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CASE REPORT

Treatment of advanced rectal cancer after renal transplantation

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Abstract

Renal transplantation is a standard procedure for end-stage renal disease today. Due to immunosuppressive drugs and increasing survival time after renal transplantation, patients with transplanted kidneys carry an increased risk of developing malignant tumors. In this case report, 3 patients with advanced rectal cancer after renal transplantation for renal failure were treated with anterior resection or abdominoperineal resection plus total mesorectal excision, followed by adjuvant chemotherapy. One patient eventually died of metastasized cancer 31 mo after therapy, although his organ grafts functioned well until his death. The other 2 patients were well during the 8 and 21 mo follow-up periods after rectal resection. We therefore strongly argue that patients with advanced rectal cancer should receive standard oncology treatment, including operation and adjuvant treatment after renal transplantation. Colorectal cancer screening in such patients appears justified.

Key words: Rectal cancer; Renal transplantation; End-stage renal disease; Treatment; Screening

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INTRODUCTION

Renal transplantation, commonly performed for end-stage renal disease (ESRD), is an alternative to dialysis. An increased incidence of malignancy in transplant recipients is well recognized, which may be related to impaired immunosurveillance, direct neoplastic action of immunosuppressive agents, oncogenic viruses such as Epstein-Bar virus or cytomegalovirus, and chronic antigenic stimulation, uremia, or genetic predisposition[1].

There is evidence that renal transplant recipients are approximately three times more likely to develop cancer than the general population[2,3]. Their risks vary in different tumors. The risk of Kaposi's sarcoma is the highest (200 times increased risk) followed by that of non-melanocytic and melanocytic skin cancer (9-20 times increased risk)[2,3]. The risk other solid-organ cancers, such as colorectal cancer, is increased by approximately 2-3 times higher in renal transplant recipients than in general population[3,4]. Cancers occurring in transplanted patients are generally de novo and mainly diagnosed after the third year with an increase after 10 years[5]. The mean onset time of colorectal malignancies is 10.4 years[1].

The prognosis of renal transplant recipients with advanced-stage cancer is extremely poor. Currently, posttransplant malignancies are an important cause of mortality and the leading reason of death within the next 20 years[6]. Immunosuppression and late diagnosis have been implicated[7]. We report 3 cases of advanced rectal cancer after renal transplantation for renal failure.

CASE REPORT

In the past 5 years, 3 male patients at a mean age of 55.3 years who developed rectal cancer (RC) after renal transplantation were diagnosed and treated in Shanxi Cancer Hospital (Taiyuan, China). The mean elapsed time from renal transplantation to development of RC was 6.5 years. The 3 patients who underwent anterior resection (AR) or abdominoperineal resection (APR) plus total mesorectal excision (TME) had an uneventful postoperative course. The clinical data about each patient are listed in Table 1.

Case 1

A 68-year-old man who underwent renal transplantation for ESRD due to hydropigenous nephritis in 1993 at the age of 54 years. He received a second left renal transplantation in 2002 for graft failure followed by immunosuppressive therapy. In 2007, he underwent colonoscopy for rectal bleeding and dyschezia, which revealed a 5.0 cm mass at the upper rectum with 80% luminal occlusion. Biopsy showed a well-differentiated adenocarcinoma. Laboratory tests showed that his preoperative CEA level was 26.20 μg/L and his cellular immune function was low. The patient underwent AR with TME. Pathologic examination revealed a 5.0 cm moderately-differentiated adenocarcinoma with invasion through the serous membrane. Of the removed 7 lymph nodes, 1 was positive ($pT_4N_1M_0$). The postoperative course was uneventful. Following the operation, the patient did not receive any chemotherapy and radiotherapy due to his refusal. In November 2009, he received 3 cycles of Xeloda after liver and lung metastasis was discovered. The patient died in March, 2010.

Case 2

A 44-year-old man who received immunosuppressive therapy for ESRD in 2004 after renal transplantation. In 2009, he underwent colonoscopy for heme-positive stools, which revealed a 4 cm mass at the rectum with 60% luminal occlusion. Biopsy showed an adenocarcinoma of the rectum. Laboratory tests showed that his preoperative CEA level was 0.04 μg/L and his cellular immune function was low. The patient underwent APR with TME. Pathologic examination revealed a 4.0 cm poorly-differentiated adenocarcinoma with invasion of the adjacent perirectal fatty tissues. Eight lymph nodes were found with no malignant lymph node involved ($pT_3N_0M_0$). The patient was recovered uneventfully. He received a course of Xeloda and was well during the 21-mo follow-up period.

Case 3

A 54-year-old man with chronic pyelonephritis who underwent renal transplantation for ESRD in 2009. After the operation, he received immunosuppressive therapy. In 2010, 6 mo after renal transplantation, the patient presented with diarrhea and rectal bleeding. Colonoscopy showed a rectal mass with 70% luminal occlusion and a pedunculated polyp in sigmoid colon which was excised by electrocautery. Histology of the rectal mass showed a well-differentiated adenocarcinoma of the rectum while histology of the polyp suggested a tubular adenoma. Laboratory tests showed that his preoperative CEA level was 1.05 μg/L and his cellular immune function was low. The patient underwent APR with TME. Pathologic examination revealed a 5 cm moderately-differentiated adenocarcinoma and partial mucinous adenocarcinoma with invasion of the pericolonic adipose tissue. Thirteen lymph nodes were found with no lymph node metastasis ($pT_3N_0M_0$). Cancer emboli were identified in vessels of the mass. He received a course of Xeloda and recovered uneventfully during the 8-mo follow-up period.

DISCUSSION

It has been shown that the incidence of cancer is significantly higher in patients who underwent renal transplantation than in those who did not undergo renal transplantation[2,3]. For example, the risk of colorectal cancer is increased by approximately 2-3 times higher in patients than in general population[3,4]. However, some of the tumors may arise in renal recipients without any relation with renal transplantation, because they might have already presented at the time of renal transplantation but not detected. As a general rule, tumors detected within the first 12 mo after renal transplantation are considered pre-existed. Such patients should be excluded from the "*de novo*" group.

In our study, the 3 RC patients who underwent renal transplantation were males, and the onset interval from renal transplantation was 14 years, 5 years and 0.5 year, respectively. One patient was diagnosed with RC within the first 12 mo after renal transplantation, and pathological stage was $pT_3N_0M_0$ (advanced cancer). The other 2 patients were diagnosed with post-transplantation RC with a mean onset interval of 9.5 years. The 3 patients had radical AR and APR with TME.

It is well known that immunosuppressive treatment increases the incidence of cancers, which is supported by the fact that the incidence of tumors is higher in patients treated with immunosuppressants following renal transplantation due to chronic renal failure than in normal population. The causes for this difference might be explained by the immunological abnormalities induced by immunosuppressants[8-10]. Therefore, screening and early diagnosis of tumors are essential both before and after renal transplantation, which means that tumors, if existed, should be detected, thus unnecessary renal transplantation can be avoided. Furthermore, annual tumor screening after renal transplantation should be conducted so that treatment can be commenced at an early stage of malignancy. In our study, the patient who was diagnosed with advanced RC within 6 mo after renal transplantation had no tumor screening before renal transplantation. It is likely that he developed RC while he was on dialysis and waiting for renal transplantation.

In general, the prognosis of transplant recipients who develop malignancy following immunotherapy are poor due to delayed diagnosis[6,8,11-14]. Most cancers are at advanced stages when they are diagnosed, and usually progress rapidly with more than 50% of such patients died within the first year of diagnosis[15]. The average survival time is proximally 25.8 mo[15]. Evidence from National Cancer Institute Surveillance Epidemiology and End Results Database suggests

Table 1 Parameters of patients with rectal cancer after renal transplantation

Age (yr)	Elapsed time (yr)	Location	Grade	pTNM	Operation	Screening	Outcome
68	14	Rectum	Moderate	$pT_4N_1M_0$	AR + TME	No	Died after 31 mo
44	5	Rectum	Poor	$pT_3N_0M_0$	APR+TME	No	Alive after 21 mo
54	0.5	Rectum	Moderate to poor	$pT_3N_0M_0$	APR + TME	No	Alive after 8 mo

that transplant patients develop colorectal cancer at a younger age (58 *vs* 70 years, $P < 0.001$) and have a worse 5-year survival rate than the general population (overall, 44% *vs* 62%, $P < 0.001$; Dukes A and B, 74% *vs* 90%, $P < 0.001$; Dukes C, 20% *vs* 66%, $P < 0.001$; and Dukes D, 0% *vs* 9%, $P = 0.08$) mainly due to chronic immunosuppression which results in a more aggressive tumor biology[16]. RC patients who underwent renal transplantation usually develop more advanced (AJCC stage > Ⅱ) colon cancer with a worse disease-specific survival rate (all stages) than those who did not undergo renal transplantation. Multivariate analyses showed that renal transplantation is a negative risk factor for survival, and cancer stage at diagnosis is the most profound negative survival predictor[17], indicating that colorectal cancers in transplant recipients are biologically more aggressive, thus resulting to a worse prognosis in such patients than in general population. Moreover, Ho *et al*[7] also highlighted that immunosuppression and late diagnosis should be blamed for the poor prognosis of colorectal cancer patients after renal transplantation. In the present study, of the 3 patients with advanced rectal cancer, 1 died of multiple liver and lung metastases 31 mo after operation, indicating that frequent colorectal cancer screening should be warranted after renal transplantation.

Zittel *et al*[18] reported a case of a 48-year-old patient who developed advanced RC 6.5 years after pancreas-kidney-transplantation for type I diabetes. The patient received neo-adjuvant radio and chemotherapy followed by low anterior rectal resection with total mesorectal excision. Within the next thirteen months, he underwent consecutive resections for a solitary hepatic metastasis, a solitary pulmonary metastasis and a chest wall metastasis. The patient eventually died of metastasis 32 mo after the initial therapy although the organ grafts functioned well until his death, suggesting that although a higher degree of morbidity might be encountered, transplantation patients should receive standard oncology treatment, including neo-adjuvant therapy, if their general condition is good and the organ graft functions well.

In conclusion, early prevention, detection and treatment of malignancies after renal transplantation are the important management strategies for improving the survival time and quality of life of cancer patients because malignancies develop more frequently in cancer patients after renal transplantation than in general population. Surgical resection is still the first choice of treatment which is a safe procedure when indicated. However, if the patients have an advanced disease (local or metastatic), the standard oncology treatment, including neo-adjuvant treatment can be used.

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