility of restorative resection are the use of pre-operative chemoradiation (c-RT)[6] and the technique of intersphincteric resection[7].

Data from Japan have shown that cancers of the lower rectum, more than cancer of the proximal rectum, tend to spread to nodes of the inferior mesenteric group as well as drain *via* the internal iliac nodes[8,9]. Some have shown internal iliac nodal involvement in up to 15 percent of cancers of the lower rectum[8]. Compared with cancer of the proximal rectum, surgical operation for cancer of the lower rectum is likely to be associated with a greater rate of local recurrence in the pelvis because of untreated internal iliac nodes. Currently, the only available approaches to treatment of rectal cancer-involved internal iliac nodes are either pelvic lymphadenectomy or pre-operative c-RT. Thus, cancer of the proximal rectum is likely to be different from cancer of the distal rectum. The aim of our prospective study was to compare the rate of curative resection, local recurrence within the pelvis and survival in patients having surgical resection for proximal rectal cancer (PRC) (> 6 cm and up to 12 cm from the anal verge) *vs* DRC (0 to 6 cm from the anal verge). We also assessed the proportion of permanent stomas that were received by patients having surgery for PRC and DRC.

MATERIALS AND METHODS

From June 1995 to April 2008 two hundred and eighteen patients [120 male (55%), 98 female (45%); median age 58 years, range 19 to 88 years] with rectal cancer confined to the pelvis, without known distal metastasis, underwent surgical treatment at the North Colombo Teaching Hospital (Table 1). Some one hundred (46%; 54 male, 46 female) had cancer > 6 cm from the anal verge (PRC) compared with 118 (54%; 66 male, 52 female) with cancer between 0 and 6 cm from the anal verge (DRC). We chose a limit of 6 cm from the anal verge to determine DRC because rectal cancer at this level would require complete removal of the rectum with a distal tumour-free margin of one to two cm with total mesorectal excision in all cases, unlike in some high PRCs, where it would suffice to remove only a part of the mesorectum[4]. Also, in addition to mesorectal spread of rectal cancer as a cause for local recurrence, rectal cancer between 0 and 6 cm from the anal verge is likely to spread to internal iliac nodes as well as to mesenteric nodes, unlike in PRC which spreads proximally to the mesenteric group of nodes[8,9].

Table 1 Comparison of patients with proximal and distal rectal cancer

Criteria	Proximal rectal cancer (n = 100)	Distal rectal cancer (n = 118)
Age (median, range, yr)	60 (23 -88)	57 (19 – 85)
Gender		
Male	54	66
Female	46	52
ASA status		
1	26	32
11	50	68
111	20	16
1V	4	2
Type of operation		
Elective	80	113
Urgent/emergent	20	5
Mean height of lower limit of tumor from anal verge (cm)	10.5	4.5

ASA: American Society of Anesthesia.

All patients were evaluated by comprehensive history and physical examination. Digital rectal examination was performed to assess tumour fixity and distance of tumour from the anal verge was also measured by rigid proctoscopy. Clinical assessment of the anal sphincter was performed by digital assessment of resting and squeezing anal tone. The proximal colon was examined to exclude synchronous polyps, tumour or polyposis syndromes and a biopsy of the tumour was obtained, morphology of the tumour documented and endoluminal ultrasound performed at the time of colonoscopy. Further investigation consisted of standard haematology and biochemical evaluation. Radiological investigations consisted of chest X-ray and trans-abdominal ultrasound and, from 2003, combined computerized tomography (CT) or magnetic resonance imaging (MRI) of the abdomen and pelvis. All patients were counseled by a stoma care nurse, stoma sites were marked preoperatively and the operation was performed after bowel preparation using polyethylene glycol 24 h preoperation, except in those presenting with obstruction or perforation.

Neoadjuvant c-RT

Patients with T3 or T4 tumours, as judged by endo-luminal US or CT/MR, were given preoperative irradiation which consisted of 5040 cGy delivered in fractions of 180 cGy per day, 5 d per week. 5-Fluorouracil was given concomitantly in a 120 h continuous intravenous infusion at a dose of 1000 mg/m^2 of body-surface area per day during the first and fifth weeks of radiotherapy. Surgery was performed 6 wk from completion of chemo-radiation following restaging of the disease. Those with PRC received preoperative c-RT on a selective basis: bulky tumours observed to involve the circumferential margin (CRM) on magnetic resonance scan and tumours that involved the circumference of the lumen.

Operative technique

Operations were performed under general anaesthesia with intermittent positive pressure ventilation. Patients were positioned in the modified Lloyd- Davies position with a 15° to 30° reverse Trendelenberg tilt. Preoperatively, patients received prophylactic antibiotics, an urethral catheter was inserted and the rectum washed with 250 mL of 5% povidone iodine solution. The abdomen was incised in the lower midline to gain access to the peritoneal cavity. Proximal extension of the incision was necessary if mobilization of the splenic flexure was deemed essential at operation, particularly if the tumour was extra-peritoneal and an extended low anterior resection was planned, as in the case of most DRCs. We performed total mesorectal excision in all distal rectal tumours. Most tumours in the upper rectum, that is, rectum enveloped by peritoneum, were managed surgically by division of the rectum at least 2 cm distal to the tumour but with mesorectal excision 5 cm distal to the lower limit of the tumour. In all cases, we performed nerve sparing resections as described previously[10]. In anterior wall rectal tumours we incorporated Denonvillier's fascia in men or a cuff of posterior vaginal wall in women to ensure a curative resection. Postoperatively, after stabilization of vital signs and satisfactory postoperative pain control was achieved, all patients were managed either in an intensive care or high dependency unit for 24 to 48 h before transfer to a general ward.

Technique of inter-sphincteric resection

Inter-sphincteric resection was performed through the anus with the aid of a 'Lone Star' (Lone Star Medical Products, Inc., Stafford, Texas, USA) retractor. The lower limit of the tumour was visualized trans-anally and a distal margin of at least 1 cm was marked by electrocautery. The incision at this predetermined site was deepened to enter the inter-sphincteric space. Inter-sphincteric dissection, usually commenced at or below the dentate line and incorporated part of or, sometimes, the whole internal anal sphincter, approached the lowermost limit of anorectal mobilisation to reach the pelvic floor by abdominal dissection in the inter-sphincteric space, wide of the tumour. The mobilized rectum with the tumour was then delivered *via* the anal canal. Reconstruction was achieved by handsewn trans-anal, colo-anal anastomosis with 3/0 polyglactin 910 sutures. A diverting loop ileostomy was performed: in all patients with DRC who underwent restoration of intestinal continuity; in those with PRC, after pre-operative c-RT, where there was a positive air leak test during insufflation of the anastomosis under water in the pelvis; or where the surgeon deemed it necessary because of excessive bleeding during the operation.

Definition of level of anterior resection

The levels of resection employed in this study are as described previously[11]. Accordingly, high anterior resection is defined as resection where the level of anastomosis is proximal to 10 cm from the anal verge. Anterior resection is where the anastomosis is less than 10 cm from the anal verge but above the level of the pelvic floor where a part of the distal rectum is left in place. A low anterior resection is defined as an anastomosis at the level of the pelvic floor. It is an extended low anterior resection, when a colo-anal anastomosis followed inter sphincteric resection in which the anastomosis was within the anal canal. Thus, PRC was treated either by high anterior resection or anterior resection whilst all DRC patients received either a low anterior resection or an extended low anterior resection. A proportion received either Hartmann's resection or an abdomino-perineal resection of the rectum.

Follow up

All patients were followed up at the outpatient clinic at 2 wk, 4 wk and at 3 monthly intervals for 3 years. Subsequently, patients were followed at 6 monthly intervals up to 5 years and in the absence of recurrent cancer, annually thereafter. Serum CEA was measured at each follow-up visit. Chest X-ray, CT scan of the abdomen to evaluate the liver and colonoscopy were undertaken at the end of the first and the second year. Thereafter, patients were advised to follow standard colonoscopy protocols for those at average risk of colorectal cancer[12]. Those who had had restorative proctocolectomy with an ileal pouch were assessed by pouchoscopy.

Local recurrence in the pelvis was confirmed if there was histologically proven cancer present in the pelvis either by fine needle aspiration, trucut biopsy or histopathological examination of a resected specimen. Median follow up after operation was 35 mo (range 12 to 126 mo). In cases of loss to follow up, survival was evaluated up to the time of the last documented visit.

End points

The endpoints of our study were: mortality at 30 d post-operation, morbidity (anastomotic leakage, pelvic sepsis, wound infection, chest infection and urine retention); curative resection, where all margins (proximal, distal and CRMs) were histologically free of tumour (R0) *vs* resection with at least one margin involved by tumour (R1); local recurrence in the pelvis; and overall survival. Concerning CRM of resection, we evaluated resection rates in

Table 2 Complications of operation for rectal cancer *n* (%)

Location complication	Proximal rectal cancer (*n* = 100)	Distal rectal cancer (*n* = 118)	
Urinary retention	2 (2)	11 (9.3)	$P = 0.41$[2]
Chest infection	4 (4)	4 (3.4)	
Wound infection	3 (3)	2 (1.7)	
Pelvic abscess	3 (3)	1 (0.8)	
Anastomotic leak[1]	2 (2.5)	7 (8)	

[1]In consideration of anastomotic leakage, those who had had a Hartmann operation, Paul-Mickulicz procedure and trans-anal resection in the proximal rectal cancer group (n = 21) and abdomino-perineal resection and trans-anal resection in the distal rectal cancer group (n = 29) were excluded; [2]Fisher's exact test.

Table 3 Operative procedures for rectal cancer in 218 patients

Operation	Proximal rectal cancer	Distal rectal cancer
High anterior resection of rectum	23 (23)	0 (0)
Anterior resection of rectum	9 (9)	3 (2.5)
Low anterior resection or extended low anterior resection	44 (44)	75 (63.5)
Abdomino-perineal excision of rectum	0 (0)	23 (19.5)
Hartmann's operation	16 (16)	5 (4.2)
Paul Mickulicz operation	4 (4)	0 (0)
Subtotal colectomy	1 (1)	4 (3.4)
Restorative proctocolectomy with ileal anal pouch anastomosis	2 (2)	7 (6)
Transanal resection	1 (1)	1 (0.8)
Total	100 (100)	118 (100)

a microscopic margin free of tumour for > 1 mm but < 2 mm and > 2 mm separately. Also, the rate of permanent stomas was compared between operations for PRC and DRC.

Statistical analysis

Data have been presented as either median and range or mean and standard deviation. Differences between PRC and DRC have been compared using the χ^2 test and Fisher's exact test in case of a number less than 5. Operative data have been compared with one way ANOVA using SPSS version 16 (SPSS, Chicago, USA). Significance was assigned to a P-value of less than 0.05. Survival was analysed using Kaplan-Meier curves. The study was approved by the National Research Council and the University of Kelaniya.

RESULTS

The mean distance of the lower margin of the tumour from the anal verge for PRC was 10.5 cm and for DRC, 4.5 cm. Overall, peri-operative mortality (deaths within 30 d of operation) was 6% [PRC 7 (7%), DRC 5 (4%)]. The most common complication encountered was urinary retention in 2 (2%) in PRC and 11 (9%) in the DRC group (P = 0.041, Fisher's exact test). Surgical wound site infection, chest infections, anastomotic leakage and pelvic abscess formation were among other reported complications and were similar in both groups (Table 2). Mean operation time for PRC was 212 min (SD ± 48) *vs* 237 min (SD ± 43) for DRC (P = 0.011, one way ANOVA). Mean operative blood loss was 691 mL (SD ± 306) and 959 mL (SD ± 425) respectively for PRC *vs* DRC (P = 0.002, one way ANOVA). Use of preoperative chemo-radiation had no significant bearing on the operation time but was associated with greater operative blood loss [c-RT; 986 mL SD ± 438 *vs* no c-RT 803 mL SD ± 378 (P = 0.034, one way ANOVA]. Compared with PRC 12 (12%), significantly more patients with DRC 44 (37%) were subjected to preoperative c-RT (χ^2: 18.2, P = 0.034).

The type of operation performed is shown in Table 3. In all, 62 (28%) patients with DRC underwent intersphincteric resection and reconstruction. Abdomino-perineal excision with a permanent colostomy was undertaken exclusively in those with DRC, 23 (19%) (Table 3). A proximal diverting loop ileostomy was performed in 47 of 79 (59%) with PRC receiving a primary anastomosis and in 86 of 89 (96%) patients with DRC who received a primary anastomosis (P < 0.001, χ^2 test). In the majority, PRC 33 (70%) and DRC 70 (81%), the ileostomy was reversed at 3 mo. The rate of permanent colostomy in our study is low; none in the PRC group received abdomino-perineal excision, while a colostomy following Hartmann operation was performed in sixteen with PRC and five with DRC, eighty percent of which have been reversed, leaving only four with a stoma likely to remain permanently. In patients with DRC, 23 (20%) received a permanent stoma consequent to abdomino-perineal excision. Thus 27 (12%) patients of 218 were left with a permanent colostomy.

Histological features of the resected specimen of rectal cancer are shown in Table 4. For CRM of clearance, a microscopic margin free of cancer greater than 2 mm, R0 resection rates were 82 (82%) for PRCs and 89 (75%) for DRCs. If a CRM of 1 to 2 mm was considered, the rate of margin-free resection was 93 (93%) for PRC and 104 (88%) for DRC. There was no significant difference between the proportion of R1 resections for PRC and DRC [PRC 18 (18%) *vs* DRC 29 (25%), P = 0.513, χ^2].

Overall, local recurrence was seen in 8% (18) of patients: 5% (5) PRC *vs* 11% (13) DRC, P = 0.001, χ^2. Seventeen patients (92%) developed local recurrence within the first 3 years after operation and 1 (8%), after 5 years. Only 3 of eighteen (17%) developed anastomotic recurrence. In the remaining 15 (83%) local recurrence was extra-anastomotic. For PRC and DRC, metachronous liver and lung metastasis (> 6 mo after operation) was seen in thirteen (6%) and three (1.25%) patients respectively. Overall survival at 3 years (65.6% *vs* 67%; Kaplan-Meier P = 0.553) and at 5 years (60.2% *vs* 64.3%; Kaplan-Meier P = 0.254) was similar (Figure 1).

DISCUSSION

In this study, which compared patients with PRC and

Table 4 Histological characteristics of patients with proximal and distal rectal cancer

Histological criteria	Proximal rectal cancer (100)	Distal rectal cancer (118)
Differentiation[1]		
Well	21 (21)	17 (14)
Moderate	69 (69)	83 (70)
Poor	8 (8)	10 (9)
Presence of mucin		
Mucinous	5 (5)	9 (8)
Signet ring	0 (0)	1 (1)
Tumour stage[2]		
T1	9 (9)	8 (7)
T2	20 (20)	28 (24)
T3	57 (57)	66 (56)
T4	14 (14)	16 (14)
Node stage[3]		
N0	58 (58)	58 (49)
N1	15 (15)	30 (25)
N2	21 (21)	28 (24)
N3	3 (3)	0 (0)

[1]Degree of differentiation not included in 10 patients (proximal rectal cancer 2 and distal rectal cancer 8) who showed complete tumour regression following pre operative chemoradiation; [2]Reported T stage in those having neo-adjuvant therapy is stage before chemoradiation; [3]Data regarding 5 patients have been withheld because either < 12 nodes were reported (n = 2) or no nodes were found after pre-operative chemoradiation (n = 3).

DRC, the overall mortality of 6 percent is comparable with a recent report of 8 percent from the United Kingdom[13]. Furthermore, data from this study examined local recurrence rates for rectal cancer during a period of transition, where, preoperative c-RT was used as adjuvant therapy on a selective basis. Thus in our study, those with T stage Ⅲ or Ⅳ rectal cancer and those with DRC were more likely to receive pre-operative c-RT compared with similar tumours in the proximal rectum. Earlier stage tumours were treated by surgical resection of the rectum without pre-operative c-RT, employing total mesorectal excision, to achieve oncologically curative circumferential and distal resection margins as proposed by Heald *et al*[4]. All those with metastasis to the liver or lung at the time of operation were excluded from analysis. Despite similar rates of curative resection of PRC and DRC, our study has shown that the rate of local recurrence after curative surgical resection of PRC was significantly less than that following resection of cancer of the distal rectum (5% *vs* 11%), which is similar to data from the Swedish cancer registry[14]. The overall local recurrence rate of five percent for PRC is acceptable and is unlikely to be reduced further by irradiation. The disadvantages of pre-operative irradiation, such as postoperative anastomotic leakage[6] and the interval after completion of c-RT up to the time of surgical excision, are likely to outweigh the benefits of reducing local recurrence any further in these patients. Thus surgical resection alone will remain the key factor in minimising local recurrence in PRC.

By contrast, pre-operative c-RT which is followed by surgical resection is likely to be of greater benefit in patients with cancer of the distal rectum; the randomized controlled trial by Sauer *et al*[6] has shown the efficacy of this modality in reducing local recurrence rates for rectal cancer staged T3 or T4[6]. Furthermore, Fujita *et al*[8] have shown involvement of nodes of the internal iliac group in up to fifteen percent of patients with DRC. Conventional surgical resection does not remove internal iliac nodes and our data may be contributory to the suggestion of extra-rectal pelvic nodal recurrence in low rectal cancer since most local pelvic recurrences were extra-anastomotic. Thus, local recurrence in the pelvis may arise from either incomplete circumferential resection or cancer in iliac nodes, a factor that may be better controlled with pre-operative chemo-radiation. Abdomino-perineal resection was only required in those with DRC. Most, with cancer proximal to six centimetres from the anal verge, were managed surgically by restorative resection except in circumstances where a Hartmann's procedure was deemed necessary. The overall rate of a permanent stoma was low. We believe that multi-disciplinary involvement in planning treatment before operation, protocol based management by high volume specialist teams and new techniques such as inter-sphincteric resection have contributed to a low stoma rate.

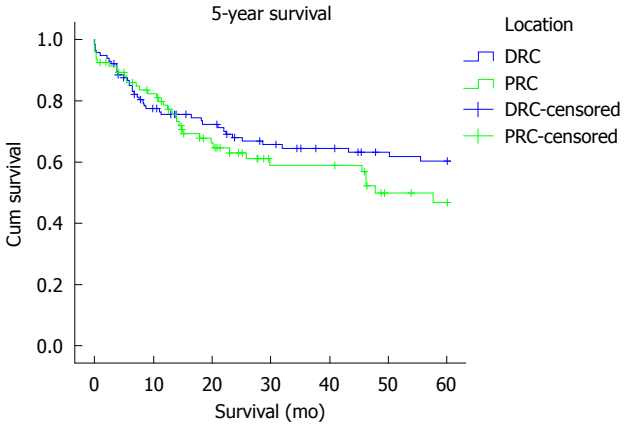

Figure 1 Kaplan Meier predicted 5 years survival curves for proximal rectal cancer and distal rectal cancer. The result indicates no significant difference in survival between the two study groups.

In conclusion, in our study, PRC differed from DRC. No patient with PRC required abdomino-perineal resection and, more importantly, local recurrence rate of cancer in the proximal rectum was significantly less than that of DRC. Urinary retention was more frequent after surgery for DRC compared with PRC. However survival was similar in both groups. In consideration of outcome trials, except for survival analysis, it would be useful to stratify rectal cancer as proximal and distal cancer.

COMMENTS

Background

Rectal cancer comprises the majority of large bowel cancers in the developing world. Local recurrence of rectal cancer after curative resection is the most dreaded complication. Surgical treatment has been based on anatomic division of the rectum as high, middle and low. However, local spread of proximal rectal

cancer (PRC) has been to inferior mesenteric nodes and spread of distal rectal cancer (DRC) mostly to middle rectal and inferior rectal nodes, referred to as pelvic nodes. The latter, cannot be addressed by surgical resection alone. Pre-operative chemoradiation (c-RT), in addition to down-staging and downsizing rectal cancer, may have a role in treatment of surgically unresected pelvic lymph nodes.

Research frontiers

In this study, the authors have considered rectal cancer as proximal or distal based on a point 6cm from the anal verge of the lowermost edge of the tumour. Despite the use of c-RT before operation in a majority of DRCs (0 to 6 cm from the anal verge), the authors have shown that curative, microscopic resection and consequently local recurrence of rectal cancer, remains significantly greater in DRC compared with PRC (6 to 12 cm from the anal verge).

Innovations and breakthroughs

New methods are required to better treat cancer of the distal rectum. Current studies are evaluating this by allowing for a longer time interval between completion of c-RT and surgical removal of the rectum, so as to enable apoptosis of rectal cancer cells to occur more completely than previously thought.

Applications

This study shows that in trained hands and with the use of a multi-disciplinary team comprising oncologic, radiological and pathologic specialists, surgeons in developing countries could achieve a remarkably low rate of permanent stomas and acceptable local recurrence.

Terminology

Rectal cancer may be better addressed as involving the proximal and distal rectum. Based on this classification of the location of a rectal cancer, most DRCs and a smaller proportion of PRC are likely to warrant pre-operative c-RT, since we have shown lower rates of local recurrence for cancer of the proximal rectum. Furthermore, all DRCs and a proportion of PRCs, will require surgical resection of the rectum by total mesorectal excision.

Peer review

It's always very interesting to evaluate the results of two different therapeutic strategies. This is a well written manuscript.

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BRIEF ARTICLE

A mathematical model for shortening waiting time in pancreas-kidney transplantation

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Abstract

AIM: To simulate a hypothetical increase of 50% in the number of pancreas-kidney (PK) transplantations using less-than-ideal donors by a mathematical model.

METHODS: We projected the size of the waiting list by taking into account the incidence of new patients per year, the number of PK transplantations carried out in the year and the number of patients who died on the waiting list or were removed from the list for other reasons. These variables were treated using a model developed elsewhere.

RESULTS: We found that the waiting list demand will meet the number of PK transplantation by the year 2022.

CONCLUSION: In future years, it is perfectly possible to minimize the waiting list time for pancreas transplantation through expansion of the donor pool using less-than-ideal donors.

Key words: Pancreas-Kidney transplantation; Waiting list; Mathematical model

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INTRODUCTION

São Paulo is a Brazilian state pioneering transplantation surgery. Brazilian law was changed (1999) and pancreas-kidney (PK) transplantation became possible because of state financial support for these procedures. Since then the patient waiting list for PK transplantation has increased and now approximately 154 cases per month are referred to a single list at the central organ procurement organization.

Simultaneous PK transplantation has become the therapy of choice for patients with end-stage renal disease and type 1 diabetes mellitus. Over the past 20 years, PK transplantation outcomes have improved significantly to the point that the majority of recent data demonstrate long-term survival benefits and some protection from progressing secondary complications[1-4].

The gap between the number of transplantable organs from deceased donors and the number of patients awaiting transplantation continues to increase each year. The number of people waiting for PK transplantation in our state is approximately 2.5-fold the number receiving transplantation.

The aim of this study is to assess the performance of our state PK transplantation program and to evaluate when the number of transplantations will meet our waiting list demand.

MATERIALS AND METHODS

We collected official data from the State Transplantation Center (Sao Paulo State Secretariat) from our PK transplantation program between January 1999 and December 2007. Only cadaveric PK transplantation was included. The data related to pancreas transplantation in our state includes: simultaneous PK transplantation, pancreas after kidney transplantation and pancreas alone. Table 1. shows the actual number of PK transplantations (Tr), the incidence of new patients on the list (I) and the number of patients who died while on the waiting list (D) in the State of Sao Paulo since 2000. As described previously[5] we projected the size of the waiting list (L) by taking into account the incidence of new patients per year (I), the number of PK transplantations carried out in the year (Tr) and the number of patients who died on the waiting list or were removed from the list for other reasons (D).

We took the data of *Tr* from Table 1 and fitted a continuous curve by the method of maximum probability[6], in order to project the number of future transplantations, *Tr*. Then we projected the size of the waiting list, *L*, by taking into account the incidence of new patients per year, *I*, the number of transplantation carried out in that year, *Tr*, and the number of patients who died on the waiting list, *D*. In other words, the list size at time $t+1$ is equal to the size of the list at the time t, plus the new patients coming onto the list at time t, minus those patients who have died on the waiting list at time t, minus those patients who have received a graft at time t. The variables *I*, and *D*, from 2007 onward were projected by fitting an equation by maximum probability, in the same way that we did for *Tr*. The dynamics of the waiting list is given by the equation: $L_{t+1} = L_t + I_t - D_t + Tr$.

RESULTS

The results can be seen in Figure 1. Note that, since 2000, both the number of transplantations (blue line) and the size of the waiting list (red line) have increased in a linear manner, and will not meet each other in the future. In other words, the list size is growing much faster than the number of PK transplantations performed in our state.

We then simulated a hypothetical 50% increase in the number of PK transplantations performed in order to check when the two curves would meet each other. The results can be seen in Figure 2.

Table 1 Number of pancreas-kidney transplantations, the incidence of new patients on the list and the number of patients who died while on the waiting list in the State of Sao Paulo since 2000

Yr	I	D	Tr
2000	163	38	33
2001	126	51	52
2002	128	46	63
2003	138	48	74
2004	143	52	82
2005	169	58	64
2006	213	69	72
2007	167	71	85

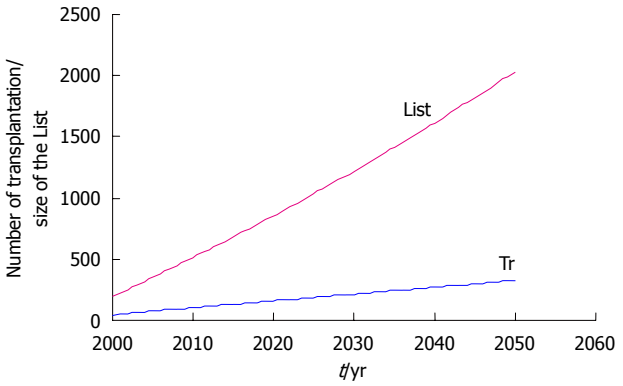

Figure 1 Number of pancreas-kidney transplantations (blue line) *vs* waiting list size (red line), State of São Paulo, Brazil.

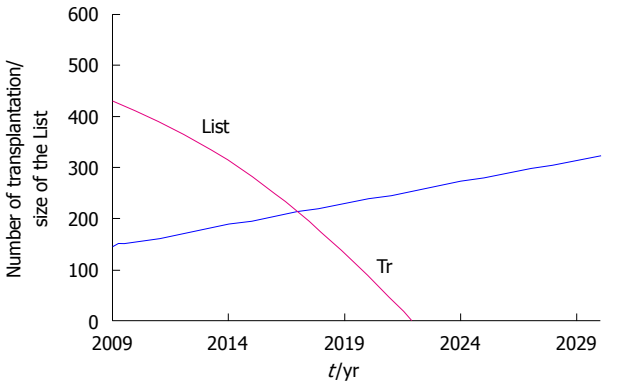

Figure 2 Projected number of pancreas-kidney transplantations (blue line) with a 50% annual increase over the current trend *vs* waiting list size (red line).

Note that by increasing the annual number of transplantation by 50%, the waiting list will come to an end in 2022.

DISCUSSION

Currently, solid-organ pancreas transplantation is the only treatment of type 1 diabetes that can restore complete insulin independence and normal blood glucose levels. The aim of a successful pancreas transplantation was not only to provide normoglycemia but also to slow

down the development or progression of diabetes-related complications[7]. Results of pancreas transplantation have improved significantly over the last 25 years. There are multiple reasons for this including superior immunosuppression, better post-transplant management, and modern surgical techniques[2,3].

In our state, current organ donation of the 7.09 per million inhabitants has not reached its full potential[8]. This fact alone is responsible for the huge demand pressure on our organ waiting list. One way to ease this pressure is to increase organ donation at least two-fold; in other words we should have been doing 15 organ retrievals per million inhabitants.

The number of PK transplantations in our state increased, approximately, 2.7-fold (33 to 85) from 2000 to 2007. On the other hand, the number of patients on the PK waiting list jumped to 2.98-fold (163 to 385) from 2000 to 2007. The gap between the number of PK transplantations and patients on the waiting list is widening fast, leading to an anticipated increase in the number of deaths.

While we have improved our performance in PK transplantation from the year 2000 to 2007, 1.8 PK transplantation/million inhabitants and 4.72 PK transplantation/million inhabitants respectively, this was not sufficient to meet our state demand for PK transplantation. During the study time frame, approximately, 3 pancreata/million inhabitants were discarded. Thus attempts to maximize pancreas utilization to satisfy the demand is a problem of increasing significance.

Another approach to expanding the donor pool for pancreas transplantation is to use pancreata from donation after cardiac death (DCD). While the use of kidneys and livers from DCD donors is increasing[9,10], the use of DCD pancreata is still low (UNOS). DCD is not a novel concept. Prior to the institution of brain death laws in the United States, all donors were DCD donors. Pancreas procurement from DCD donors was described for the first time in 1968[11]. However, routine implementation of DCD recovery at many centers has been impeded by ethical concerns, logistical considerations, and fear of poor functional outcomes. Limited experience with DCD pancreas transplantation is available, and this is primarily short term follow-up in a small number of patients[12,13]. In comparison to a contemporaneous cohort of recipients of conventional heart-beating donors organs, SPK transplantation from selected DCD donors resulted in similar excellent patient, kidney, and pancreas graft survival[14].

The lengthening waiting lists caused by the shortage of available organs and the increasing number of patients with end-stage organ disease have led to predictable rise in deaths; therefore the search for new sources of transplantable organs is imperative[15,16]. It has been suggested that, with the current standard of practice, the pancreas is the least likely abdominal organ to be deemed suitable for transplantation[17]. Waiting list time for simultaneous PK transplantation is increasing. In the United States of America at the end of 1993, there were 855 patients awaiting simultaneous PK transplantation, whereas at the end of 2002 there were 2425 (Organ Procurement and Transplantation Network, OPTN, USA).

Since pancreas is a limited national resource our proposal is: (1) Improve the organ donation campaign; (2) Concentrate funding resources in public university hospitals in order to improve PK performance; and (3) Expand the donor pool using less-than-ideal donors such as: DCD[12-14], living donors[18-20] and pediatric donors[21].

In this study, we simulated a hypothetical increase of 50% in the number of PK transplantations and we found that the waiting list demand will meet the number of PK transplantations by the year 2022 (Figure 2). This means that is perfectly possible in the years ahead to minimize the waiting time for pancreas transplantation if we expand the donor pool using less-than-ideal donors.

In conclusion, the implementation of the measures mentioned above would immediately ease the pressure on our waiting list for PK transplantation and this, coupled with the potential future 50 % increase in the number of PK transplantations, should minimize transplant patient waiting time.

COMMENTS

Background

Simultaneous pancreas-kidney (PK) transplantation has become the therapy of choice for patients with end-stage renal disease and type 1 diabetes mellitus. Over the past 20 years, PK transplantation outcomes have improved significantly to the point where the majority of recent data demonstrate long-term survival benefits and some protection from progressing secondary complications.

Research frontiers

Since pancreas is a limited national resource, our proposal is: (1) improve the organ donation campaign; (2) concentrate funding resources in public university hospitals in order to improve PK performance; and (3) expand the donor pool using less-than-ideal donors such as: donation after cardiac death, living donors and pediatric donors.

Innovations and breakthroughs

The authors projected the size of the waiting list (L) by taking into account the incidence of new patients per year (I), the number of PK transplantations carried out in the year (Tr) and the number of patients who died on the waiting list or were removed from the list for other reasons (D).

Applications

In this study the authors simulated a hypothetical increase of 50% in the number of PK transplantations and we have found that the waiting list demand will meet the number of PK transplantation by the year 2022. This means that is perfectly possible in the years ahead to minimize the waiting time for pancreas transplantation by expanding the donor pool using less-than-ideal donors.

Peer review

It is an interesting work and thus could be published.

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CASE REPORT

Inverted Meckel's diverticulum manifested as adult intussusception: Age does not matter

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Abstract

Adult intussusception due to Meckel's diverticulum (MD) is an uncommon cause of intestinal obstruction. However, the surgeon should still be suspicious of this condition since the non specific symptoms and the rarity of it make a preoperative diagnosis uncertain. Considering the secondary nature of adult intussusception and the necessity of early surgical intervention to avoid morbidity and mortality, we report two cases of intussusception due to MD in adults. A diverticulectomy using a TA stapler was performed in the first patient. In the second patient extensive fibrosis of the adjacent mesentery and thickening of jejunal mucosa were observed, so a segmental resection of the small bowel or affected ileal part and a hand-sewn anastomosis was performed. The postoperative period along with the long term follow-up was uneventful for both patients. The decision between diverticulectomy *vs* bowel resection can be based on the intussuscepted bowel condition. Early surgical intervention may ensure a favorable outcome.

Key words: Inverted Meckel's Diverticulum; Adult intussusception; Emergency surgery; Intestinal obstruction; Computed tomography; Diverticulectomy

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INTRODUCTION

Meckel's diverticulum (MD) is the most common congenital abnormality of the gastrointestinal tract, occurring in 1% to 2% of the population[1]. It is usually asymptomatic and becomes evident when complicated. Although MD appears equally in both sexes, it causes complications more frequently in males[2,3]. Lower gastrointestinal bleeding, obstruction and inflammation are the most common complications which usually occur in children under 10 years old. Occasionally, inversion of MD into the lumen of the bowel can cause intussusception, ischemia and infarction[4].

The incidence of intussesception attributed to an inversion of MD accounts for 4% of all cases presenting with intestinal obstruction due to intussusception[5]. It occurs when the MD sags into the bowel lumen and then serves as a lead point to allow telescoping of the small intestine, first into the distal ileum and then in to the large intestine, causing ileo-ileal and ileocolic type of intussusceptions. The vast majority of cases with ileocolic intussusception is idiopathic and has a tendency to appear in children under 2 years of age[1,6]. The incidence of MD complications has been reported to decrease with advancing age. However, intussusception attributed to an

inversion of MD may appear in older ages[2].

Regarding the physiognomy of this occurrence, we report two cases of intussusception due to inverted Meckel's diverticulum in 15 and 80 years old females.

CASE REPORT

Patient 1

A 15-year-old female presented to the emergency room complaining of abdominal pain and vomiting for the last 12 h. She had no significant past medical history or previous abdominal surgery. There was no family history of any hereditary illnesses.

On admission she had normal vital signs and a temperature of 37.3℃. Physical examination showed a slightly distended abdomen with hyperactive bowel sounds. The patient had moderate abdominal tenderness without guarding. No masses or hernias were identified. Laboratory tests revealed increased white blood cells (WBC) of 13 200 μ/L with shift to the left.

Plain abdominal X-ray demonstrated air fluid levels of the small bowel (Figure 1). Computed tomography (CT) revealed distension of the small intestine, especially of the jejunum and ileus. Furthermore, a mass lesion with concentric rings of fat and soft tissue attenuation was identified (Figure 2). These findings were consistent with a bowel obstruction secondary to an enteric intussusception.

A decision to operate was made based on the above findings. A midline laparotomy was carried out. The intra operative findings were distention of the small bowel and intussusception of ileus due to an inverted MD located 20 cm from the ileocecal valve. The bowel was deployed and examined for signs of ischemia. No ischemic loop was identified. A diverticulectomy was performed using a TA stapler in parallel with the longitudinal axon of the bowel lumen (Figure 3). The operating time was 45 min. Histopathology revealed MD measuring 4 cm × 2 cm × 0.7 cm without ectopic mucosa or malignancy.

The postoperative period was uneventful and after 6 d the patient was discharged. At the 12 mo follow-up, the patient had no evidence of complications.

Patient 2

An 80-year-old female with no previous laparotomies presented to the emergency room complaining of colicky abdominal pain, relieved after vomiting for the last 24 h. Her past medical history identified symptoms of anorexia for the past year, weight loss, repeated episodes of small bowel obstruction and readmissions for the last 3 mo. She had been investigated for these symptoms with a colonoscopy that was negative. Her family history was free of any hereditary illnesses.

On admission she had normal vital signs and a temperature of 37℃. Physical examination showed a distended abdomen with normal bowel sounds. The patient had moderate abdominal tenderness without concomitant peritoneal irritation. No masses or hernias were identified. Laboratory tests revealed increased WBC of 14 500 μ/L with shift to the left.

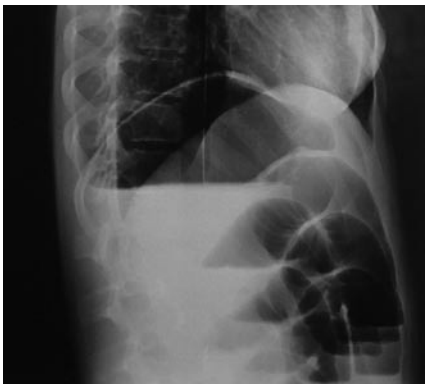

Figure 1 Plain abdominal X-ray demonstrated air fluid levels of the small bowel.

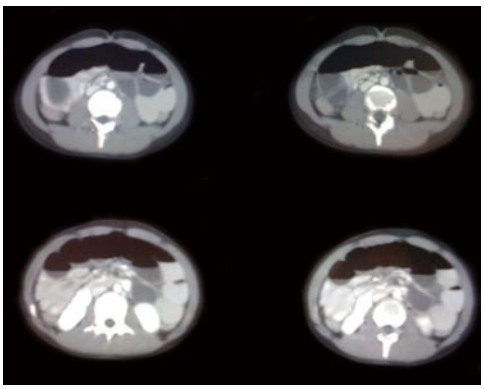

Figure 2 Computed tomography revealed distention of the small intestine at the level of jejunum and ileus. A mass lesion was identified with concentric rings of fat and soft- tissue attenuation.

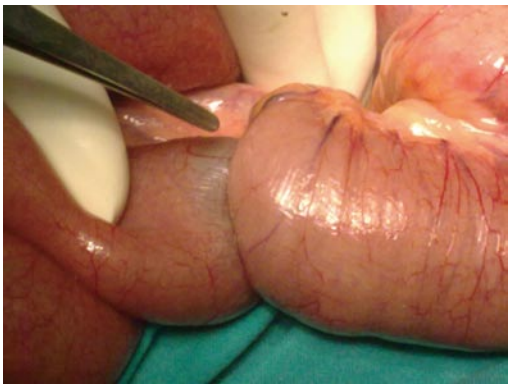

Figure 3 Intussuscepted portion of ileus attributed to inverted Meckel's diverticulum.

Plain abdominal X-ray demonstrated air fluid levels of small bowel. CT with contrast revealed distension of the small intestine and wall thickening. She was managed conservatively for the first 24 h but the patient did not respond well to the analgesics and severe distention was observed.

After a surgical consultation, the patient was admitted to the operating room. A midline laparotomy was carried

Figure 4 Intraoperative image of a free diverticulum located at an approximate distance of 70 cm from ileocecal valve.

out. The intra operative findings were distention of the small bowel and intussusception of ileus due to an inverted MD located 70 cm from the ileocecal valve (Figure 4). The free diverticulum acted as a lead point for intussusception. Extensive fibrosis of the adjacent mesentery and thickening of jejunal mucosa were also identified. No ischemic loop was identified. A segmental small bowel resection and hand-sewn anastomosis was performed. The operating time was 50 min. Histopathology distinguished MD measuring 3.5 cm × 2.5 cm × 1 cm and no signs of malignancy. The postoperative period was uneventful and after 7 d the patient was discharged. At 6 mo follow-up, the patient remains asymptomatic and without recurrence.

DISCUSSION

There is a paucity of data regarding the true incidence of intussusception due to MD. Only a few cases have been reported in the literature[7-13]. Epidemiological data confirm that the chronic clinical course paces patients with inverted MD to the operating room in older ages[14-16]. However, the presented first case occurred in a young patient 15 years old. The second case occurred in an 80-year-old female who had multiple admissions for partial bowel obstruction. That implies that ileo-ileal intussusception can be observed in any age group.

Preoperative clinical diagnosis for adults remains a challenge as the classic triad of childhood intussusception occurs in only 15%-20% of cases[17]. The usual concept embraces long lasting symptoms of partial obstruction[18,19].

Therefore, several clinical characteristics such as history of previous attacks, the chronic course of disease with vomiting and possibly rectal bleeding and a palpable mass have been identified to distinguish the intussusception from an inverted Meckel diverticulum[20]. However, our first patient did not have any of these features and presented acutely, whereas our second patient had had readmissions for a long time.

CT is the most sensitive imaging modality for diagnosis of bowel obstruction with reported accuracy of 58%-100%[21]. In the early stage, the characteristic point is the target lesion, described as enveloped, eccentrically located areas of low density, which represents the intussuscepted bowel viewed in cross section[22]. That was identified only in our first case. However, this imaging stamp is noticed in intussusceptions caused by other pathological lesions, which limit the sensitivity and specificity of CT to identify the cause of intussusception[23]. CT enteroclysis and magnetic resonance enteroclysis are up-to-date alternative studies for successful diagnosis of MD[24]. Other findings, such as vascular compromise, layering or stratification effect to bowel wall thickening and amorphous mass recognized later in the natural history of unrelieved intussusception were not revealed in our cases[22]. Thus, CT is recommended not only as a strong diagnostic tool but also as a determinator of progression and severity of this process.

Referring to the location, MD is usually found within 100 cm of the ileocecal valve[2]. In our two cases, the distance was calculated as 20 and 70 cm respectively.

Concerning the surgical treatment, the available techniques reported in the literature are classified based on the location of MD and the progression and the severity of the process. Simple diverticulectomy or segmental resection is preferred for the small bowel, since the malignancy rate is low (17%)[25-27]. Diverticulectomy is predicated as a simple, minimal and cost effective technique which can resolve the problem[19].

Resection with anastomosis is clearly indicated in cases of inflammation and ischemia of ileum and is also recommended in edematous, inflamed or perforated base of MD. Laparoscopy represents an alternative method of treatment with techniques varied from segmental resection of MD[28] to reduction of intussusception, diverticulectomy and intracorporeal anastomosis[29].

The authors preferred the open approach due to the uncertainty of the diagnosis. Laparoscopy seems to be safe and effective as a treatment option in emergency surgery for small bowel obstruction. However, in routine practice there are obstacles such as proper instrumentation and facilities available in the setting of emergency surgery. Moreover, there is an absence of level I evidence knowledge to support the proper treatment options[30].

Intra operatively, the intussuscepted bowel was deployed and examined for ischemia. There is no doubt that in case of transmural ischemia, the bowel needs to be resected along with the diverticulum. Intussusception due to MD is an absolute indication for MD resection. In one of the cases, simple diverticulectomy was performed using a TA stapler. There is currently a lack of strong evidence to support the use of a stapler for the MD diverticulectomy. The morbidity and leak rates seem to be equivalent or even better than that reported in a hand-sewn technique[31]. Few published series have addressed the results from this surgical technique. More specifically, Vadalà *et al*[32] described his experience in treating seven cases of diverticulectomies in the emergency setting with the use of staplers, emphasizing the reduction of operative time and the decreased postoperative complications.

Additionally, Patsner *et al*[33] reported diverticulectomies in sixteen patients during gynecological cancer surgery without morbidity.

In our study, we report two cases of successful management of adult ileus intussusception due to inverted MD. The novel information is that this uncommon entity can be observed even in extreme adult ages, since the first patient was only 15 years old while the second patient was 80 years old. Age might be a predictor factor for the type of the operation although this needs to be further investigated.

In adult cases there are usually previous episodes or even readmissions. It could be assumed that age may influence the clinical course along with the surgical treatment. A long life period with multiple episodes of partial obstruction seems to be related to structural effects in the wall of the small bowel and the adjustment structures, as confirmed in the elderly patient. That predisposes the severity of the intraoperative findings and the type of the proper surgical procedure since only diverticulectomy was adequate for the very young patient and a wider resection was considered necessary for the old patient.

In conclusion, adult intussusception caused by inverted MD may be observed in any age. Diverticulectomy *vs* bowel resection are the standard treatment. Age should be considered as a predictive factor for the surgical strategy.

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CASE REPORT

Intestinal duplication in adulthood: A rare entity, difficult to diagnose

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Abstract

Duplications of the alimentary tract (ATD) are rare congenital anomalies often found early in life. They may occur anywhere in the intestinal tract but the ileum is the most frequently affected site. Clinical presentation of ATD in adults is variable and because these lesions occur so infrequently they are rarely suspected. In the present report we describe a case of ileal duplication in a 61-year-old patient with Crohn's disease. Despite various radiological investigations and medical consultations, the diagnosis was only made on the surgical specimen.

Key words: Intestinal duplication; Adulthood; Intestinal obstruction; Surgical resection; Abdominal pain

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INTRODUCTION

Duplications of the alimentary tract (ATD) are rare congenital anomalies. Eighty percent of ATD are diagnosed in children before the age of 2 years. They may occur anywhere in the intestinal tract but the ileum is the most frequent affected site[1-3].

Due to the infrequency of ATD and its major relevance in the pediatric population, the analyses of patient characteristics and clinical manifestations in the adult are limited.

In the present report we describe a case of ileal duplication in a 61-year-old patient with Crohn's disease.

CASE REPORT

A 61-year-old Caucasian patient with a 5-mo history of intermittent diffuse abdominal pain associated with nausea, vomiting and weight loss was referred to our Gastroenterology Unit with a diagnosis of ileal Crohn's disease. A small bowel follow through (SBFT) showed an ileal stricture associated with dilation above a stenosis and a suspected entero-enteric fistula at about 30 cm from the ileocecal valve (Figure 1). However, no radiological evidence of mucosal lesions, including ulcers, was detectable. Steroid treatment was given, followed by incomplete remission.

Figure 1 Small bowel follow through shows an ileal stricture associated with dilation above stenosis and suspected entero-enteric fistula at about 30 cm from the ileo-cecal valve. No conclusive diagnosis was made on the basis of this examination.

Figure 2 Entero-computed tomography showing a marked ileal dilatation, with no evidence of mucosal lesions or fistulae.

Clinical examination and blood tests at admission were normal. The patient had no family history of inflammatory bowel disease (IBD) and there were no abdominal masses, cutaneous fistulas or other stigmata of Crohn's disease. A Small Bowel Contrast Ultrasonography (SICUS) was performed that showed findings comparable to SBFT. Oral budesonide (9 mg/d) was given with temporary and partial benefit. Entero-computed tomography (CT) scan confirmed the ileal stenosis associated with dilation above the stricture but it also visualized a blind loop of the intestine close to the stenosis (resembling a diverticulum) and enlarged mesenteric lymph-nodes (Figure 2). At this point, a differential diagnosis between CD and intestinal lymphoma was made in a symptomatic patient, giving an indication for an explorative laparotomy.

At surgery, an inflammatory mass was found in the right iliac fossa. The terminal and pre-terminal ileum, the cecum and the great omentum were involved. Tight adhesions were found between the above mentioned structures and both the terminal ileum and regional mesentery. The intestine at this level was thickened and a pre-stenotic dilation was present. A standard ileo-cecal resection was performed and the surgeon described the intra-operative findings compatible with an inflammatory mass of unknown origin. The patient made an uneventful recovery and was discharged home within a week.

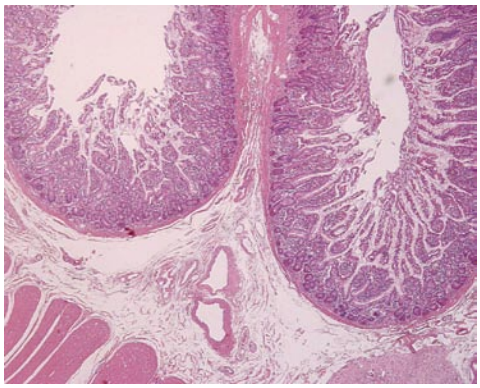

Figure 3 Histological section of the intestinal duplication at low magnification, showing the wall structure including the mucosa, the submucosa and the inner circular layer of the muscolaris própria (hematoxilin-eosin, original magnification 20 ×).

Macroscopic examination showed a tubular structure communicating with the ileal lumen that measured 5.5 cm × 2.5 cm × 2 cm. The cut surface was morphologically indistinguishable from the normal ileal wall. Light microscopy (Figure 3) highlighted the four layered organization of the ATD wall, including a mucosa with an intestinal-type epithelial lining and a muscularis propria, with an inner circular and outer longitudinal smooth muscle layers. A myenteric plexus was present between the two muscle coats.

The mucosa showed patchy features of ischemic injury. A diagnosis of ileal duplication was finally made.

DISCUSSION

ATD are congenital anomalies of the intestine, first described by Fitz[4]. They can be spherical or tubular and can be attached or adherent to the ATD. These conditions are rare (1/10000 live births), usually encountered in the ileum[1,2] and the vast majority are found in infants[5,6]. The differential diagnosis is with mesenteric cysts and true and false diverticula. However, a duplication shares a portion of its wall with the adjacent small intestine, usually sharing a common blood supply. The epithelial lining is always of some part of the ATD and may include heterotopic gastric mucosa. Malignant degeneration has been described in the adult series[7].

According to the review published by Johnson *et al*[8] in 1994, cancer was found in 3 (23%) of 13 reported cases of ileal duplications in adults (2 adenocarcinoma and 1 squamous cell carcinoma). This evidence of epithelial instability might suggest a tendency toward malignant transformation in long standing duplications. This also supports complete resection of the duplication as the most appropriate method of treatment.

Clinical presentation of ATD in adults is variable and, because these lesions occur so infrequently, they are not suspected. A palpable mass can be found in approximate-

ly one half of patients; abdominal pain is often present but the most common clinical presentations include intestinal obstruction and bleeding[1,9-11]. It is worthwhile to highlight that the clinical presentation is strictly related to the site and type of ATD. In cases of ATD of the hindgut, the diagnosis is often made within the first years of life and the most frequent symptom is biliary vomits. These malformations are usually cystic and localized on the mesenteric border of the first or second duodenum. In the jejunum, the most frequent aspect includes a tubular duplication with a common lumen, whilst in the ileum ADT can resemble a diverticulum. Ileal duplication affecting the distal part of the intestine should be distinguished from a Meckel's diverticulum, even though this is present on the anti-mesenteric border of the intestine. Complications of ATD include volvulus, invagination, bleeding, perforation and malignancy.

Twenty-seven cases of ileal duplications in adults are described in the world literature in over 100 years. In one of these cases, the correct diagnosis was made preoperatively. In this case, clinical presentation and pre-operative studies supported a diagnosis of complicated CD. Biopsies were not taken because it was not possible to enter the ileo-cecal valve during diagnostic colonoscopy and the rest of colonic mucosa was normal. Laparotomy is also often indicated in these settings to make a differential diagnosis[12]. Abdominal scans such as SICUS, CT or MRI and conventional contrast x-ray studies are useful tools to detect ATD. The diagnostic problems arise from the extreme rarity of this entity in the adult population.

We hereby describe a case of an adult patient who underwent various radiological studies and was referred to different physicians during the year before the correct diagnosis was made. The patient had 3 previous admissions to A&E and was on oral steroids when referred to our Gastroenterology Unit. ATD was not suspected and the diagnosis was made on the surgical specimen.

In conclusion, ATD are congenital abnormalities that can arise at any level from the mouth to the anus. They are rare and often found early in life. A minority of cases may remain undiscovered until adulthood when they may give rise to different symptoms, depending on the location. The ileum is the most frequent affected site and abdominal pain is the most referred symptom. Diagnosis is difficult due to the rarity of this entity. Symptoms are not specific and intestinal duplication is not considered in differential diagnoses. We believe therefore that it is useful to report new cases and to review the most relevant aspects of this entity. Surgical correction is the treatment of choice and, in the adult, resection of the entire duplication should be undertaken due to the reported incidence of malignancy.

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EAES Advanced Laparoscopic GI Surgery Course, Cairo, Egypt

January 20-22, 2011
Gastrointestinal Cancers Symposium (ASCO GI), San Francisco, CA, United States

January 26-30, 2011
5th UK Alpine Liver and Pancreatic Surgery Meeting, Carlo Magno Zeledria Hotel, Madonna di Campiglio, Italy

February 01-03, 2011
6th Annual Academic Surgical Congress, Huntington Beach, CA, United States

February 21-26, 2011
Minimally Invasive Surgery Symposium 2011, The Grand America Hotel, Salt Lake City, Utah, United States

March 03-06, 2011
The Society of Surgical Oncology 63rd Annual Meeting, San Antonio, TX, United States

March 10-13, 2011
The American Hepato-Pancreato-Biliary Association Annual Meeting, Miami Beach, FL, United States

March 14-17, 2011
British Society for Gastroenterology Annual Meeting, International Convention Centre, Birmingham, United Kingdom

March 25-27, 2011
NZAGS Conference 2011 GI Surgery, New Plymouth, New Zealand

March 30-April 02, 2011
The Society of American Gastrointestinal and Endoscopic Surgeons 2011 Annual Meeting, San Antonio Convention Center, San Antonio, TX, United States

April 02-06, 2011
The American Association for Cancer Research 102nd Annual Meeting, Orlando, FL, United States

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The American Association of Endocrine Surgeons 32nd Annual Meeting, Houston, TX, United States

April 14-16, 2011
The American Surgical Association 131st Annual Meeting, Boca Raton, FL, United States

May 07-10, 2011
Digestive Disease Week, Chicago, IL, United States

May 07-10, 2011
45th Annual Meeting of the Pancreas Club, Chicago, IL, United States

June 15-18, 2011
19th International Congress of the European Association for Endoscopic Surgery, in collaboration with and incorporating the 15th National Congress of the Italian Society of Endoscopic Surgery, Torino, Italy

September 10-14, 2011
International Congress of Endoscopy, Los Angeles, CA, United States

September 22-24, 2011
5th joint EAES and ESGE, European Workshop on NOTES, Frankfurt, Germany

September 23-25, 2011
The New England Surgical Society 92nd Annual Meeting, Breton Woods, NH, United States

September 23-27, 2011
ECCO-European Society for Medical Oncology Congress, Stockholm, Sweden

October 23-27, 2011
The American College of Surgeons 97th Annual Clinical Congress, San Francisco, CA, United States

November 02-05, 2011
American Pancreatic Association 42nd Annual Meeting, Chicago, IL, United States

November 13-16, 2011
The Western Surgical Association 119th Scientific Session, Tucson, AZ, United States

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2 **Lin GZ**, Wang XZ, Wang P, Lin J, Yang FD. Immunologic effect of Jianpi Yishen decoction in treatment of Pixu-diarrhoea. *Shijie Huaren Xiaohua Zazhi* 1999; **7**: 285-287

In press

3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

Organization as author

4 **Diabetes Prevention Program Research Group**. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462 PMCID:2516377 DOI:10.1161/01.HYP.0000035706.28494.09]

Both personal authors and an organization as author

5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

No author given

6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

Volume with supplement

7 **Geraud G**, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache* 2002; **42** Suppl 2: S93-99 [PMID: 12028325 DOI:10.1046/j.1526-4610.42.s2.7.x]

Issue with no volume

8 **Banit DM**, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. *Clin Orthop Relat Res* 2002; (**401**): 230-238 [PMID: 12151900 DOI:10.1097/00003086-200208000-00026]

No volume or issue

9 Outreach: Bringing HIV-positive individuals into care. *HRSA Careaction* 2002; 1-6 [PMID: 12154804]

Books

Personal author(s)

10 **Sherlock S**, Dooley J. Diseases of the liver and billiary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

Chapter in a book (list all authors)

11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

Author(s) and editor(s)

12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wieczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

Conference proceedings

13 **Harnden P**, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

Conference paper

14 **Christensen S**, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

Electronic journal (list all authors)

15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: http://www.cdc.gov/ncidod/eid/index.htm

Patent (list all authors)

16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

Statistical data

Write as mean ± SD or mean ± SE.

Statistical expression

Express *t* test as *t* (in italics), *F* test as *F* (in italics), chi square test as χ^2 (in Greek), related coefficient as *r* (in italics), degree of freedom as υ (in Greek), sample number as *n* (in italics), and probability as *P* (in italics).

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Quantities: *t* time or temperature, *c* concentration, *A* area, *l* length, *m* mass, *V* volume.
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