Donor Choriocarcinoma Transmission From Solid Organ Transplantation: A Case Report

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ABSTRACT

Transplantation of any organ has some inherent risk of disease transmission, such as infection and malignancy. The present study aims to describe 2 cases of choriocarcinoma transmission after kidney and liver transplantation originating from the same patient. The donor was a 17-year-old woman who died of cerebral hemorrhage. Both organ recipients died of metastatic choriocarcinoma few months after the transplantation, within days after starting chemotherapy. Retrospective hCG (human chorionic gonadotropin hormone) analysis in donor's blood stored at the time of donation had a result of 9324 mIU/mL. Despite its rarity, clinicians should be aware of the risk of transplant-related choriocarcinoma from female donors in childbearing age. In some cases, hCG dosage should be performed before donation.

TRANSPLANTATION of any biological material has an inherent risk of disease transmission, whether infectious or neoplastic. Because there are few cases reported in literature, it is believed that the incidence of neoplasm transmitted by solid organ transplants is underestimated [1,2], in the order of 0.02 to 0.2% [2].

The most frequent donor-transmitted neoplasms are of renal, melanoma, lymphoma, pulmonary, Kaposi's sarcoma, breast, and prostate origin [1–4]. Transmission of choriocarcinoma is rarely described (5.5% of cases) [1]. Despite its rarity, the association with high mortality makes the theme of great clinical importance.

In recent decades, the prevalence of chronic kidney disease is increasing, as is the number of patients on the waiting list for kidney transplantation. In order to meet this growing need, it is essential to increase the spectrum of potential donors by expanding pre-existing criteria. There is still no consensus on the possibility of acceptance of donors with previous or current neoplasia history [1], and better elucidation of this aspect is necessary.

This article aims to report 2 cases of transmission of choriocarcinoma after kidney and liver transplantation originating from the same donor.

CASE REPORT

Donor

A 17-year-old woman whose death was attributed to hemorrhagic vascular accident due to arteriovenous malformation was evaluated for organ donation. She had no known history of neoplasms nor previous comorbidities. Her terminal creatinine was 1.0 mg/dL. The macroscopic evaluation of the organs referred for transplantation showed no alteration, and 2 kidneys and the liver were donated. However, one of the kidneys was not used due to a long time of cold ischemia.

Kidney Recipient

A 65-year-old male patient with stage V chronic kidney disease, under conservative treatment, received the donor's kidney. He was eutrophic, had no previous or current malignancy history and had a Charlson Comorbidity Index (CCI) of 4.

Induction immunosuppression was thymoglobulin and maintenance immunosuppressive therapy was tacrolimus and

mycophenolate. Transplantation evolved without complications, with hospital discharge after 9 days with creatinine of 2.3 mg/dL. After 2 months, the patient was treated for urinary tract infection and the creatinine increased to 4.2 mg/dL. On this occasion, a renal ultrasound revealed a solid, hypoechoic nodule with vascularization, in the medium third of the renal graft measuring 3.0 x 2.8 cm.

A magnetic resonance-guided biopsy was done, which revealed poorly differentiated neoplasm (Fig 1). Allograft nephrectomy (Fig 2) and immunosuppression withdrawal were performed. Extensive angiolymphatic invasion with compromised circumferential surgical margins was detected, and immunohistochemistry showed the presence of diffuse polyclonal chorionic gonadotropin compatible with choriocarcinoma.

The patient was readmitted after 28 days with worsening renal function and dyspnea. Staging evaluation performed 115 days after the transplantation revealed multiple pulmonary neoplastic nodules (Fig 3) and implants permeating the abdominal wall overlying the kidney graft area and splenic nodules, compatible with metastases. No testicular, mediastinal, or retroperitoneal lesion suggestive of primary germ cell tumor (GCT) was found. At that time, human chorionic gonadotropin hormone (hCG) dosing was >255,000 mIU/mL.

Systemic chemotherapy with etoposide and cisplatin (in reduced doses for 4 days, as recommended for dialytic patients) was quickly initiated [5]. After 3 days of treatment and 4 months of transplantation, the patient evolved to respiratory failure and death.

Liver Recipient

A 66-year-old female patient was diagnosed with cryptogenic liver cirrhosis in association with a 6.5-cm hepatocellular carcinoma in the hepatic segment V/VI. The patient was referred for chemoembolization and the lesion decreased from 6.5 cm to 2.4 cm. Therefore, she was referred to the preoperative evaluation for liver transplantation.

The staging of hepatocellular carcinoma was performed with bone scintigraphy and chest and abdominal tomography with no evidence of metastatic lesions. The patient was listed for transplantation gaining special status due to the hepatocellular carcinoma.
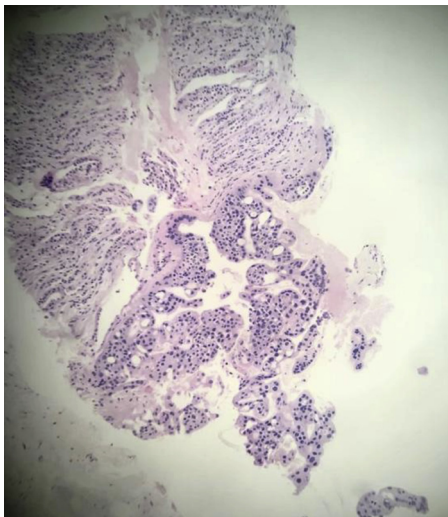

Fig 2. Allograft nephrectomy revealing a solid mass of 3.0 x 2.8 cm.

Immunosuppression was initiated with tacrolimus, prednisone, and mycophenolate. The patient was discharged on the seventh day with good allograft function.

After information that the kidney recipient of the same donor had been diagnosed with choriocarcinoma, an abdominal tomography (Fig 4) was performed showing the liver with hypodense lesions, with peripheral vascular enhancement, disseminated by the right lobe, and a chest tomography (Fig 5) showing multiple nodules with miliary pattern. At that time, the hCG of the patient was >255,000 mIU/mL. The percutaneous biopsy of liver mass
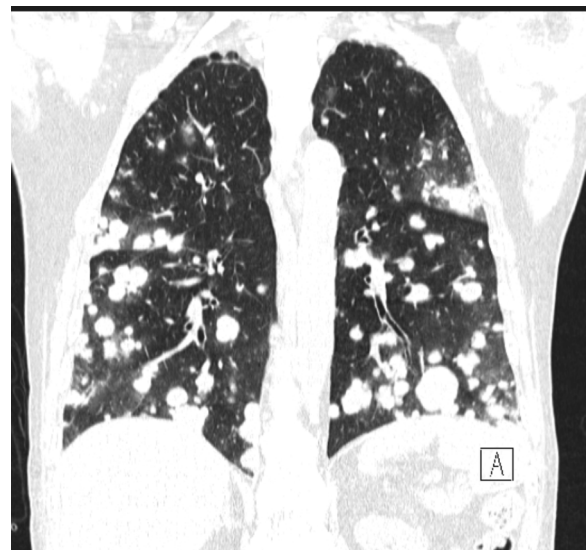

Fig 1. Kidney allograft biopsy showing poorly differentiated neoplasm.

Fig 3. Kidney recipient chest tomography showing images of neoplastic implants in pulmonary parenchyma.

evidenced poorly differentiated, epithelioid, malignant neoplasm. Immunohistochemistry showed the presence of diffuse polyclonal chorionic gonadotropin.

A very high-risk gestational trophoblastic neoplasia chemotherapy protocol with low-dose etoposide and cisplatin was initiated, with the intention of switching to the association of etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine (EMA-CO) after 2 cycles. In addition, tacrolimus was discontinued and replaced by everolimus.

After 7 days of treatment and 5 months after transplantation, the patient evolved with pancytopenia and sepsis and died despite the efforts undertaken.

DISCUSSION

This article reports 2 cases of choriocarcinoma transmission from the same donor. The kidney recipient underwent nephrectomy, followed by chemotherapy, but evolved to death rapidly. The liver recipient underwent chemotherapy but also died after infectious complications. Both cases revealed the high aggressiveness of these tumors.

Due to its low prevalence, the management and treatment of donation-borne choriocarcinoma is difficult. Most of them are neoplasms that appear shortly after transplantation (1 day to 3 months, average of 45 days), and its early diagnosis is essential in an attempt to improve the prognosis, which is already very poor [1].

The first case was reported in 1977 after a kidney transplant [6]. The donor was a 30-year-old woman diagnosed with choriocarcinoma 2 years earlier. She underwent hysterectomy and posterior clinical follow-up with no sign of metastasis. Her death was also from intracerebral hemorrhage. The recipient, a 47-year-old man, presented initial graft dysfunction and, 6 days after transplantation, choriocarcinoma was diagnosed by kidney biopsy. The recipient underwent nephrectomy and immunosuppression suspension, obtaining complete remission [6].

Marsh et al (1987) reported another case of transmission of choriocarcinoma after transplantation of 4 organs from the same 36-year-old donor [7]. The cause of the donor's death was intracerebral hemorrhage. The liver recipient died after 85 days of transplantation due to acute respiratory failure. The diagnosis of choriocarcinoma was done through autopsy, with metastatic lesions in the liver and lungs. Kidney recipients underwent nephrectomy immediately after

receiving this information. The first of them died quickly and the other presented the disease, remaining alive after 5 months, undergoing chemotherapy. The heart recipient showed no signs of cancer transmission [7].

Another study published in 1993 described cases of complete remission after 14 cycles of actinomycin D and etoposide in renal transplant recipient, and the liver recipient died of pulmonary metastasis, despite chemotherapy with methotrexate [8]. Through these few cases described, it is believed that the transmissibility of choriocarcinoma is approximately 93% [4].

In the present case, the donor had no known history of neoplasms, but after the diagnosis of neoplasia in the recipients, an active search for her previous hospital records was performed. A history of abortion was observed 2 years before donation and the pathology was compatible with partial hydatidiform mole. One month after the incident, the beta-hCG dosage was 283 mIU/mL. After 6 months, the beta-hCG dropped to 22 mIU/mL. The patient abandoned follow-up. This clinical-laboratory follow-up is necessary, even when the decline in hCG levels are indicating disease remission [9]. It is worth mentioning that this information was not provided by family members at the time of donation and that hCG levels are not routinely measured in young patients of reproductive age in our service.

After the transmission of the choriocarcinoma, beta-hCG dosage was performed in the donor's stored blood at the time of donation, with a result of 9324 mU/mL.

Choriocarcinoma is a rare type of cancer and characterized by high levels of hCG. It is considered the most aggressive type of gestational trophoblastic neoplasia, due to its early hematogenous spread. Its diagnosis occurs, in half of cases, after a normal pregnancy, abortion, or ectopic pregnancy. In the other 50% of cases it may evolve from a trophoblastic disease (hydatidiform mole, partial or complete, invasive mole, and choriocarcinomas) [2,10,11].

It is regrettable that the initial diagnosis and management were adequate for this donor, but there has been loss of follow-up, as well as the absence of the report of this previous complication, perhaps by little understanding by the family members of the seriousness of that diagnosis.

Choriocarcinoma may present in men as a component of testicular or, less commonly, extragonadal GCT. A search for testicular or extragonadal (mediastinal or
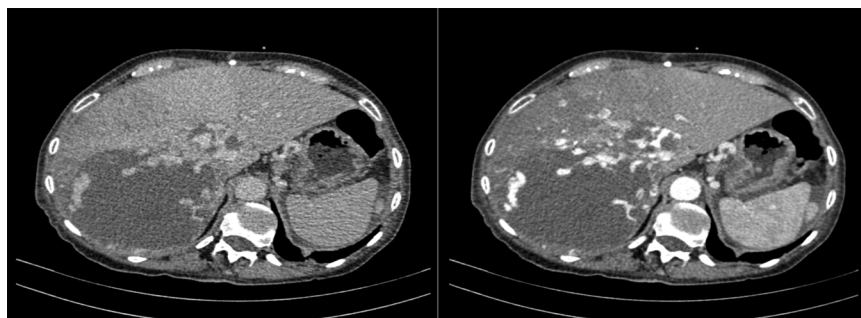

Fig 4. Liver recipient abdominal computed tomography revealing hypodense expansive lesions, with peripheral vascular enhancement, disseminated by the right lobe.
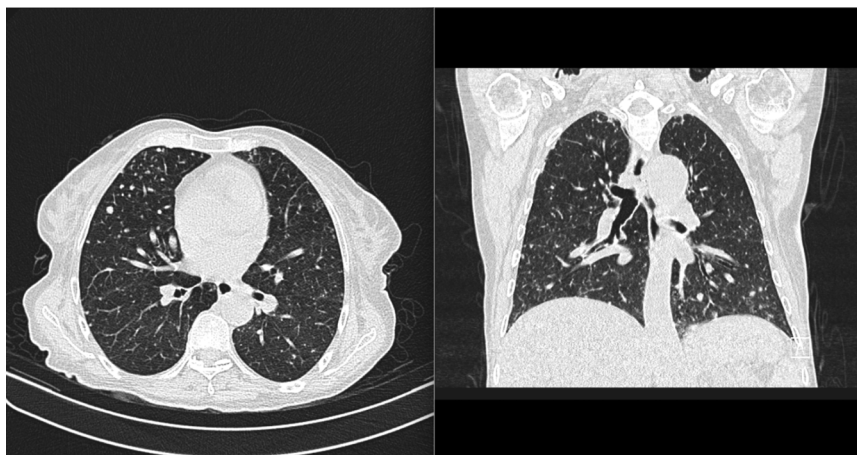
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Fig 5. Liver recipient chest computed tomography showing multiple nodules with miliary pattern compatible with secondary implants.

retroperitoneal) primary GCT was performed in the kidney recipient. The chemotherapy regimen used was chosen considering both the possibilities of an endogenous metastatic GCT or a choriocarcinoma transmitted by the donor. Later, the high level of hCG in the donor's stored blood made it clear that the origin of the tumor was exogenous. This case represents an extraordinary example of a gestational trophoblastic neoplasia in a male patient.

The diagnosis of choriocarcinoma occurs more frequently in a late phase of the disease, after the appearance of metastases [12]. The lungs are the most common site of choriocarcinoma metastases (80%), followed by the liver and then, more uncommonly, the brain [13]. We believe that the bleeding that led to the donor's brain death may have actually been caused by brain metastases of choriocarcinoma. Choriocarcinoma mortality is mainly due to brain metastases [14].

The performance of kidney allograft biopsy was questioned in that scenario, in face of the potential for contribution to the metastatic dissemination. The estimated risk of implant along the needle path is less than 0.01% [15], and there are only 6 cases reported in the literature [16]. The risk seems to be associated with the number of removed fragments, and the use of ultrasound for guidance contributes to a lower risk [17].

After the introduction of chemotherapy, the prognosis of this pathology was modified radically [9]. Patients with metastases are subdivided, depending of risk factors as follows: age >39 years; antecedent of normal pregnancy, in opposition to mole or abortion; pretreatment hCG >100,000 mIU/mL; largest tumor mass ≥5 cm; presence of metastasis, especially if in brain or liver; more than 8 metastases; and failure to previous chemotherapy [18]. Furthermore, transmission through donated organs in the context of more vigorous initial immunosuppression is thought to result in early spread of the disease and poor therapeutic response.

Very high-risk gestational trophoblastic neoplasia is associated with poor survival because of chemoresistance

and early complications, such as hemorrhagic metastasis and multisystem organ failure. The most common regimen used for high-risk choriocarcinoma is the EMA-CO regimen. When given to very high-risk patients with a large disease burden, low-dose induction etoposide chemotherapy for 1 to 2 cycles before commencing EMA-CO decreased early death rate from 7.2% to 0.7% [19,20].

The treatment of choice for renal transplant recipients is early nephrectomy [1]. The possibility of graft nephrectomy and suspension of immunosuppression in kidney transplantation is an advantage when compared with other solid organ transplants that cannot be removed.

Physicians working with transplantation should be aware of the high potential of transmission of choriocarcinoma, as well as its high mortality. Detailed anamnesis should be performed on all female donors at gestational age. In suspected cases, hCG dosages should be provided [9]. Currently, after the outcome of the reported case, the State Transplant Center has made it mandatory to measure beta-hCG in potential donors of childbearing age. High levels of this hormone can correspond to a normal pregnancy, as well as trophoblastic neoplasms. Ultrasound is the first choice method to investigate this diagnosis. Any patient with suspected choriocarcinoma should have the donation of their organs contraindicated [1].

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