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CASE REPORT

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Long-term survival after choriocarcinoma transmitted by liver graft: A successful report in pediatric transplantation

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Abstract

Background: LT is the standard of care for many pediatric liver disorders. Although long-term outcomes have improved, some rare complications such as transmission of occult donor tumors have been reported.

Case report: An adolescent diagnosed with tyrosinemia was submitted to LT from a previous healthy donor due to HCC. Almost 8 months after LT, the patient presented a nodular hepatic lesion. Clinically, he had mild weight loss, lower limb edema, and gynecomastia. Thorax CT found lesions in the left lung parenchyma, which showed no increased uptake in PET SCAN. Liver biopsy revealed a carcinoma with desmoplastic stroma. ISS was withdrawn, and palliative chemotherapy was started for presumptive HCC relapse. AFP remained normal, but HCG had reached unexpected values of 1984 IU/L. As we requested detailed information about the other organ recipients from the same donor, we found that one of them passed away due to disseminated tumor. Five months after the beginning of chemotherapy, the patient underwent resection of liver segments V and VI. Histological examination confirmed liver metastatic choriocarcinoma. At the time of writing, with 11 years of follow-up, the patient had sustained remission with no signs of relapse.

Discussion: This case reports a diagnostic challenge in an adolescent with a particular unique background and a very rare pattern of tumor transmission. The authors aim to highlight the risk of cancer-bearing organs reveled post-LT and to testimony the experience of the successful outcome after a choriocarcinoma transmitted by liver graft.

KEYWORDS
children, liver transplantation, misdiagnosed choriocarcinoma

1 | INTRODUCTION

LT is the standard of care for many metabolic or end-stage pediatric liver disorders. Although long-term outcomes have improved over the last three decades for both patient and graft, some rare complications as occult tumors in liver donors need greater exposure.[1-4] The priorities in transplant allocation emphasize the hemodynamic stability and harvestability of the potential donor, a process that needs to be expeditious.[1] When there is no suggestion of significant medical history or intra-abdominal disease, an autopsy is seldom performed and it is possible that a cancer-bearing graft is used in LT.[1] Cancer transmission following LT has been sporadically reported in case series. Although it is rare (estimated incidence of 0.02%-0.2%), it is an unavoidable risk in organ transplantation.[5]

Abbreviations: AFP, alpha-fetoprotein; ALK, alcalin phosphatase; CT, computerized tomography; HCC, hepatocellular carcinoma; HCG, human chorionic gonadotropin; ISS, immunosuppression; LT, liver transplantation; NTBC, 2-(2-nitro-4-trifluoromethylbenzoyl)-1,3-cyclohexanedione; PET, positron emission tomography; US, ultrasound.

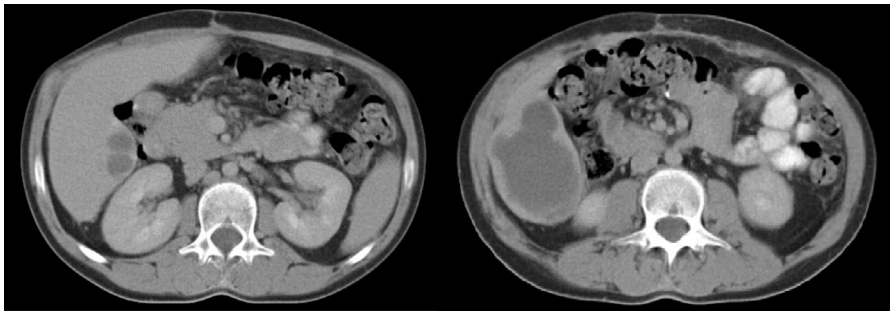

FIGURE 1 Liver CT. Hipervascular lesion in segments V/VI, hypodense in the central portion, and contrast uptake to the periphery

Liver tumors represent about 1% of all pediatric malignancies, with hepatoblastoma and HCC accounting for over 90% of all primary hepatic malignancies.[6] HCC is the second most common and has a well-established association with viral hepatitis, hereditary tyrosinemia, hereditary hemochromatosis, genetic intrahepatic cholestasis, among other conditions.

Tyrosinemia type I (or hepatorenal tyrosinemia) is an autosomal recessive condition resulting from an enzymatic deficiency in the tyrosine catabolic pathway. It results in hepatic failure and other comorbidities involving the renal and neurologic systems and represents a long-term risk for HCC.[7] In the last two decades, NTBC has been used as a therapeutic option for tyrosinemia along with diet restriction. When tyrosinemia patients develop liver or neurological complications, orthotopic LT restores liver function and reduces the inherent lifelong risk of HCC.[7]

The following case reports a patient diagnosed with HCC who received a different occult carcinoma within the transplanted liver. Despite the diagnostic challenge, chemotherapy and tumor resection both allowed for a successful outcome. The aim of this report was to highlight the risk of cancer-bearing organs in transplantation and to share our experience in this particular scenario.

2 | CASE REPORT

This case reports an adolescent male diagnosed with tyrosinemia type I at age 12 months. He was receiving a low-protein diet and NTBC since diagnosis. Besides this, he had associated risk for thrombosis (Factor V Leyden pathogenic variant).

At the age 13 years, he presented a multinodular liver, suspected to be HCC with concomitant elevation of AFP. A percutaneous biopsy confirmed HCC, and he was listed to LT without any complementary treatment. He received a whole liver graft which was apparently healthy on inspection and palpation and without any gross signs of disease that might have disqualified it. The donor was a previously healthy 42-year-old woman with brain hemorrhage as the cause of death.

The transplantation procedure was uneventful, and histological examination of the explanted liver described a moderately differentiated HCC in the right lobe with vascular invasion and micronodular hepatic cirrhosis (pTNM—T2 NO Mx).

The early post-transplant period was complicated with a Budd-Chiari Syndrome with partial occlusion of the hepatic veins. The patient was treated by primary angioplasty with stent placement at 4th post-transplant month. Monthly US were performed as follow-up.

Almost 8 months after LT, the patient presented a 6.7 cm poorly defined nodular lesion on US. The lesion was described as a heterogeneous nodule with a central liquid content, and heterogeneity with areas of greater echogenicity as well as hypoechoic areas. A month before, a smaller lesion with poorly defined edges was described at the same location. However, previous monthly US described consistently the liver parenchyma as being slightly heterogeneous with a diffuse micronodular pattern without focal lesions identified. Liver CT confirmed the hypervascular focal lesion in segments V/VI (Figure 1). Serum AFP was within normal range at this point.

Clinically, he had a mild weight loss, minor edema of the lower limbs, moderate gynecomastia, and morning nausea. Since there was a concern about HCC relapse, the investigation proceeded with thorax CT scan disclosing four lesions in the left lung parenchyma. PET SCAN showed no increased tracer uptake of these lesions and bone scintigram was negative for bone metastatic disease.

The most accessible lung lesion was biopsied by fine-needle aspiration for cytological examination, and the liver nodule was also percutaneously biopsied. Percutaneous liver biopsy revealed a carcinoma with abundant desmoplasic stroma compatible with HCC relapse, and lung biopsy raised suspicion of metastatic lesions, with bulky cells with high nucleo-cytoplasm ratio and nuclear pseudo-inclusions.

Tumoral arterial chemoembolization was performed, and palliative chemotherapeutic (Sorafenib®) was administered for a month along with ISS withdrawal. A week after embolization, the lesion was unchanged in US except for a more liquefied core. Laboratory evaluation showed normal cell blood count, normal aminotransferases, and a moderate increase in GGT 391 IU/L and ALF 528 IU/L. AFP maintained normal values, but HCG reached unexpected values of 1984 IU/L.

Meanwhile, a request to the transplantation coordination group for more details about donor past medical history and outcome of the other organ recipients revealed that only one kidney had been grafted and the recipient had passed away due to disseminated tumor difficult to characterize, but assumed to be a choriocarcinoma.

The patient completed four cycles of chemotherapy (cisplatin, ifosfamide, and etoposide). Five months later, HCG levels were <1 IU/L, and the patient underwent resection of liver segments V and VI. There were no postoperative complications reported.

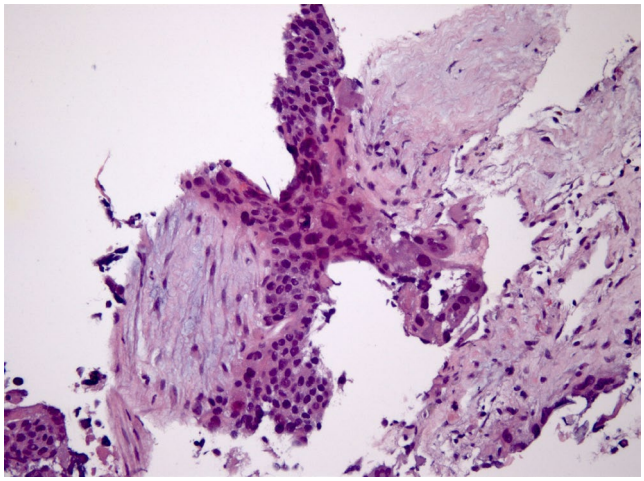

FIGURE 2 Histological examination. Formaline-embed sections, Hematoxylin-eosin staining. The tumor composed of mononucleate cytotrophoblasts and multinucleate syncytiotrophoblasts with hemorrhage

Histological examination of the resected segments confirmed liver metastatic choriocarcinoma with clear margins (Figure 2).

He had a very satisfying response to chemotherapy and partial hepatectomy with no signs of relapse (normal imagological studies and normal levels of AFP and HCG). The pulmonary lesions were no longer visualized. During chemotherapy, ISS was based on steroid monotherapy and liver enzymes were normal. Thereafter, sirolimus was added.

At 2 years post-liver transplant, there was progressive worsening of his renal function. This was interpreted as a consequence of his baseline disease and chemotherapy, since sirolimus levels were very low and proteinuria was not significant.

By the age of 18 years, he transitioned to the adult group of LT and nephrology. The identified comorbidities included stage 3 chronic kidney disease and a non-functioning pituitary adenoma.

At the time of writing, with an 11-year follow-up, he is in complete remission, with normal levels of AFP and HCG. Latest liver biopsy reported peri-centrilobular and sinusoidal distention with diffuse perisinusoidal fibrosis. The upper digestive endoscopy showed incipient esophageal varices.

3 | DISCUSSION

Transplantation has become an exceptional opportunity not only to treat patients with acute liver failure and end-stage liver disease, but also a way to improve the quality of life and the proper development of children and adolescents with metabolic diseases.[1,2] Post-transplant lymphoproliferative disease and other *de novo* tumors are well described as a potential complication in LT.[1,8,9] Occult tumors of the graft are fortunately very rare but almost impossible to predict and hard to explain to patients and families. A wide range of experimental findings supports the concept of "immunologic surveillance" where a healthy immune system eliminates the growth potential of the transplanted malignant cells. However, due to ISS therapy used after LT, there is a greater chance malignant cells could survive and flourish.[10,11]

Since the availability of NTBC, the need for LT has been limited to cases of malignancy.[7] Unfortunately, this case, which was a delicate quiz, reports a late diagnosis which prevented the potential benefits of NTBC, and the patient developed HCC.

A few months after LT, this patient presented a mass in the graft raising suspicion about HCC relapse. Although the primary tumor had been diagnosed at an early stage without distant metastasis, it also showed vascular invasion on pathological examination, which could jeopardize the prognosis.[12] In contrast, AFP, a very well-known biological factor to follow the course of HCC, was persistently maintained within normal range after LT. In fact, AFP may be normal in a quarter of pediatric patients with HCC, but it would be surprising that the primary tumor changed its biological behavior in a relapse.[13] Against all odds and after an exhausting investigation, the tumor turned up to be a choriocarcinoma transmitted from the donor graft.

Donor selection guidelines and improved imaging techniques allowed for huge advances in the identification of graft malignancies.[1,5] However, young donors whose cause of brain death had been intracranial hemorrhage without any evidence of tumor during the harvest of the organs are commonly report as a source of graft malignancies in literature.[1,4,5,10,11] A meticulous physical examination along with intraoperative US should help finding some undiagnosed donor malignancies. Some authors even propose that all female donors in their child-bearing age should be screened for HCG levels[1,5] and that high HCG values in non-pregnant donors should exclude donation.[5]

Published reports on choriocarcinoma transmission are rare and have poor prognosis for liver recipients, with a high chance of metastatic lesions.[9] Moreover, it seems to have a high malignant potential in immunosuppressed patients.[4,5]

In this report, the transplanted organ was not removed due to initially good response to chemotherapy and because of the presence of distant metastases. Higher ISS required after a retransplant, would promote a great chance of metastatic expansion.

Falling the utopic goal of finding every cancer-bearing grafts, case reports function as important tools in creating a cancerous donor profile. Online platforms as the NOTIFY library (https://www.notifylibrary.org/) allow experts from around the world to collaborate and share didactic information on adverse outcomes such as presence of malignancy after liver and kidney transplantation.

The Cincinnati Transplant Tumor Registry reported a rate of 93% in transmission of choriocarcinoma, with the majority of recipients presenting metastatic disease. All kidney grafts underwent transplantectomy. As it is not possible to do, an immediate transplantectomy for a liver graft or to retransplant when metastatic disease is present the prognosis was worse for liver recipients.[5,14,15]

As the best of our knowledge, this is the first report of a successful outcome using a liver graft with choriocarcinoma. Long follow-up free of disease and no need for retransplant are also worth to notice.

This case suggests the benefit of donor screening for HCG value in female donors of child-bearing age with intracranial hemorrhage.

CONFLICT OF INTEREST

No financial or personal interests to declare.

AUTHOR CONTRIBUTION

All authors attest that they meet the current ICMJE criteria for Authorship. IP, FH. EF, APC, IG involved in planning and design. IP, APC, and IG involved in acquisition of data, performing the procedures, reporting, and conception. IP, FH. EF, APC, and IG involved in analysis and interpretation of data.

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