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Original Scientific Paper

KIDNEY TRANSPLANTATION FROM DECEASED DONORS WITH PROSTATE CANCER

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SUMMARY – **Introduction**: Kidney transplantation is associated with the risk of unrecognized cancer transmission from donor to recipient. There have been no reported cases of prostate cancer transmission in kidney transplantation.

Methods: We conducted a retrospective search of all cadaveric kidney allograft donors from August 2007 to November 2022 with available autopsy findings. Our primary interest were patients diagnosed with prostate cancer on autopsy. In further analysis, we recorded the data from the recipients of these kidneys, including further management and malignant disease development.

Results: Overall, there were 1360 kidney transplantations at our center in the studied period. Three donors were diagnosed with prostate cancer at autopsy. Two recipients received kidney allografts from donors with a Gleason score 6 for intraprostatic cancer and one from a donor with a Gleason score of 7. After the appropriate information, all recipients decided to continue renal replacement with transplanted organs. Patients were switched to an mTOR inhibitor and are currently in regular and meticulous follow-up.

Conclusion: Prostate cancer may be diagnosed on autopsy, and its prevalence has been increasing with the age of donors. The risk of transmission should be individually assessed based on the pathology findings.

Key words: *prostate cancer; kidney donor; cancer transmission*

Introduction

Kidney transplantation is the method of choice to treat end-stage kidney failure[1]. However, transplantation of any biological material may be associated with the risk of disease transmission from donors to recipients.

The prevalence of malignancies increases with age. Cancer is one of the leading causes of death in older populations since half of all malignancies occur in patients aged 70 years or older[2]. The widening gap between the number of patients on transplantation waiting lists and the number of available organs requires using older donors, which increases the risk of cancer transmission. Transmission of cancer may occur from donors with a history of malignancies as well as donors with no history of malignancy at the time of organ procurement, which is not easy to predict. Some recipients never develop malignancies, but others develop cancers suspicious of donor origin.

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Despite the efforts of the transplant community to incorporate evidence of donor transmission risk into guidelines for organ screening and acceptance[3], the current recommendations for considering a donor organ with a history of malignancy are based predominantly on single case reports[4]. Additionally, guidelines for screening have been inconsistent, particularly among donors with borderline transmission risk.

Herein we present our experience with kidney transplant recipients who received kidneys from deceased donors diagnosed with prostate cancer at autopsy.

Patients and methods

A retrospective observational cohort study recruited participants from the University Hospital Center Zagreb to determine kidney donor malignancies. The study included all adult renal transplant recipients between August 2007 and November 2022. Data were retrospectively obtained from hospital charts and records.

The study was approved by the University Hospital Center Zagreb Ethics committee, 8.1-21/252-2.

The recorded variables included patient demographics (age, gender), primary kidney disease, comorbidities, and type of immunosuppressive regimen. Donor characteristics of interest included age, gender, cause of death, history, radiological findings, and laboratory findings. Descriptive statistics were used, and continuous variables were depicted as means, with interquartile ranges reported where appropriate.

Results

Characteristics of donors and recipients – a whole cohort analysis

From August 2007 to November 2022, 1360 kidney transplantations were performed at our institution. The average age of donors was 53 years (IQR 42-60 years), and 58 % were male. Causes of death included cerebrovascular disease in 55%, trauma in 31%, and other causes in 14% of donors. The average estimated glomerular filtration rate was 89.2 mL/min/m^2. History of hypertension was present in 57% and diabetes in 5% of donors.

The most common primary kidney disease was glomerulonephritis (52%), followed by autosomal dominant polycystic kidney disease (14%), nephroangiosclerosis (12%), and chronic pyelonephritis (11%), while other diagnoses were less frequent. Recipients were more commonly male (60%), averaging 52 years of age (IQR 32-62). Before kidney transplantation, 85% replaced kidney function by hemodialysis, 5% were treated with peritoneal dialysis, and 10% had a combination of both treatments in their medical history. Five percent had a history of hepatitis C, while only 0.5% had hepatitis B. Average dialysis vintage was six years (IQR 1-12 years).

Characteristics of donors with prostate cancer and kidney recipients

A 66-year-old man with a history of alcohol abuse and smoking died from cerebral ischemia. His laboratory findings were within the reference range and abdominal ultrasound revealed a slightly enlarged (14 cm) steatotic liver. Other radiologic findings were unremarkable. His left kidney was offered to a patient from our center. The recipient was a 66-year-old man with end-stage renal failure caused by diabetic kidney disease. He had a history of cardiovascular surgery, including aortic valve replacement and a coronary artery bypass graft. The immunosuppressive protocol included basiliximab induction followed by tacrolimus, mycophenolate, and steroid maintenance. Two weeks later, the center received an autopsy finding revealing colon and prostate cancer. Colon adenocarcinoma was stage T1N0M0, and the prostate cancer was graded a Gleason score of 6.

The patient was informed about the finding and all options were discussed with him and his family. The patient decided to proceed with kidney transplantation. His immunosuppressive protocol was modified with the substitution of mycophenolate with everolimus. During follow-up, there were no signs of either prostate cancer or colon adenocarcinoma.

The second donor was a 55-year-old man who died from a rupture of a brain artery aneurysm. He was a smoker without comorbidities. All laboratory findings and ultrasound evaluations were normal. His right kidney was transplanted to a 36-year-old female patient with adult autosomal dominant polycystic kidney disease. She had been treated with hemodialysis for 2.5 years before transplantation. Twenty days after the transplantation, an autopsy finding of the donor revealed intraprostatic cancer with a Gleason score of 7. She was informed about the discovery and

decided to continue with immunosuppression and kidney transplantation. Her posttransplant course is uneventful to date.

The third donor was a 66-year-old man who died from subdural hematoma. His history included alcohol abuse lasting 22 years. Laboratory evaluation was unremarkable, while computed tomography showed an enlarged liver (16 cm) with signs of steatosis and no focal lesions. Other organs were described as normal. His right kidney was allocated to a 67-year-old man with adult autosomal dominant polycystic kidney disease treated with hemodialysis for seven months. After basiliximab induction, he received tacrolimus, steroids, and mycophenolate. Allograft function was delayed, and the patient was treated with hemodialysis for eight days after the transplantation. The posttransplantation course was complicated by steroid psychosis and *Pseudomonas aeruginosa* sepsis. Eighteen days after the transplantation, the autopsy finding of the donor revealed prostate cancer with a Gleason score of 6. The patient was informed and continued with his immunosuppressive treatment.

Discussion

In our institution's large cohort of kidney transplantations, prostate cancer was found on autopsy in only three donors. All were low-to-intermediate-risk intraprostatic cancers. All recipients decided to continue with kidney transplantation as the method of renal replacement therapy.

The risk for cancer transmission from donor to recipient is low but still exists. Measures to prevent cancer transmission from donor to recipient include:

- Detailed preoperative screening of donors.
- Meticulous examination of all organs at the time of procurement.
- Immediate biopsy of any suspicious lesions.

Routine donor autopsy should be promoted whenever possible as it may discover cancers, particularly those which are difficult to detect[5,6]. However, autopsies are not frequently performed. Possible reasons include the cost of the procedure[7] but also the hesitancy of the donor's family. Additionally, autopsies can provide a definitive diagnosis of malignancy only a few days or weeks after the transplantation[8]. Despite these limitations, every suspicious lesion should be investigated because diagnosing a malignancy can drive the management of recipients, even when a precise diagnosis is determined some days after the procedure[6,8,9].

The risk of transmission depends on the type of malignancy and its staging. In a study by Desai et al. which included 30765 transplants from 14986 donors from the United Kingdom Transplant Registry, there were 15 donor-transmitted cancers, all of them diagnosed after the donation (6 renal cell cancer, five lung cancer, two lymphomas, one neuroendocrine cancer, and one colon cancer). Kidney transplant nephrectomy was performed in 11 patients, chemotherapy was used in 4, and radiotherapy was administered in one patient. Three patients (20%) died directly from cancer[10].

There are several meta-analyses in the literature that focus on donor-transmitted cancers. Xiao et al. identified 69 studies with 104 donor-transmitted cancer cases. Renal cancer was the most commonly transmitted cancer, followed by melanoma, lymphoma, and lung cancer. The prognosis was poor for patients with melanoma and lung cancers, with less than 50% of recipients surviving two years after transplantation[11]. Eccher et al. included a total of 128 published papers with 234 recipients. In their analysis, the most commonly transmitted cancers were lymphoma, renal cancer, and melanoma[6]. Neither paper recorded transmission of prostate cancer.

In a meta-analysis of 16 studies which included more than 120 solid-organ transplantations performed with organs coming from deceased donors with proven prostate cancer, there were no recorded cases of cancer transmission or death related to malignancy in kidney transplantation and only 1 case of transmission after a heart transplant[12].

According to the Council of Europe, donors with extra-prostatic tumor extension should be excluded from donation because their use is associated with an unacceptable risk. While small intra-prostatic, low-grade tumors with a Gleason score ≤6 are considered minimal risk, intra-prostatic tumors with a Gleason score of seven are considered a low-to-intermediate risk. Intra-prostatic (pT2c) tumors with a Gleason score >7 are considered high risk[13]. Donors with a history of treated prostate cancer ≤pT2 and Gleason score ≤6 and donors with minimal prostate cancers and Gleason ≤6 under "regular surveillance" can be accepted for organ donation. They are considered

minimal transmission risk at any time after diagnosis, requiring frequent and meticulous follow-ups.

In the case of prostate cancer, which is limited to the prostate with a Gleason score ≤7 after curative treatment, the risk is considered minimal after a cancer-free period longer than five years. Individual risk assessment is required for donors with higher stages and Gleason scores[13].

It is important to stress that kidney transplant recipients can receive maximal treatment if a transmitted cancer is found because of the option of returning to dialysis. Additional treatment options include changing, decreasing, or completely withdrawing immunosuppression, kidney allograft nephrectomy and chemotherapy, and a meticulous follow-up of the recipients. The recipient should make the decision after receiving detailed information about potential risks and outcomes.

Our patients were informed about the autopsy findings and the risk of cancer transmission. They all refused kidney allograft nephrectomy. Immunosuppression was switched to mTOR inhibitors, and they are in regular follow-up.

Some limitations of our study need to be emphasized. It was a retrospective single-center study with all limitations typical for this type of investigation. We do not have data on the number of donors in whom an autopsy was performed. Therefore, the actual prevalence of prostate cancer in kidney donors may be underestimated.

In conclusion, the transmission of cancer from the donor to the recipient is rare. However, it may lead to graft loss and death. Unfortunately, the risk of cancer transmission cannot be completely eliminated, while the presence of cancer remains unknown at the time of organ donation. Prostate cancer transmission is sporadic. Every case should be assessed individually to find the optimal solution for the patient.

References

1. Bašić Jukić N, Kaštelan Ž. Transplantacija bubrega. 1st ed. Zagreb: Medicinska Naklada; 2016.
2. Navarrete-Reyes AP, Soto-Pérez-de-Celis E, Hurria A. Cancer and Aging: A Complex Biological Association. Rev Investig Clin organo del Hosp Enfermedades la Nutr. 2016;68(1):17-24.
3. Nanni Costa A, Grossi P, Gianelli Castiglione A, Grigioni WF. Quality and safety in the Italian donor evaluation process. Transplantation. 2008 Apr;85(8 Suppl):S52-6.
4. Nalesnik MA, Ison MG. Organ transplantation from deceased donors with cancer: is it safe? Open Access Surg. 2011;11.
5. Dziewanowski K, Drozd R, Parczewski M, Klinke M. Multiorgan transplantation from a deceased donor with intravascular diffuse large B-cell lymphoma: transmission of the disease and results of treatment. Clin Transplant. 2014 Oct;28(10):1080-3.
6. Eccher A, Girolami I, Motter JD, Marletta S, Gambaro G, Momo REN, et al. Donor-transmitted cancer in kidney transplant recipients: a systematic review. J Nephrol. 2020 Dec;33(6):1321-32.
7. Turnbull A, Osborn M, Nicholas N. Hospital autopsy: Endangered or extinct? J Clin Pathol. 2015 Aug;68(8):601-4.
8. Girolami I, Neil D, Segev DL, Furian L, Zaza G, Boggi U, et al. Discovered cancers at postmortem donor examination: A starting point for quality improvement of donor assessment. Transplant Rev (Orlando). 2021 Apr;35(2):100608.
9. Herzig KA, Falk MC, Jonsson JR, Axelsen RA, Griffin AD, Hawley CM, et al. Novel surveillance and cure of a donor-transmitted lymphoma in a renal allograft recipient. Transplantation. 2000 Jul;70(1):149-52.
10. Desai R, Collett D, Watson CJ, Johnson P, Evans T, Neuberger J. Cancer transmission from organ donors-unavoidable but low risk. Transplantation. 2012 Dec;94(12):1200-7.
11. Xiao D, Craig JC, Chapman JR, Dominguez-Gil B, Tong A, Wong G. Donor cancer transmission in kidney transplantation: a systematic review. Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg. 2013 Oct;13(10):2645-52.
12. Doerfler A, Tillou X, Le Gal S, Desmonts A, Orczyk C, Bensadoun H. Prostate cancer in deceased organ donors: a review. Transplant Rev (Orlando). 2014 Jan;28(1):1-5.
13. European Committee (Partial Agreement) on Organ Transplantation. Guide to the quality and safety of organs for transplantation [Internet]. 2018. Available from: https://www.edqm.eu/en/reports-and-publications

Sažetak

TRANSPLANTACIJA BUBREGA OD KADAVERIČNIH DARIVATELJA S RAKOM PROSTATE

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Uvod: Transplantacija bubrega povezana je s rizikom prijenosa neprepoznatog raka s darivatelja na primatelja. Nema objavljenih slučajeva prijenosa raka prostate u transplantaciji bubrega.

Metode: Provedena je retrospektivna analiza svih kadaveričnih darivatelja bubrega u našem centru s dostupnim nalazima obdukcije, u periodu kolovoz 2007.-studeni 2022. Izdvojeni su svi darivatelji kod kojih je dijagnosticiran karcinom prostate na obdukciji. U daljnjoj analizi izdvojili smo podatke o tijeku liječenja i razvoju maligne bolesti kod primatelja ovih bubrega.

Rezultati: Sveukupno, bilo je 1360 transplantacija u našem centru. Dva bolesnika primila su bubrežni presadak darivatelja s Gleason zbrojem 6 za intraprostatični karcinom, a jedan od darivatelja s Gleason zbrojem 7. Nakon prikladnog informiranja, svi primatelji su odlučili nastaviti nadomještati bubrežnu funkciju s dobivenim presatkom. Kod svih bolesnika imunosupresija je zamijenjena u mTOR inhibitore i provode se redovite i detaljne kontrole.

Zaključak: Karcinom prostate može biti dijagnosticiran prilikom obdukcije a njegova prevalencija raste s dobi darivatelja. Rizik prijenosa bolesti treba biti individualno procijenjen ovisno o patohistološkim nalazima.

Ključne riječi: *karcinom prostate; darivatelj bubrega; prijenos karcinoma*