Received: 26 February 2021 | Revised: 15 July 2021 | Accepted: 22 August 2021

DOI: 10.1002/ccr3.4810

CASE REPORT

Clinical Case Reports Open Access WILEY

Overall of kidney transplant recipients with a pretransplantation cancer history

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Funding information
NO Funding/NO Support

Abstract

No significant morbidity from recurrence cancer and no development of secondary type of cancers in pre-existing malignancies. We must be careful about risk of rejection.

KEYWORDS

kidney, malignancy, recurrence, transplantation

1 | INTRODUCTION

Pretransplant malignancy (PTM) in remission has long been considered a relative contraindication for organ transplantation due to the heightened risk of cancer recurrence associated with immunosuppression used after transplantation. In recent years, older patients are being accepted for transplantation. We report the overall of three cases with a history of malignancy before kidney transplantation. Our findings indicate that there is no significant morbidity from recurrence cancer and no development of secondary type of cancers in pre-existing malignancies. But we must be careful about risk of rejection.

Patients with cancer history in need of organ transplantation represent a special challenge. Pretransplant malignancy (PTM) even in remission has been considered a contraindication for organ transplantation due to the heightened risk of cancer recurrence associated with immunosuppression used after transplantation. In recent years, older patients are being accepted for transplantation, it is expected that more transplant recipients will present with a history of pretransplantation malignancy. So the number of candidates to transplantation with history of malignancy continues to grow.

The cancer-free waiting time has been related to the type of malignancy, a wait between 2 and 5 years has been deemed sufficient for most cancers. This is in the aim to avoid the recurrence of cancer after transplantation on the assumption that development of micrometastases will be enhanced by the immunosuppressants.

Over the last decades, malignancy is one of the principal causes of death in kidney transplant recipients with functioning grafts beyond the first year of kidney transplantation; however, there has been an encouraging decrease in mortality after kidney transplantation.

The purpose of this study was to investigate overall and cause-specific mortality in kidney transplant patients with a history of malignancy, to appraise overall survival and cancer-related consequences.

2 | METHODS

We conducted a retrospective descriptive study collecting all cases of kidney transplanted patient with cancer history in the department of Internal Medicine over a period of forty years (1978 à 2018).

Recipients with a diagnosis of cancer (disregarding basal cell carcinoma) within 60 days before transplantation or within the first 60 post-transplantation days were excluded from the analysis. Patients likely transplanted because of a malignancy were also excluded from the analysis.

The underlying renal disease, duration of dialysis, delay between cancer diagnosis and kidney transplantation, clinical presentations, biochemistry data, microbiology study, post-transplantation immunosuppressive strategies, and outcomes of the patients were analyzed.

Main causes of death were categorized as cancer or noncancer-specific and noncancer deaths were further categorized as cardiovascular, infectious, or other.

The immunosuppression dosages, incidence of rejection and infection, and immunosuppression induction were noted.

We reported the age, sex, immunosuppressive therapy and corticoids, type of pretransplantation cancer and time interval between cancer and kidney transplantation, and post-transplant de novo malignancies.

3 | RESULTS

A total of three patients with cancer history underwent a kidney transplantation during forty years in our department. All candidates were considered cured of their cancer before undergoing transplantation (Tables 1 and 2).

3.1 | Case 1

A 56-year-old man underwent kidney transplantation because of bilateral nephrectomy. Right nephrectomy indicated in front of non-functional lithiasis kidney and a left nephrectomy indicated in front of vesical tumor invasion. Sixteen years before the transplant he was diagnosed as having a vesical tumor GII PT1 witch was treated with BCG therapy during five years and since then he has been considered cured. Current immunosuppressive therapy includes corticosteroid and mofetil mycophenolate (MMF). During his nine years of follow-up, he has had an episode of urinary infection, an episode of rejection, and an episode of endocarditis. There has been no recurrence of malignancy.

What is already know on this topic

- Pretrasplant malignancy is a relative contraindication for organ transplantation.
- 2 and 5 years are enough for most cancers.

What this study adds

- No higher incidence of infections in patients with pre-existing neoplasms.
- No rejection or recurrence of malignancy.

3.2 | Case 2

A 45-year-old women underwent kidney transplantation because of vascular nephropathy. Two years before the transplant she underwent a thyroidectomy as treatment of papillary thyroid carcinoma and since then she has been considered cured. Current immunosuppressive therapy includes corticosteroid, tacrolimus, and mofetil mycophenolate (MMF). During her three years of follow-up, she has had an episode of rejection, an episode of urinary infection, a serous cystadenoma after one year of transplantation indicated the switch by sirolimus and cortico-induced diabetes. There has been no recurrence of malignancy.

3.3 | Case 3

A 65-year-old women underwent kidney transplantation because of chronic glomerular nephropathy. Eleven years before the transplant she underwent a radical mastectomy followed by hormonal therapy as treatment for breast cancer. Current immunosuppressive therapy includes prednisone and mofetil mycophenolate. During her five years of follow-up, she has had many episode of urinary infection, cortico-induced diabetes, and an episode of ischemic cerebrovascular accident. There has been no recurrence of malignancy.

4 | DISCUSSION

In our study, the number of the kidney transplanted patients with a history of malignancy before kidney transplantation is lower than the number of patients reported by Chapman et al.[1] and Kauffman et al.[2]

Immunosuppression is related to a major risk of cancer in kidney transplant recipients compared to the general population. Several studies suggest that

TABLE 1 Characteristic of patients collected in our study

	Gender	Age[a]	Type of cancer	Duration on dialysis (year)	TR[b]	FU[c]	Creat[d]
Case 1	Man	56	Vesical tumor	16	16	9	97
Case 2	Women	45	Papillary thyroid carcinoma	5	2	3	110
Case 3	women	65	Breast cancer	2	11	5	87

[a]Age at the end of the study (years).
[b]Time between cancer and transplantation (year).
[c]Follow-up after transplantation (years).
[d]Serum creatinine at the end of the study (μmol/l).

TABLE 2 Characteristic of immunosuppressive therapy

	Induction immunosuppressive therapy	Current immunosuppressive therapy
Case 1	ATG	Corticosteroid
	Solumedrol	MMf
	MMF	
Case 2	ATG	Corticosteroid
	Solumedrol	MMF
	MMF	Tacrolimus
Case 3	ATG	Corticosteroid
	Solumedrol	MMf
	MMF	

Abbreviations: ATG, Thymoglobulin; MMF, mofetilmycophenolate.

immunosuppression may favor the growth of existing cancer cells.[3-5] It was not the case in our study.

Kauffman et al.[2] and other authors,[6,7] found that patient survival was significantly lower in kidney graft recipients with previous malignancies. These findings are in disaccordance with our material. However, because no multivariate analysis was performed in the Kauffman et al. study (eg, with adjustment for age), they were unable to assess the extent to which survival differences were explained by different factors. Other research is needed to inquire into the etiologies of mortality in kidney graft recipients with PTM. Is it explained by the increased cancer mortality or by cardiovascular disease or graft failure.

According to Brattstrom et al[8] and Kiberd et al,[6] the range of overall death from various recurrent malignancies varying between 5 and 12% of the recipients with a pretransplantation cancer. In contrast, Bavinck et al[9] reported that there is no greater risk of cancer-specific mortality in 46 kidney recipients with pretransplant malignancy, our results support these findings.

Common recommendations or listing transplant candidates with PTM have been based on the high risk of cancer recurrence reported by the Israel Penn International Transplant Tumor Registry and the natural history of the malignancy.[10-12]

For Penn, the prevalence of recurrence after transplantation was excessive in case of cancer in the breast, kidney, sarcoma, or multiple myeloma. In CTTR database, the risk of cancer recurrence has been reported to be 21% overall and in Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOS) the risk of cancer recurrence has been reported to be 2.4%. In fact, in our study, there is no recurrent malignancy and the impact of cancer history on post-transplantation mortality in our study was small in absolute terms. We have not recorded deaths.

The most evident approach in attempting to prevent cancer recurrence after transplantation is to delay transplantation.[8] However, prolonging the period of remission before transplantation may not have a positive influence on survival outcomes in patients with PTM. Also prolonging the dialysis period before transplantation amplified the risks of cardiovascular mortality and graft failure.[13,14]

For low-risk cancers, it seems that a waiting time of 2 years would be enough. Penn proposed that the risk of recurrence depends on the type of cancer and on the waiting period between treatment of cancer and transplantation. It has been advised to delay transplantation for 2, 2 to 5, and more than 5 years depending on the type of pretransplantation malignancy.[15] The median waiting period between treatment of cancer and transplantation in our study was 9.6 years.

We do not found a higher incidence of infections in patients with pre-existing neoplasms despite the fact of immunosuppression therapy.

In the literature, many study showed that PTM is associated with increased risk of de novo post-transplant malignancy.[16,17] In fact, in our study, there are no cases of post-transplant de novo malignancy.

5 | CONCLUSION

In conclusion, our findings indicate that there is no significant morbidity from recurrence cancer and no development of secondary type of cancers in pre-existing malignancies. But we must be careful about risk of rejection. The pronostic factors that should be considered in each individual case are the type and extent of cancer and the duration between diagnosis and the proposed transplant.

ACKNOWLEDGEMENTS
None.

CONFLICTS OF INTEREST
The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS
All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

CONSENT
Published with written consent of the patient.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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How to cite this article: Chargui S, Braiek N, Bacha MM, et al. Overall of kidney transplant recipients with a pretransplantation cancer history. *Clin Case Rep*. 2021;9:e04810. https://doi.org/10.1002/ccr3.4810