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Case report

Unusual Clinical Presentation of Colorectal Cancer in a Kidney Transplant Recipient

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Abstract

Introduction. Kidney transplant recipients (KTRs) from around the world are at greater risk of developing cancer compared to the general population. In addition, some common cancers in the general population occur at a higher incidence rate in KTRs (e.g. colorectal cancer).
Case report. In this report, we describe a case of a 54-year-old male with an advanced stage colorectal cancer (CRC) causing urinary obstruction as cardinal symptom for its diagnosis. He underwent living-related kidney transplantation from his 70-years-old mother in 2005 with a stable renal function in the following years (serum creatinine around 180 µmol/l). However, the patient had a poor compliance not regularly attending our outpatient clinic. Thus, at his last visit a slight progression of anaemia was found, although, he denied a possibility for bleeding from any part of the gastrointestinal tract. The motive for his next consultation to the hospital was the problem of voiding urine. The pain from the bladder glob at admission immediately disappeared after the urocatheterisation with ensuing poliuria and serum creatinine (278 µmol/l) decreased gradually in the following days. CT scan showed a tumour mass from an advanced CRC pressuring the lower bladder wall and distant metastasis and disseminated lymph-nodes. The surgical revision was not considered as treatment option, thereby chemotherapy was initiated. Two years after the diagnosis of the CRC he passed away with an advanced chronic allograft nephropathy, yet without a need for renal replacement therapy.
Conclusion. There is a possibility to develop CRC as an advanced metastatic form at diagnosis in relatively short period after renal transplantation as in our case. Periodic CRC screening pre and post-transplant in this population is important as treatment options are limited and survival of such KTRs is very poor. Since an older age is the most important risk factor, a more aggressive screening for malignancy in transplant recipients after 50 years of age, especially in those with poor compliance and anaemia development, should be employed in the hospital condition.

Keywords: kidney transplantation, malignancies, colorectal cancer, obstructive nephropathy

Introduction

Immunosuppressive therapy in solid organ transplantation has short- and long-term side-effects, such as infections, cardiovascular accidents and malignancies [1,2]. Post-transplant malignancies have become an important cause of mortality and are expected to become the leading cause of death within the next 20 years [2]. Moreover, the incidence of malignancy in transplant recipients is known to be several times higher than that in the general population, with more aggressive course and worse prognosis [3-5]. However, for some common cancers in the general population such as colorectal cancer (CRC), there are still not unified parameters related to his appearance, associated risk, recommended screening, etc. We present a case of CRC in kidney transplant patient with a poor compliance, advanced cancer stage at the time of diagnosis and discuss options on whether/when an early screening should be performed in KTRs.

Case report

A 54-year-old male with medical history of diabetic nephropathy and no family history of any cancer underwent living-related kidney transplantation from his 74-years mother with 36 ml/min of GFR at the donated kidney. Induction therapy consisted of methylprednisolone and Daclizumab® and no complications were encountered perioperatively. At the time of discharge he was on standard triple maintenance therapy with prednizolone 0.1 mg/kg, mofetil mycophenolate (MMF) 2x1000 mg and cyclosporine A of 2.5 mg/kg in two doses (adapted at the lower level of C2 normal range). Expectedly, at 6-month protocol biopsy the histology of tubular atrophy, intimal fibrosis, chronic allograft nephropathy and initial diabetic nephropathy characteristics were found and a consecutive mild reduction of the cyclosporine dose was prescribed. At his irregular visits at our outpatient clinic serum creatinine levels were ranging between 170-200 µmol/l. At almost four years

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after transplantation, the routine laboratory showed he is becoming severely anaemic. He denied any change of the stool colour or any other problem being reluctant to perform any proposed examination of the lower gastrointestinal tract. He received 2 units of blood transfusion, MMF was slightly reduced (2x750 mg), the depleted ferritin reserve was gradually supplemented and erythropoietin treatment was initiated. Three months latter he admitted having a "negligible" haemorrhoidal bleeding, but refused hospitalisation, indicated rectoscopy and eventual ligation or surgical treatment. A few weeks later (December 2009), the patient was admitted at our Department with urinary retention into the bladder causing obstructive nephropathy with an increase in serum creatinine of 278 µmol/l. In addition, he admitted having intermittent bleeding in his stool, sporadic fever, feeling malaise and fatigue. The ultrasound examination revealed tumour mass adjacent to the urethral neck predominantly from the posterior and left bladder wall and urinary retention. Urinary catheter was placed, and postopstructive diuresis of more than 3000 ml was obtained. The tumour mass was highly suspicious for a bladder penetration from a CRC that was confirmed by the abdominal CT scan (Figure 1).

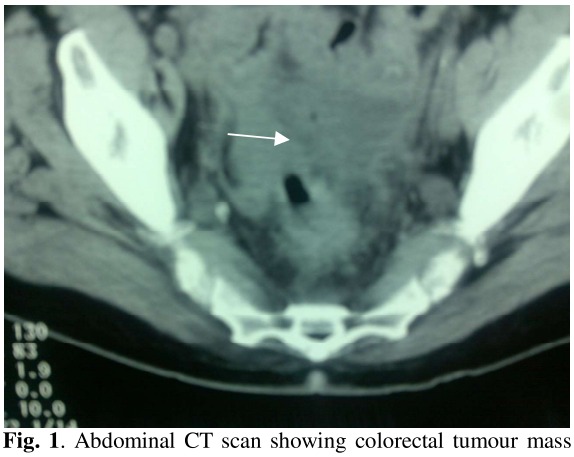

Fig. 1. Abdominal CT scan showing colorectal tumour mass infiltrating the lower and posterior wall of the bladder and urethral neck (arrow)

With the histology of colorectal carcinoma and imaging findings of disseminated metastatic infiltrations were obtained, the patient was referred to oncological section for further chemotherapy with 5-fluorouracil and irinotecan. The immunosuppression was further modulated with drawing calcineurin inhibitors and MMF, while Azathioprine and prednizolone was maintained since our patient did not agree on complete cessation of the immunosuppression. Meanwhile, the deterioration of the graft function and condition of the patient required several intermittent dialysis treatments. However, at two years after the diagnosis of the CRC the patient died with an advanced chronic allograft nephropathy, yet without a need for renal replacement therapy.

Discussion

The risk of developing malignancy is increased after transplantation, which is believed to be related to an additional risk of the use of immunosuppression. The incidence and specific risk for CRC has been difficult to calculate [6-8], although, according to the USRDS database, the incidence of common malignancies, such as colon, lung and stomach, is approximately 2-fold times higher after renal transplantation than in the general population [9-11]. A variety of conventional and those specific to transplant recipients risk factors contribute to the incidence of cancers. The "age at the time of transplantation" (especially an age >50 years) has been extensively reported as risk factor for post-transplant malignancies in many studies [12,13]. The duration of immunosuppression, its intensity and type of immunosuppressive agent used, all might have an impact on the development of post-transplant malignancy, rendering the immunosuppressive regimen an important risk factor requiring further consideration [14]. However, the association of a particular immunosuppressive agent with the incidence and outcome of post-transplant malignancies is still controversial since all immunosuppressive regimens contain a combination of a variety of agents [5,7,15,16].

At present, CRC after renal transplantation is controversial and the reported time interval from transplant to its development range from 3.8 to 12.3 years [1,17]. In addition, Kasiske *et al.*, reported two-fold higher risk of CRC development in the first post-transplant year, which increases to 2.2-fold times higher risk after the third post-transplant year compared with the general population [8]. In contrast to our case, the pattern of increased risk appears to be greatest among younger recipients, being increased at least 20-times in patients <35 years, compared to around 1.5-fold time increased risk among those >50 years [2,14]. Interestingly, Johnson *et al.* reported a median age of 58.7 years at the time of diagnosis of CRC and concluded that more than 25% of the at-risk population would have their tumors missed if adhered to the current screening guidelines [18]. They suggested in those >50 years, a baselyne pretransplant screening colonoscopy should be obtained along with a follow-up surveillance exam 2 years after transplantation.

Expectedly, kidney transplant recipients diagnosed with CRC have a worse prognosis than patients without transplants. The overall five-year survival rate of CRC is less than 20%. In addition, these cancers are often found at a much later stage due to the tumour growth either into the lumen or adjacent structures, being with more aggressive and worse oncological outcomes than cancers in the general population [19,20]. Although the common signs of presentation may be abdominal pain, melena and unexplained iron deficiency anaemia, the most unusual presentation of CRC is the local invasion or a contained perforation that is sometimes causing malignant fistula formation into adjacent organs of bladder or small bowel.

Our unusual case presentation is of a relatively young transplant patient with advanced CRC causing opstructive nephropathy. It appeared to be at relatively short period after

transplantation and with limited treatment options and a poor survival. We highlight the paramount importance of a good compliance for early detection of malignancies, and the potential benefit of a preventative screening in KTRs with possible benefit of lower morbidity and mortality through reduced incidence or early interventions. Finally, it's the patient's choice for a complete or partial immunosuppression withdrawal or eventual conversion to sirolimus which is still under debate (21).

Conclusion

There is a possibility of development of an advanced CRC with metastases within relatively short period after renal transplantation. Periodic CRC screening pre and post-transplant in this population is important as treatment options are limited and survival of such KTRs is very poor. Thus, we should adopt the tumor screening schedules in post-transplant recipients as recommended in the guidelines for the general population. Since an older age is the most important risk factor, a more aggressive screening for malignancy in transplant recipients after 50 years of age, especially in those with poor compliance and anaemia development, should be a regular clinical practice.

Conflict of interest statement. None declared.

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