Laparoscopic assisted low anterior resection for advanced rectal cancer in a kidney transplant recipient

A case report

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Abstract

Introduction: Development of de novo malignancy has become a major cause of late mortality in solid organ transplant recipients. Surgery is currently the most important treatment of choice for transplant patients with resectable CRC. However, conventional open surgery represents a great risk to these high-risk patients. They seem to benefit more from laparoscopic surgery, based on the favorable oncological outcome and remarkable short-term advantages of this approach.

Patient concerns: In this study, we have reported a case of a 50-year-old man who had undergone kidney transplantation for 4 years. He presented with recurrent hematochezia and frequent loose stools for 1 year, and consulted a doctor for recent progressive general malaise and weight loss.

Diagnoses: Colonoscopy revealed a near-circumferential mass at the middle rectum about 8 cm from anal verge. Further biopsy confirmed a diagnosis of adenocarcinoma. Following computed tomography demonstrated peripheral lymph node metastasis, but no signs of distant metastasis.

Interventions: The patient underwent a laparoscopic assisted low anterior resection with total mesorectal excision for rectal cancer. Concomitantly, a loop transverse colostomy was performed to prevent anastomotic leakage. The surgery was completed within 120 min with a blood loss of 100 mL, and immunosuppressive therapy was not stopped perioperatively. Considering the tumor stage of pT3N1MO, the patient also received adjuvant chemotherapy with a regimen of FOLFOX for 8 cycles.

Outcomes: Anastomotic bleeding occurred in this patient about 4 h after surgery, and a control of hemorrhage per anus was performed timely. The following postoperative course was uneventful without any complications, and graft function stayed well. After 4 months of follow-up period, the patient was in a good condition. No evidences of local recurrence and distant metastasis were found.

Conclusion: We have presented a case of successful laparoscopic resection for advanced rectal cancer in a kidney transplant recipient. We believe laparoscopic surgery for CRC in transplant recipients is technically feasible and oncologically safe, which could be a preferred option of surgical procedure in the near future.

Abbreviations: AJCC = American joint committee on cancer, CNI = calcineurin inhibitor, CRC = colorectal cancer, ESRD = end-stage renal disease, mTOR = mammalian target of rapamycin, TME = total mesorectal excision.

Keywords: case report, kidney transplantation, laparoscopic surgery, low anterior resection, rectal cancer

1. Introduction

Colorectal cancer (CRC) is one of the most common malignancies and the leading causes of cancer-related death worldwide.[1] Surgery is the cornerstone of curative treatment for patients with resectable CRC. A number of earlier randomized trials and meta-analyses confirmed that laparoscopic surgery for CRC was not inferior to open surgery in terms of survival and recurrence rates, but provides significant short-term advantages, including a shorter hospital stay, reduced analgesic use, faster recovery of intestinal function, and earlier return to activities of daily life.[2,3] Therefore, laparoscopic-assisted surgery has been widely accepted as an alternative to conventional open surgery for CRC.[4]

Currently, due to the development of minimally invasive techniques, the indications for laparoscopic surgery have gradually expanded to high-risk patients with CRC.[5] Recipients of solid organ transplantation not only have associated problems of chronic immunosuppression and allograft dysfunction, but also suffer from numerous comorbidities, as the primary etiology of their organ failure.[6,7] Conventional surgical treatment for CRC represents a great risk to these high-risk patients, and the benefits of minimal access surgery seem to be shared by them.[8]
However, there is still some lack of literature about the evaluation on outcome of laparoscopic surgery for CRC in patients after organ transplantation. Herein, we report a case of a patient who presented with advanced rectal cancer 4 years after kidney transplantation, and underwent laparoscopic assisted low anterior resection.

2. Case report

A 51-year-old Chinese male had undergone living-donor kidney transplantation for end-stage renal disease (ESRD) due to 8 years of nephrotic syndrome in 2011 at the age of 46 years. His immunosuppression regimen included a combination therapy with tacrolimus 2.5mg/d, mycophenolate mofetil 1.5g/d, and prednisolone 10mg/d. The blood concentration of tacrolimus (FK-506) was monitored regularly at a target level of 4 to 10ng/mL. No colonscopy had been performed prior to transplantation, and he did not receive colonscopic surveillance postoperatively. Renal graft function remained stable in him without any rejection episodes.

Four years after transplantation, the patient presented with recurrent hematochezia (bright red blood per rectum mixed with stools), and a change in bowel habits manifested by frequent loose stools. He did not pay attention to these abnormal conditions until he began to suffer from progressive general malaise and weight loss of 3kg during the period of 1 month. A colonscopy was taken subsequently in January 2016, which revealed a near-circumferential mass at the middle rectum about 8cm from anal verge accompanied by moderate luminal stenosis. The friable lesion proved to be adenocarcinoma by further biopsy. Having made a definite diagnosis, the patient was admitted to our institution in February 2016. He had a previous history of hypertension for 7 years that could be generally controlled by medication, and cigarette smoking for more than 30 years. Regarding his family history, there were no remarkable findings.

On admission, detailed physical examination revealed a temperature of 36.5°C, pulse of 80 bpm, and blood pressure of 106/60 mmHg. No special signs were noted except for a healed surgery scar on his right lower abdominal wall. The lower margin of a solid, irregular mass was touched about 6cm from anal verge through a digital rectal examination. Laboratory tests showed hemoglobin was 133g/L, fecal occult blood test was positive, serum creatinine was 88μmol/L, liver function test was normal, and most serum tumor markers (AFP, CEA, CA19-9, and CA72-4) were within the normal range but CA242 was slightly elevated. The following computed tomography (CT) scan demonstrated a soft tissue density mass protruding into the lumen of upper-middle rectum, with the wall thickening and peripheral lymph node metastasis and the transplant kidney was located in the right pelvic cavity (Fig. 1). No evidences of distant metastasis were suggested. FK-506 was 4.7ng/mL at that time. According to recommendation of interdisciplinary team including urologists, medical physicians, and general surgeons, immunosuppressive therapy with previous regimen was extended perioperatively. FK-506 was monitored regularly at a target level of 4 to 10ng/mL. No colonoscopy had been performed prior to transplantation, and he did not receive colonscopic surveillance postoperatively.

Figure 1. Computed tomography scan showed a soft tissue density mass (arrow) protruding into the lumen of rectum (A) and a transplant kidney (arrow) in the right pelvic cavity (B).

The operation was completed successfully within 2h with a proximate blood loss of 100 mL. Histopathology revealed a well/moderately differentiated adenocarcinoma measuring 4.2 × 5 × 2.3cm, with invasion through the muscularis propria into pericolectal tissues (Fig. 5). The resection margins were free of peritoneal carcinomatosis. The tumor was identified locating at the middle-lower rectum. Specific surgical procedures started with lysis of abdominal adhesions from previous surgery. The sigmoid mesocolon and mesorectum were dissected along the inner side of the ureters by harmonic scalpel, and the vessels and lymphatics were ligated at the root of the superior rectal vessel with Hem-o-lock. The distal rectum was transected intracorporeally 3cm from the distal margin of tumor with a EC45-A laparoscopic linear stapler (Johnson & Johnson, Cincinnati, OH, USA). After that, a 6cm left supraumbilical incision was made to remove the proximal rectum, the distal sigmoid colon, and the surrounding tissues of the rectum 10cm from the proximal margin of tumor. The specimen was obtained for further pathological evaluation (Fig. 2). Reconstruction was performed intracorporeally in the manner of straight end-to-end colorectal anastomosis using a 28mm transanal circular stapler (COVIDIEN, Mansfield, MA, USA) (Fig. 3). Finally, 2 drainage tubes were placed in the pelvic cavity surrounding the anastomosis site. In order to prevent postoperative anastomotic leakage, a loop transverse colostomy was performed (Fig. 4).
tumor. Among the removed 14 lymph nodes, 3 contained metastatic cancer, indicating the tumor stage of pT3N1M0. Furthermore, immunohistochemistry showed the tumor was negative for MLH-1, MLH-2, MLH-6, and PMS-2.

Approximately 4h after surgery, the patient developed archorrhagia (dark red blood and clots per rectum), and the amount of blood loss increased up to 200 mL within 1 h. After exploration per anus, a bleeding wound near the anastomosis was identified and the control of hemorrhage was performed timely. There was no recurrence of archorrhagia ever since. The further postoperative course was uneventful. Graft function stayed well, and serum creatinine levels were always within the normal limits, ranging from 80 to 104 μmol/L. The ostomy was opened on the third postoperative day, and flatus was passed then. The patient went on a liquid diet 4 days after surgery and made a recovery soon. He stayed in hospital for 9 days after surgery, and drainage tubes were removed at discharge.

During 4 months of follow-up period, immunosuppressive therapy with tacrolimus 2.5 mg/d, mycophenolate mofetil 1.5 g/d, and prednisolone 10 mg/d continued, no allograft rejection and complications were observed. Considering his tumor stage, he received adjuvant chemotherapy with a regimen of FOLFOX (oxaliplatin/5-fluorouracil/calcium folinate). After 8 cycles of chemotherapy, repeated CT scan indicated no evidences of local recurrence and distant metastasis. To date, the patient was in a good condition.

3. Discussion

We have reported the detailed case of a patient after kidney transplantation, in whom laparoscopic surgery for advanced rectal cancer had been performed. Our case demonstrates that
laparoscopic assisted surgery for advanced rectal cancer can be
tolerated by kidney transplant recipients, and its short as well as
long-term outcomes are acceptable and encouraging.

Kidney transplantation is a definite treatment for patients with
ESRD. As surgical techniques, organ procurement, immunosuppres-
sion regimen, and postoperative monitoring have improved, kidney
transplant recipients have a higher treatment success rate and a longer life span. However, the development of de novo malignancy has become a major cause of late mortality in these patients.

The increased risk of CRC after kidney transplantation has been
documented. Moreover, compared with the general population, CRC that are diagnosed in kidney transplant recipients often display a more aggressive behavior, and the aggressive behavior is characterized by an earlier age of cancer diagnosis. A more advanced cancer stage (American joint committee on cancer stage > II) and a lower 5-year survival.

Interestingly, a significantly reduced risk of rectal cancer was observed in the transplant recipients when separated from colon cancer, and it seems that the elevated risk of CRC was driven by excess of proximal colon cancer. One possible explanation to these results might be that transplant recipients were screened more frequently than the general population primarily through sigmoidoscopy, which did not occur in the transplant recipients.

Based on the general rule, cancer was observed in the transplant recipients when separated from colon cancer, and it seems that the elevated risk of CRC was driven by excess of proximal colon cancer. One possible explanation to these results might be that transplant recipients were screened more frequently than the general population primarily through sigmoidoscopy, which did not occur in the transplant recipients. Interestingly, a significantly reduced risk of rectal cancer was observed in the transplant recipients when separated from colon cancer, and it seems that the elevated risk of CRC was driven by excess of proximal colon cancer.

The de novo malignancy has become a major cause of late mortality in these patients.

Compared with conventional open surgery, laparoscopic surgery for rectal cancer possesses comparable oncologic outcomes, and remarkable short-term advantages, particularly, a lower intra-postoperative complication rate.

It is generally accepted that surgery plays a role in the treatment of transplant patients with CRC. Most concerns exerted a positive effect on survival of transplant patients with CRC. The patient in our report developed advanced rectal cancer (pT3N1M0) 4 years after kidney transplantation at an age of 50 years. Based on the general rule, tumors detected within the first 12 months after transplantation are correlated with pre-existing condition. Despite the fact that he had not received colonoscopic surveillance before or at the time of transplantation, we considered the diagnosed rectal cancer as the de novo malignancy. While, long-term exposure to CNI-based triple immunosuppressive agents together with an absence of colonoscopic surveillance are speculated to be the 2 major hazards of occurrence of rectal cancer in our case.

It is generally accepted that surgery plays a role in the treatment for CRC after transplantation. Several studies found surgeries exerted a positive effect on survival of transplant patients with CRC. Theoretically, these patients were supposed to be more susceptible to perioperative complications. However, Krzyśka assessed the outcome of 21 kidney transplant recipients undergoing elective colorectal surgery, and suggested the results were favorable, with no transplant rejection, low morbidity and mortality.

Wisam also compared postoperative morbidity and oncologic outcome between patients with CRC in chronic immunosuppressive therapy and control groups. No significant difference was observed in wound infection, intra-abdominal abscess, anastomotic leak, urinary tract infection, or pneumonia, but lower in 3- and 5-year overall and disease-free survival. Consistently, several other reports demonstrated standard surgical treatment for CRC could be done safely in transplant recipients as long as the general condition and graft function were allowable.

Regarding the relationship between option for timing of surgery and surgical outcomes, Le found kidney transplant recipients undergoing colorectal resection <1 year of transplant had a higher perioperative mortality rate than those with grafts >1 year, likely due to more emergent surgeries in the early post-transplant period. Emergent colorectal surgery in kidney transplant patients was reported to have a significant risk of anastomotic leak; moreover, the overall major complication rate after emergent surgery was 81%, much higher than 19% of that after elective surgery. Therefore, emergent surgery for CRC in transplant recipients is not recommended considering its worse surgical outcomes.

In addition, much more fluid loss after loop ileostomy than loop transverse colostomy leads to a higher incidence of renal insufficiency. For these reasons, loop transverse colostomy
seemed to be a better option in this case. Anastomotic bleeding after laparoscopic rectal surgery is not rare. The use of a circular side stapling technique in laparoscopic low anterior resection for rectal cancer proved to be safe and did not increase the risk of anastomotic complications. Possible reason for bleeding in our case was likely to be attributed to the lower location of tumor.

### 3.2. Long-term oncologic outcome

Laparoscopic resection for CRC in kidney transplant patients is oncologically safe. Oncologic outcome is usually measured by the extent of resection, disease-free survival and overall survival. Curative extent of resection represents radical tumor removal with negative margins, TME, and a sufficient number of lymph nodes (>12). During our surgery, resection achieved adequate range of intestinal segment and total mesorectum. In addition, 14 lymph nodes were harvested, which fulfilled the standard of radical operation. Similar outcomes could be achieved by Rivas during the laparoscopic resection for colon cancer in transplant patients, as long as the allograft was placed in the contralateral side of the colon resection. As for disease-free survival and overall survival, our patient was alive without recurrence and metastasis after 4 months of follow-up. Further follow-up is needed to evaluate his long-term survival.

### 3.3. Graft function and immunosuppression modification

In this case, 2 trocars were placed away from the incision scar of the transplant surgery and the position of graft. Slightly lower pneumoperitoneum pressure during the surgery was maintained to preserving an adequate allograft function. Immunosuppressive therapy was not stopped perioperatively to avoid danger of resection, and postoperative serum creatinine levels stayed within the normal limits. In recent years, immunosuppressive medication modification including CNI-free regimens, substitution by mammalian target of rapamycin inhibitors or reduction in dosage of immunosuppression has been utilized as a treatment after cancer diagnosis in some transplant patients. It has been speculated that the use of rapamycin, instead of CNI might reduce the recurrence of cancer in transplant patients. In a case of adenocarcinoma in the stage of III B, as in our patient, switching immunosuppression regimen from cyclosporin to rapamycin might be helpful for his survival after surgery.

Based on the favorable oncologic outcome and low operative complications, laparoscopic assisted resection might be a preferred option for transplant patients with CRC. Indeed, decisions regarding surgical approach should also take into consideration of surgeon experience, tumor stage, potential contraindications, and patient expectations.

In summary, we have reported a case of a patient after kidney transplantation, in whom laparoscopic assisted low anterior resection for advanced rectal cancer had been performed successfully. The de novo rectal cancer was speculated to associate with long-term exposure to CNI-based immunosuppressive agents and an absence of colonoscopic surveillance. We believe laparoscopic surgery for CRC in transplant recipients is technically feasible and oncologically safe, which could be a preferred option of surgical procedure in the near future.

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