Choriocarcinoma transmitted with the transplant: Case study

Ziba Aghsaeifard1, Marzieh Latifi2, Farzaneh Bagherpour2, Maryam Rahbar, MD1, Hormat Rahimzadeh3, Farshad Namdari4, Hossein Dialameh5, Mohsen Taheri Mahmoudi5 and Sanaz Dehghani2,6

Abstract
Choriocarcinoma is a rare kind of cancer, which may be either gestational or non-gestational. Choriocarcinoma is responsible for about a quarter of all documented neoplastic aneurysms. It is a descriptive case report of choriocarcinoma transmission from a donor, following kidney donation. A 45-year-old woman got a kidney from a 25-year-old woman who was taken to the hospital due to a non-traumatic cerebral hemorrhage. She delivered a healthy baby 48 days before her brain death. The transplant was successfully done. Five weeks’ post-transplantation, the recipient had pain and erythema in the surgical area. Regarding the high level of beta-human chorionic gonadotropin in her blood, diagnostic tests were performed. Following the confirmation of the cancer, a five-phase chemotherapy plan with various pharmaceutical regimens was initiated. Liver function test values rose after the final round of chemotherapy, and the patient developed hepatic encephalopathy. Considering the thrombocytopenia, dialysis, or hemoperfusion, which are normally performed to reduce liver enzymes, were not initiated. Finally, she died due to the hepatic failure and disseminated intravascular coagulation. Although the nephrologists disagree on the optimal course of treatment, it seems that nephrectomy would be helpful in such instances. Physicians should be aware of the possibility of transplant-related choriocarcinoma in female donors of reproductive age who die because of intracerebral brain hemorrhage for unclear reasons. Every donor must undergo a thorough examination. It is critical to get documents, clarify history, and interview relatives.

Keywords
Choriocarcinoma, brain death, organ donation, cadaveric

Date received: 14 August 2021; accepted: 27 February 2022

Introduction
Kidney transplantation as the best treatment for end-stage renal disease (ESRD) can improve the patients’ survival and quality of life.1 On average, the number of people with ESRD increases by 5%-7% annually.2 On the contrary, only about 14% of patients on waiting lists receive a kidney in the first year after diagnosis of ESRD.3

When the organs from donors with a history of continuous malignancy are retrieved for the transplantation, the risk of transfer of malignant illnesses is increased.4 Several studies suggested factors that should be considered before the organ procurement at the time of admission to the hospital. These factors include age, recent malignancy, active and untreated current opportunistic infection, mental illness, drug abuse, severe liver or lung disease, and ischemic heart disease.2,5

1Department of Internal Medicine, School of Medicine, Sina Hospital, Tehran University of Medical Sciences (TUMS), Tehran, Iran
2Organ Procurement Unit, Sina Hospital, Tehran University of Medical Sciences (TUMS), Tehran, Iran
3Department of Nephrology Disease, Sina Hospital, Tehran University of Medical Sciences (TUMS), Tehran, Iran
4Department of Urology, AJA University of Medical Sciences, Tehran, Iran
5Department of Urology, Sina Hospital, Tehran University of Medical Sciences (TUMS), Tehran, Iran
6Iranian Tissue Bank & Research Center, Tehran University of Medical Sciences, Tehran, Iran

Corresponding Author:
Sanaz Dehghani, Organ Procurement Unit, Sina Hospital, Tehran University of Medical Sciences (TUMS) & Iranian Tissue Bank & Research Center, Tehran University of Medical Sciences, Tehran, Iran
Email: sanaz_dehghani2002@yahoo.com
One of the inevitabilities of transplantation is the possibility of cancer transmission from the donor to the recipient, which is dependent on donors’ and recipients’ variables, such as age, underlying illness, immunologic match, and donors’ cause of death. The incidence of malignancy among transplanted patients, according to Villeneuve and Mihalov, was roughly 12% and 11.7%, respectively. About one-quarter of reported neoplastic aneurysms account for choriocarcinoma. Almost 30% of the cases of choriocarcinoma have metastasis when diagnosed. According to studies, the rate of malignant tumors of the donor in recipients of organs reportedly varies.

Choriocarcinoma is a highly malignant kind of gestational trophoblastic disease that affects roughly 1 in 40,000 pregnancies (in normal pregnancies, it may reach 1 in 160,000) and can quickly proceed to malignancy and distant metastases. Choriocarcinoma is a cancer that develops after a hydatidiform mole pregnancy. It might even occur after a child is born. This is a descriptive case report of choriocarcinoma transmission from the donor following kidney donation.

Case presentation

The cadaveric donor was a 25-year-old female referred to the hospital with a headache and suffering from brain death after several days due to a cerebral hemorrhage of non-traumatic origin. She had a successful delivery 48 days before the brain death.

Recipients

Liver: Two people had liver transplants (a 42-year-old male and a 32-year-old female). Female liver transplant patient had a high beta-human chorionic gonadotropin (B-hCG) level and died 2 months later from metastatic choriocarcinoma. The male liver recipient achieved a complete recovery after getting adequate medication, and his liver function was normal for 18 months. There were no issues in the postoperative phase. The patient was given standard care.

Kidneys: Kidney recipient was a 45-year-old female with ESRD. The salient and relevant past medical history included (a) kidney stone under treatment, (b) high blood pressure and diabetes with a history of 11 months of hemodialysis, (c) decreased urine volume, and (d) a history of right kidney nephrectomy and laparoscopic cholecystectomy. In this descriptive case report, we show the issues related to the detection of malignancy after the kidney transplant.

The transplant was successfully done. For 4 weeks, a double J (DJ) catheter was implanted. The amount of creatinine was 3.73 mg/dl on the first day after transplantation, but it dropped to 1.35 mg/dl 2 days later. Cyclosporine, prednisolone, mycophenolate mofetil, and insulin were all recommended. Antibiotic therapy was started 1-week post-transplantation regarding a detected urinary tract infection in her urine test. She got discharged from the hospital 18 days’ post-transplantation while her blood sugar and white blood cell (WBC) were normal, her creatinine level was fixed at 1.5 mg/dl, and her urine culture result was negative.

Five weeks after the transplant, the patient was referred to the nephrology clinic with discomfort and erythema in the operative region. She was admitted to the hospital with a fever, chills, active cough, hematuria, dysuria, and frequent urine. The transplanted kidney was subjected to an ultrasonic color Doppler scan, which came back normal. Her cytomegalovirus antigen (CMV Ag) was negative as well. One week post-admission, her creatinine reached 1.37 mg/dl and the urine culture was negative. As a result, the patient’s DJ catheter was removed, and she was discharged from the hospital. Nitrofurantoin 100 mg per day was added to the patient’s medications.

After the diagnosis of malignancy in the partial liver transplant recipient, the kidney recipient was checked up as well, whose B-hCG titer test result was 6077 Miu/ml.

After the malignancy was confirmed, a team comprising a nephrologist, transplant surgeon, oncologist, radiologist, and pathologist was tasked with assessing the patient’s health and administering comprehensive therapy. In addition, the whole-body magnetic resonance imaging (MRI; with and without contrast) and computed tomography (CT)-scan were performed, there was no evidence of a brain metastatic lesion, the kidney function was acceptable and B-hCG levels increased to 6176 Miu/ml. One day after admission, viral markers were negative. Fortunately, the creatinine levels were stable during the hospitalization and slightly fluctuated between 1.1 and 1.5 mg/dl.

One week after admission, B-hCG level increased to 73,593.46 Miu/ml, while alpha phytoprotein was in normal level (1.58 ng/ml).

After confirming the cancer, the medication was changed to sirolimus (2 mg/day). Plus, cyclosporine and mycophenolate mofetil were discontinued.

The first phase of chemotherapy. Six-day period methotrexate. Following treatment, the patient’s WBC and red blood cell counts started to decline until the white blood cell count hit 1000. When Amp GCF 300 mg was administered to her in two stages, her B-hCG level dropped 10 days after the first round of chemotherapy ended.

The second and third phases of chemotherapy. Five-day period MTX plus kytril. After these phases, the patient had pain at the end of limbs, although the patient’s kidney transplant history limited non-steroidal anti-inflammatory drugs prescription.

The fourth phase of chemotherapy. Considering patient’s delayed referral for further treatment, B-hCG had risen from 103 to 1023 Miu/ml.

The fifth phase of chemotherapy. Performed 5 days after the elimination of fever, with a chemotherapy regimen of Amp dactinomycine 0.5 mg, Amp etoposide 170 mg, Amp...
enoxaparin 40mg, Amp methotrexate (MTX) 500mg and Cap abitant.

After the last phase of chemotherapy, liver functional test (LFT) index level was increased. The corticosteroid dose was reduced to 10mg, regarding the patient’s diabetic history.

In supplemental Table 1, all procedures and treatments are listed (see supplemental material).

She was taken to the hospital with the hepatic encephalopathy, jaundice, and thrombocytopenia as her symptoms. The patient’s liver biopsy revealed acute hepatitis with cholestatic hepatitis as the predominant diagnosis. Necrosis was observed in all parts of liver. Based on the hepatic encephalopathy and low blood pressure, supportive treatment began. Even though she should have undergone dialysis, it was not possible before the correction of her platelet count. The patient succumbed to hepatic failure and disseminated intravascular coagulation (DIC).

One of the kidneys was transplanted to a 24-year-old male, in which case nephrectomy was performed as soon as choriocarcinoma in cadaveric donor was diagnosed. In the 18-month follow-up, the recipient shows no signs of malignancy.

Discussion

The cadaveric donor in this report was a young woman in her reproductive years who appeared with intracerebral brain hemorrhage without a history of high blood pressure. According to reports, high B-hCG levels are known as a symptom of choriocarcinoma. At the moment of brain death, regarding the level of B-hCG level her blood, which was higher than normal in the last test, the procurement team should have been suspicious of choriocarcinoma, but unfortunately did not pay proper attention to this matter.

Based on the precise standards for donor evaluations prior to any donation, the transplant team may be required to complete checklists to conduct a comprehensive donor screening.

We support the contention that B-hCG levels of all female cadaveric donors in their reproductive years should be screened, specifically when they are at childbearing age and become brain dead due to intracerebral brain hemorrhage (ICH). It confirms the vital importance of checking medical history, followed by a complete examination and laboratory tests for donors. Hence, our results are consistent with those of McCanty and Detrey.

According to Penn, the transmission rate of choriocarcinoma was 93% by 64% mortality rate. If all cadaveric donors were thoroughly evaluated at the time of procurement and any suspicious lesions are biopsied, the risk of disease transmission would be minimal. It needs accurate and accessible registries, as well as legislation that permits access to and exchange of personal data across administrative boundaries. To summarize, paying respect to current guidelines about the comprehensive assessment of the donor, that is, a rigorous examination of the cause of ICH in young donors, particularly women of reproductive age, is one of the most crucial actions to take before deciding on donation. Therefore, retrieval of records, clarification of history, and interview with relatives are all vital.

Conclusion

Although the nephrologists suggested nephrectomy for kidney recipient after detecting the malignancy in the cadaveric donor, the recipient refused the nephrectomy. She continued chemotherapy sessions with written consent form. Because the second kidney recipient was diagnosed with malignancy in the donor, a nephrectomy was done soon after the diagnosis. Presently, nephrologists do not agree on the best action if this problem occurs, but it seems that a transplanted kidney nephrectomy could have been effective. If this kidney, had a nephrectomy earlier, we would no longer need chemotherapy for micro-metastasis.

Finally, B-hCG level should be evaluated in the women of reproductive age who have brain death due to unexplained causes of intra-cerebral brain hemorrhage and the procurement team should be wary of choriocarcinoma based on the amount of B-hCG in their blood. According to the findings of this descriptive case report, rigorous assessment of the donor and attention to their medical history, as well as adherence to all organ transplantation standards, are critical prior to donation.

Acknowledgements

The authors of this article would like to thank the patients and their families who participated in this study.

Authors and roles

Z.A., M.R., and H.R. are the kidney transplant surgeons for this case. M.T. and F.N. are the transplantation coordinators for this case. H.D. and S.D. are responsible for management team for this case. F.B. contributed to first draft writing. M.L. contributed to editing and reviewing the first draft. S.D. played a role as a supervisor.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.
Informed consent

Written informed consent was obtained from the family/legally authorized representative of the patient(s) for their anonymized information to be published in this article.

ORCID iD
Sanaz Dehghani https://orcid.org/0000-0001-5946-2611

Supplemental material
Supplemental material for this article is available online.

References
1. Liu N, Yang L, Long Y, et al. Endometrial cancer in a renal transplant recipient: a case report. Open Med 2020; 15(1): 981–985.
2. Lee S, Yoo KD, An JN, et al. Factors affecting mortality during the waiting time for kidney transplantation: a nationwide population-based cohort study using the Korean Network for Organ Sharing (KONOS) database. PLoS ONE 2019; 14(4): e0212748.
3. Gander JC, Zhang X, Ross K, et al. Association between dialysis facility ownership and access to kidney transplantation. JAMA 2019; 322(10): 957–973.
4. Eccher A, Girolami I, Motter JD, et al. Donor-transmitted cancer in kidney transplant recipients: a systematic review. J Nephrol 2020; 33: 1321–1332.
5. Kim C-D. Kidney transplantation. Korean J Medicine 2014; 86(2): 142–151.
6. Desai R, Collett D, Watson C, et al. Estimated risk of cancer transmission from organ donor to graft recipient in a national transplantation registry. Br J Surg 2014; 101(7): 768–774.
7. Gandhi MJ and Strong DM. Donor derived malignancy following transplantation: a review. Cell Tissue Banking 2007; 8: 267–286.
8. Mangus RS, Bajpai S, Lutz AJ, et al. Contrast administration to the deceased kidney donor has no impact on post-transplant outcomes. J Surg Res 2020; 254: 261–267.
9. Villeneuve P, Schaubel D, Fenton S, et al. Cancer incidence among Canadian kidney transplant recipients. Am J Transplant 2007; 7(4): 941–948.
10. Mihalov M, Gattuso P, Abraham K, et al. Incidence of post-transplant malignancy among 674 solid-organ-transplant recipients at a single center. Clin Transplant 1996; 10(3): 248–255.
11. Kalafat M, Vinuela F, Saver JL, et al. Multiple cerebral pseudoaneurysms and hemorrhages: the expanding spectrum of metastatic cerebral choriocarcinoma. J Neuroimaging 1998; 8(1): 44–47.
12. Mangla M, Singla D, Kaur H, et al. Unusual clinical presentations of choriocarcinoma: a systematic review of case reports. Taiwan J Obstet Gynecol 2017; 56(1): 1–8.
13. Weir B, MacDonald N and Mielke B. Intracranial vascular complications of choriocarcinoma. Neurosurgery 1978; 2(2): 138–142.
14. Birkeland SA and Storm HH. Risk for tumor and other disease transmission by transplantation: a population-based study of unrecognized malignancies and other diseases in organ donors. Transplantation 2002; 74(10): 1409–1413.
15. Garrido G and Matesanz R. The Spanish national transplant organization (ONT) tumor registry. Transplantation 2008; 85(8S): S61–S63.
16. Braga A, Campos V, Filho JR, et al. Is chemotherapy always necessary for patients with nonmetastatic gestational trophoblastic neoplasia with histopathological diagnosis of choriocarcinoma. Gynecol Oncol 2018; 148(2): 239–246.
17. Soper JT, Mutch DG, Schink JC, et al. Diagnosis and treatment of gestational trophoblastic disease: ACOG practice bulletin no. 53. Gynecol Oncol 2004; 93(3): 575–585.
18. Zhao J, Xiang Y, Wan XR, et al. Molecular genetic analyses of choriocarcinoma. Placenta 2009; 30(9): 816–820.
19. Álvarez-Sarrado L, González Ballano I, Herrero-Serrano R, et al. Hemoptysis as the first symptom in the diagnosis of metastatic choriocarcinoma in the third trimester of pregnancy: a case report. Case Rep Womens Health 2020; 27: e00211.
20. Pang Y, Rajesh H and Tan L. Molar pregnancy with false negative urine hCG: the hook effect. Singapore Med J 2010; 51(3): e58–e61.
21. Namburi RP, Kancherla V and Ponna RA. High-dose hook effect. J NTR Univ Health Sci 2014; 3(1): 5–7.
22. McCanty TC, Jonsson J, Khawand N, et al. Transferral of a malignancy with a transplanted kidney. Transplantation 1989; 48(5): 877–879.
23. Penn I. Transmission of cancer from organ donors. Ann Transp 1997; 2(4): 7–12.
24. McKeown DW, Bonser RS and Kellum JA. Management of the heartbeating brain-dead organ donor. Br J Anaesth 2012; 108(Suppl. 1): i96–i107.