American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2021; 22: e933168
DOI: 10.12659/AJCR.933168

Received: 2021.05.17
Accepted: 2021.08.19
Available online: 2021.09.01
Published: 2021.10.08

Chromophobe Renal Cell Carcinoma of a Renal Allograft

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF Jamilya Saparbay
BCF Melss Assykbayev
ABCDEF Saitkarim Abdugafarov

Department of Hepatobiliary and Transplant Surgery, National Research Oncology Center, Nur-Sultan, Kazakhstan

Corresponding Author: Jamilya Saparbay, e-mail: dzhamilyasaparbay@gmail.com
Financial support: None declared
Conflict of interest: None declared

Patient: Female, 30-year-old
Final Diagnosis: Chromophobe renal cell carcinoma
Symptoms: Pain
Medication: —
Clinical Procedure: —
Specialty: Transplantology

Objective: Rare disease

Background: Kidney transplantation is a treatment option for patients with end-stage renal disease. However, life-long immunosuppressive therapy, which is obligatory for renal transplant recipients, increases the risk of cancer recurrence and de novo tumor formation. Cancer is one of the leading causes of death in kidney transplant recipients. Renal cell carcinoma (RCC) of an allograft kidney is an extremely rare type of neoplasm and occurs in only about 0.22-0.25% of all kidney recipients. RCC is often asymptomatic and can be an incidental finding on routine examination.

Case Report: In this case study, we describe a patient who developed chromophobe renal cell carcinoma 3 years after kidney transplantation from a living related donor. At the time of detection of the tumor, the graft function was impaired. A renal allograft biopsy was performed, and the pathological examination showed signs of chronic inflammation and chronic graft rejection. The graft biopsy failed to differentiate between oncocytoma and chromophobe carcinoma. Due to impaired graft function, presence of neoplasm in the graft, and morphologic chronic rejection, it was decided to perform a transplantectomy. The final histological examination showed the eosinophilic type of chromophobe carcinoma.

Conclusions: Chromophobe carcinoma in a kidney allograft is extremely rare in kidney transplant recipients. This clinical observation confirms the necessity and effectiveness of regular ultrasound and magnetic resonance imaging of the graft, not only for monitoring the functioning of the graft, but also for early detection of neoplasms in the transplanted kidney.

Keywords: Kidney Transplantation • Immunosuppression • Carcinoma, Renal Cell

Abbreviations: **RCC** – renal cell carcinoma; **ESRD** – end-stage renal disease; **PET-CT** – positron-emission tomography-computed tomography; **MRI** – magnetic resonance imaging

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/933168

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

Background

Currently, kidney transplantation is the best treatment option for end-stage kidney disease [1]. However, after transplantation, patients are on lifelong immunosuppressive therapy, which increases the risk of developing neoplasms in this cohort of patients [2]. Cancer is one of the leading causes of death in kidney transplant recipients [3]. RCC is one of the most lethal urologic malignancies and accounts for 90% of adult renal cancer [4]. There are 3 main subtypes of RCC: clear cell (70%), papillary (10-15%), and chromophobe (5%). Rare subtypes of RCC include carcinoma of the collecting ducts of Bellini, renal medullary carcinoma, multilocular clear cell RCC, mucinous tubular and spindle cell carcinoma, and other unclassified RCC [5]. The incidence of various types of renal cell carcinoma (RCC) in the recipient's native kidneys is 15-30 times higher than in the general population, and the development of RCC in the graft occurs in 0.22-0.25% of cases [6]. In this clinical case report, we describe the development of the eosinophilic variant of chromophobe renal cell carcinoma in a transplanted kidney 3 years after kidney transplantation from a living related donor.

Case Report

A 42-year-old woman, diagnosed with end-stage renal disease related to chronic glomerulonephritis, underwent a kidney transplantation from a living related donor in May 2016. The patient had been on programmed hemodialysis since 2013. She had no history of blood transfusions or solid organ transplantation. The duration of cold ischemia was 30 min. The induction of immunosuppression was performed with Basiliximab. We began maintenance immunosuppressive therapy with tacrolimus (starting dose 0.1 mg/kg), mycophenolate, and steroid. The postoperative period was uneventful. Three years after kidney transplantation, during a regular checkup, an abdominal sonogram showed a solid mass in the transplanted kidney. Magnetic resonance imaging confirmed the presence of a kidney mass (**Figure 1A, 1B**). A biopsy of the renal allograft was performed, and the pathology examination showed signs of chronic inflammation and chronic graft rejection, and the tumor tissue was more consistent with an oncocytoma. Differentiation from chromophobe carcinoma was required. Graft biopsy failed to differentiate between oncocytoma and chromophobe carcinoma. PET-CT was conducted to determine the neoplasms of other localizations or metastases. PET-CT showed metabolically active growth of a renal transplant, and no signs of regional and distant metastases were detected (**Figure 2**). The graft function was impaired; diuresis decreased to 800 ml per day and creatinine level increased up to 250 mkmol/l (normal range-53-97 mkmol/l).

It was decided to perform open surgery with intraoperative biopsy from several sites of the graft. The intraoperative repeated biopsy showed eosinophilic variant of chromophobe carcinoma. Graftectomy was performed. The patient was returned to hemodialysis. The patient underwent another PET scan 3 months after the transplantectomy. No neoplasms were found. The patient did not show any new or metastatic tumors within 2 years after graftectomy.

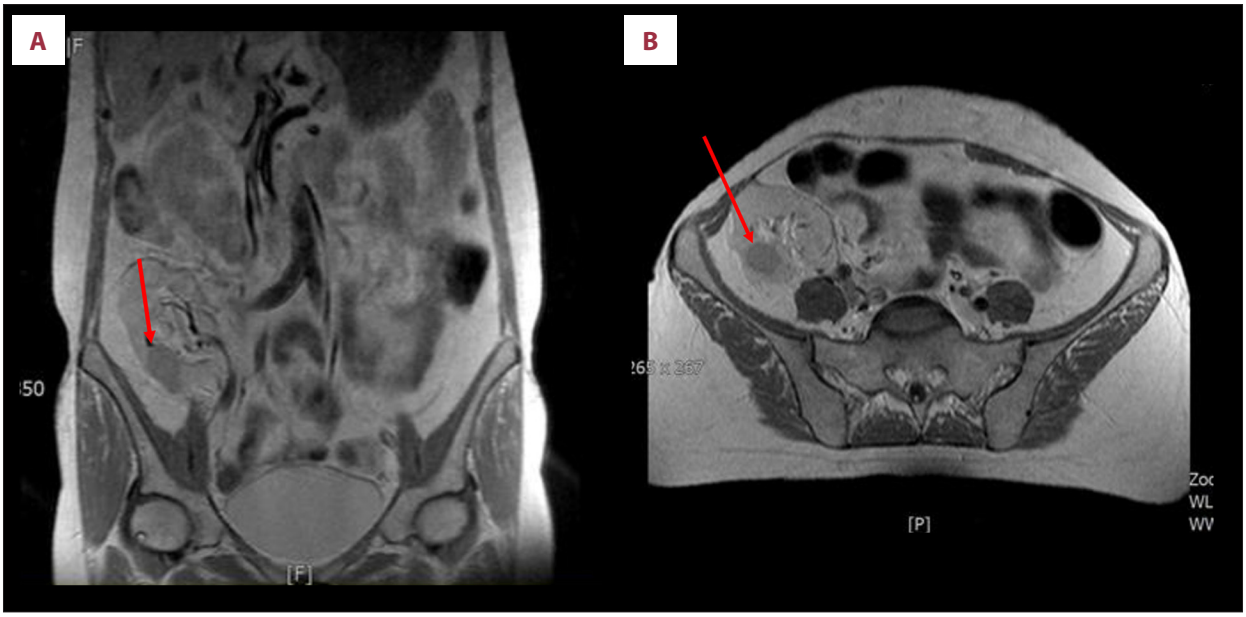

Figure 1. MRI of the abdomen. (**A**) MRI of the abdomen, frontal view; the tumor of the renal allograft indicated with red arrow. (**B**) MRI of the abdomen, saggital view; the tumor of the renal allograft indicated with red arrow.

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

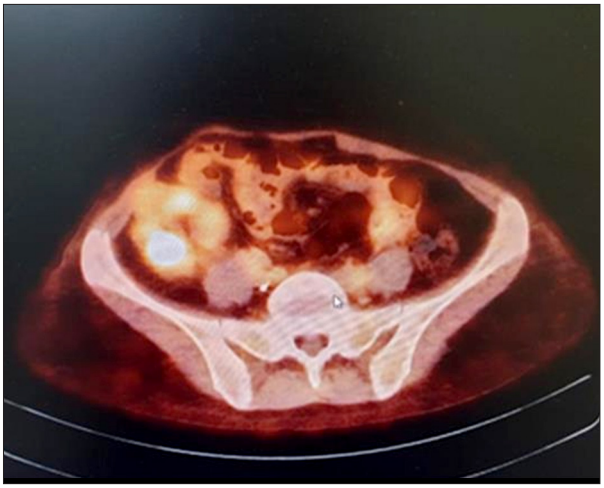

Figure 2. PET-CT. Metabolically active mass in the renal allograft.

Discussion

Chromophobe renal cell carcinoma is a rare form of malignant neoplasms of the kidney, accounting for less than 10% of all types of RCC [7]. It was first described in 1985 by Thöenes and was classified as a form of papillary RCC; later, it was categorized as a separate morphological type. There are 2 morphological types of chromophobe renal cancer: classical and eosinophilic [8]. The eosinophilic variant is less common and differs from the classical type in localization of neoplastic cells and in the density of cell cytoplasm. [9]. The eosinophilic variant of chromophobe RCC is characterized by pronounced cytoplasmic eosinophilia; as a result of which, this variant is difficult to differentiate from oncocytoma [10]. Patients with chromophobe RCC have a better prognosis compared to those with clear cell carcinoma, with a mortality rate of less than 10%. Large tumor size and the disintegration of the malignancy worsen the prognosis. The incidence of the chromophobe form of carcinoma in the kidney transplant is unclear because fewer than 10 cases have been described in the world literature [11].

Treatment options for kidney transplant recipients with chromophobe graft carcinoma include transplantectomy, cryoablation, and radiofrequency ablation. The method of treatment depends on the size of the tumor. In our clinical observation, the size of the tumor in the graft exceeded 2 cm. The pathologist could not differentiate the type of tumor between oncocytoma and the eosinophilic variant of the chromophobe RCC according to the results of a diagnostic biopsy. Considering the above factors, as well as a decrease in graft function and an increase in creatinine levels, the patient was referred for transplantectomy.

In this case, we observed the RCC of the renal allograft in combination with renal allograft rejection. Immune cell infiltration of the tumor mass and surrounding vessels is typical for RCC. Cell infiltration is composed of different immune cell types, including CD4 and CD8 T cells, B cells, APCs, and natural killer cells (NK) [12]. Immunosuppressive (IS) agents provide the necessary immune state, which is important for host tolerance to the graft [13]. However, currently-used IS agents target the adaptive component of host immunity. The concept of "danger theory" says that any extracellular or intracellular perturbation of the microenvironment can activate innate immune cells [14]. Carcinogenesis can be the origin of allograft rejection.

There is a lack of information on the eosinophilic form of chromophobe RCC due to its low incidence and difficulty in distinguishing it from the classical form of ChRCC and oncocytoma. Our literature search showed that sex is not a risk factor for de novo RCC in allografts [11,15,16]. However, it was clear that patients can experience ChRCC a long time after kidney transplantation (eg, 11 and 13 years), and at older ages (eg, 67 and 73 years) [11,15,16]. The period of allograft tumor development after transplantation varies depending on several risk factors; however, in our case, it was only 36 months, which may indicate a donor-derived tumor.

RCC is often asymptomatic; therefore, this cancer type may be difficult to diagnose early. However, patients undergo a routine examination after kidney transplantation, including ultrasound examination of the graft, which allows diagnosis of the neoplasm in transplanted and native kidneys. Differential diagnosis of a solid mass in the kidney remains a challenging issue. Imaging plays an important role in diagnosis of different types of RCC. Ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) are commonly used in RCC diagnosis. According to our national guidelines, transplant recipients undergo routine US of the graft once every month during the first 6 months after transplantation, and then once every 3 months thereafter. However, MRI is a more effective diagnostic option in kidney solid tumor identification. The specificity of MRI in distinguishing between benign and malignant tumors is 89% [17]. Therefore, for differential diagnosis, we suggest MRI as the best diagnostic option.

In the literature, only 2 out of 4 cases presented at the hospital emergency department due to conditions such as fever, vomiting, diarrhea, weakness, and abdominal pain [9-11]. The rest were found incidentally during a follow-up check-up, as in the present case.

Conclusions

In this case report, we described the development of a rare eosinophilic form of chromophobe RCC in a transplanted kidney after kidney transplantation from a living related donor. The graft function was impaired, and the lesion was discovered

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

by chance during the examination. Several cases of non-functioning graft RCC have been described in the literature. We believe that regular examinations of kidney recipients, especially the combination of US and MRI, should be carried out regardless of graft function.

Acknowledgments

We would like to thank the patient for allowing us to publish this work.

Declaration of Figures Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

References:

1. Suthanthiran M, Strom TB. Renal transplantation. N Engl J Med. 1994;331(6):365-76
2. Ferreiro AO, Vazquez-Millan MA, Lopez FS, et al. Everolimus-based immunosuppression in patients with hepatocellular carcinoma at high risk of recurrence after liver transplantation: A case series. Transplant Proc. 2014;46:3496-501
3. Chapman ACW Jr, Wong G. Cancer in the transplant recipient. Cold Spring Harb Perspect Med. 2013;3(7):a015677
4. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. Cancer J Clin. 2015;65:5-29
5. Eble JN, Sauter G, Epstein JI, Sesterhenn IA. World Health Organization Classification of Tumours. Pathology and genetics of tumours of the urinary system and male genital organs. Lyon: IARC Press, 2004
6. Althalf MMA, Al-Sunaid MS, Abdelsalam MSA, et al. Chromophobe renal cell carcinoma occurring in the renal allograft of a transplant recipient presenting with weight loss. Saudi J Kidney Dis Transpl. 2016;27(1):139-43
7. Reuter VE. The pathology of renal epithelial neoplasms. Semin Oncol. 2000;27(2):124-37
8. Reuter VE, Presti JC Jr. Contemporary approach to the classification of renal epithelial tumors. Semin Oncol. 2000;27(2):124-37
9. Hsieh JJ, Purdue MP, Signoretti S, et al. Renal cell carcinoma. Nat Rev Dis Primers. 2017;3:17009
10. Thöenes W, Storkel S, Rumpelt HJ, et al. Chromophobe cell renal carcinoma and its variants – a report on 32 cases. J Pathol. 1988;155:277-87
11. Podduturi V, Yourshaw CJ, Zhang H. Eosinophilic variant of chromophobe renal cell carcinoma. Proc (Bayl Univ Med Cent). 2015;28(1):57-58
12. Gouttefangeas C, Stenzl A, Stevanovic S, Rammensee HG. Immunotherapy of renal cell carcinoma. Cancer Immunol Immunother. 2007;56:117-28
13. Ebrahimi A, Hosseini SA, Rahim F. Immunosuppressive therapy in allograft transplantation: From novel insights and strategies to tolerance and challenges. Cent Eur J Immunol. 2014;39(3):400-9
14. Matzinger P. Tolerance, danger and the extended family. Annu Rev Immunol. 1994;12:991-1045
15. Alharbi A, Al Turki MS, Aloudah N, Alsaad KO. Incidental eosinophilic chromophobe renal cell carcinoma in renal allograft. Case Rep Transplant. 2017;2017:4232474
16. Ajabnoor R, Al-Sisi E, Zafer G, Al-Maghrabi J. Chromophobe renal cell carcinoma in renal allograft: Case report. Life Science Journal. 2014;11(7):9-14
17. Taouli B, Thakur RK, Kim S, et al. Renal lesions: Characterisation with diffusion-weighted imaging versus contrast-enhanced MR imaging. Radiology. 2009;251(2):398-407

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]