

# Living Donor Liver Transplantation for Hepatic Epithelioid Hemangio Endothelioma: Two Case Reports

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## ABSTRACT

*Hepatic epithelioid hemangio endothelioma (HEHE) is a rare tumor of the liver, vascular in origin. Orthotopic liver transplantation (OLT) is the accepted treatment option for bilobar infiltrating tumors. In case of limited and stable extrahepatic invasion, OLT is not strictly contraindicated. This study presents two HEHE cases treated with living donor liver transplantation (LDLT). The first patient, a 39-year-old female, had a rapid clinical onset of one month, and the tumor was unresectable at the time of diagnosis. The second patient was a 31-year-old male presenting with unresectable tumor and extrahepatic dissemination of the disease. In similar patients on the waiting list for cadaveric liver transplantation, undue delay can be avoided through LDLT. Both of the presented patients are in an uncomplicated state as of postoperative month 11.*

**Key words:** Living donor liver transplantation, Hepatic epithelioid hemangio endothelioma

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## ÖZET

### Hepatik Epiteloid Hemanjiyo Endotelilyomada Canlı Vericili Karaciğer Nakli: İki Olgu Sunumu

*Hepatik epiteloid hemanjiyo endotelilyoma (HEHE) karaciğerin nadir görülen, vasküler kökenli tümörlerindedir. Her iki lobu infiltrate eden tümörlerde ortotopik karaciğer transplantasyonu (OLT) kabul edilen bir tedavi yöntemidir. İyi seçilmiş, stabil seyirli ekstrahepatik tutulum olan olgularda da OLT kesin olarak kontrendike değildir. Çalışma, canlı vericili karaciğer nakli (CVKN) ile tedavi edilen 2 adet HEHE olgusuna dair sonuçları sunmaktadır. İlk olgu 39 yaşında bir kadın hasta olup, bir ay içinde hızla gelişen klinik tablo ile başvurduğunda, tanı anında tümör unrezektabl idi. İkinci olgu 31 yaşında erkek hasta olup unrezektabl tümöre ek olarak karaciğer dışı yayılım tablosuyla başvurmuştu. Bu olgular gibi organ bekleme listesinde olan hastaların tedaviye ulaşacakları zamanın uzamasının önüne CVKN ile geçilebilir. Her 2 hastanın da postoperatif ilk 11 ayı sorunsuz olarak geçmiştir.*

**Anahtar kelimeler:** Canlı vericili karaciğer nakli, Hepatik epiteloid hemanjiyo endotelilyoma

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**INTRODUCTION**

Hepatic epithelioid hemangioendothelioma (HEHE) is a rare tumor, low grade in malignancy and vascular in origin, with a frequency of 0.00001% and a peak incidence in the early decades. The clinical course of the disease varies from asymptomatic state to liver failure parallel to the treatment options varying from clinical follow-up to liver transplantation<sup>[1-4]</sup>. Orthotopic liver transplantation (OLT) is the accepted treatment for unresectable HEHE. Extrahepatic dissemination and lymph node invasion are not absolute contraindications for liver transplantation<sup>[1,4]</sup>. There have been reports of living donor liver transplantation (LDLT) for the treatment of HEHE, and the procedure is approved for well-selected cases with bilobar disease without extrahepatic dissemination<sup>[4-7]</sup>. This report presents two unresectable HEHE cases treated with LDLT in our institution due to rapidly progressing liver failure.

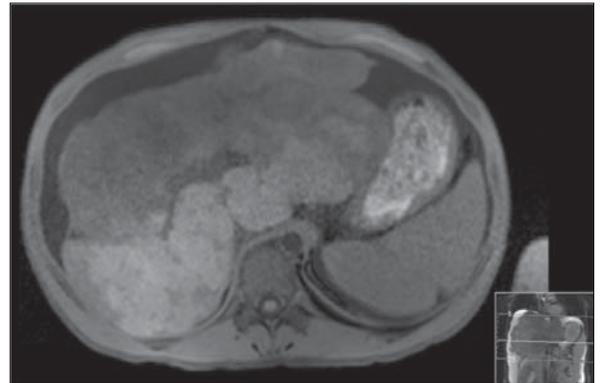
**CASE REPORTS**

**Case 1**

A 31-year-old male patient applied with complaints of abdominal distention and fatigue for one month. The physical examination revealed extensive ascites. Magnetic resonance imaging (MRI) studies revealed lobulated contoured lesions in both hepatic lobes, which were hypointense on T1A and hyperintense in T2A slides, tending to unify, containing cystic necrotic areas, and displaying localized contrast enhancement (Figure 1). Alpha fetoprotein (AFP) level was within normal range (1.5 IU/mL). Following liver biopsy, the immunohistochemical study detected CD31 to be positive, and the diagnosis was HEHE. Computerized tomography (CT) of the thorax revealed pulmonary millimetric metastatic lesions. Hepatic functions deteriorated rapidly; the CHILD class was determined to be C and MELD score was 32. Due to the unresectability of the tumor, LDLT was performed. The operation and the postoperative follow-up were uneventful, and the patient was discharged. In postoperative month 6, percutaneous internal-external biliary catheter was applied due to biliary stricture; the remaining follow-up was without complication. As of postoperative month 11, follow-up CT scans did not reveal any increase in the dimension or number of the pulmonary lesions, and no tumoral lesion was seen in the liver.

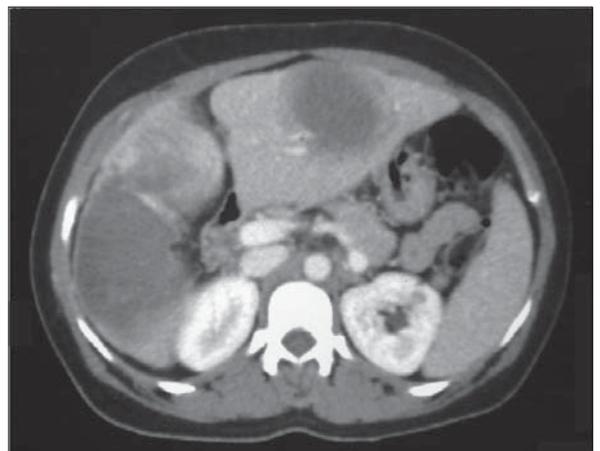
**Case 2**

A 39-year-old female patient applied with the complaint of fatigue for one month. The physical



**Figure 1. Lobulated contoured lesions in both hepatic lobes, tending to unify, containing cystic necrotic areas and displaying localized contrast enhancement.**

examination revealed jaundice. Multi-slice CT studies revealed a semi-solid mass lesion occupying the right hepatic lobe, 15 x 10 cm in craniocaudal dimensions, consisting of calcified areas and compressing the bile duct bifurcation. Multiple masses with similar properties were detected - one located in segment III and 7.5 cm in diameter and the remaining in segment VII, with the largest being 2.5 cm in diameter (Figure 2). AFP level was within normal range (1.1 IU/mL). Following liver biopsy, immunohistochemical study detected factor VIII-RAg and CD31 to be positive, and the diagnosis of HEHE was made. No extrahepatic dissemination of the disease was detected. Percutaneous transhepatic cholangiography (PTC) was performed due to tumor compression resulting in



**Figure 2. Semi-solid mass lesion occupying the right hepatic lobe, 15 x 10 cm in craniocaudal dimensions, consisting of calcified areas and compressing the bile duct bifurcation.**

intrahepatic bile-duct dilatation. Following PTC, the patient was followed in the intensive care unit due to hemobilia. Gastrointestinal bleeding triggered the onset of liver failure. CHILD class was determined to be C and MELD score was 14. LDLT was performed. During the postoperative follow-up, pneumonia resulting in sepsis was treated. As of postoperative month 11, no recurrence of the disease was detected.

## DISCUSSION

HEHE was initially presented in a case series of 32 patients by Ishak et al.<sup>[8]</sup>. To date, small case series about the disease have been presented. At the time of diagnosis, 81% of the cases present with multifocal lesion, and 27-37% of the cases present with metastasis. Clinical manifestation may vary from asymptomatic state to the most common complaints of abdominal pain and weight loss<sup>[1,7,10]</sup>. This insidious disease resulted in liver failure in our cases and was diagnosed when it occupied both hepatic lobes. Oral contraceptive intake history, exposure to vinyl-chloride and major trauma are among the risk factors, but none of these risk factors was detected in our patients<sup>[1,3]</sup>.

HEHE displays tumoral masses on CT and MRI scans, which cause retractions of the hepatic capsule due to their fibrotic structure. They are centrally hypervascular and peripherally dense in contrast enhancement (target-shaped), tending to unify<sup>[3]</sup>. Definitive diagnosis requires the demonstration of factor VIII-RAg, CD31, CD34, and cytokeratin in immunohistochemical studies following liver biopsy<sup>[3]</sup>. Factor VIII-RAg is 98% positive in HEHE; therefore, this marker is suggested as a diagnostic marker. In our cases, the diagnosis of HEHE was achieved by biopsies taken from the lesions, which displayed semisolid masses tending to unify on CT and MRI scans, and immunohistochemical studies displaying the presence of CD31 and factor VIII-RAg.

Prognosis of the disease varies from survival over 5 years without any treatment, to a case of spontaneous complete cure in 10 years, to death of the patient in a few weeks<sup>[4,8,11]</sup>. Prediction as to the outcome of the disease is difficult, since there seems to be no relation between the nuclear atypia, number of mitoses, and capsule invasion, which are well-known biological behavioral markers of the tumor and the clinical outcome. Only tumor necrosis has been found to be related with a poor prognosis<sup>[11]</sup>. Additionally, liver failure and portal hypertension, which were present in our cases, are also findings of an aggressive tumor and poor prognosis<sup>[3]</sup>.

Development of a structured clinical approach algorithm for a tumor with various probable clinical outcomes is not easy<sup>[10]</sup>. Treatment options consist of local ablation, liver resection, liver transplantation, chemotherapy, and radiotherapy<sup>[4]</sup>. Medical treatment options are limited, with variability in outcomes<sup>[3]</sup>. Surgery is the essential treatment. The best treatment option for localized disease is liver resection. However, the most accepted treatment is OLT due to the high incidence of multicentric presence of the tumor. Extrahepatic dissemination is not related with poor prognosis; therefore, this situation and lymph node invasion are not absolute contraindications for OLT (especially when extrahepatic metastatic lesions are resected)<sup>[1-3]</sup>. In fact, the number of LDLT cases with a history of HEHE is less than 10. Cases with bilobar diseases without extrahepatic dissemination are encouraged for expansion of the organ donation pool<sup>[5-7]</sup>. A patient subjected to LDLT died in postoperative month 8 due to disease recurrence<sup>[12]</sup>. One of our cases with extrahepatic dissemination did not experience an increase in dimension or in number of the pulmonary metastatic lesions. As reported in the literature, 5-year survival and 5-year disease-free survival rates are 64-83% and 43-60.2%, respectively<sup>[1-3]</sup>. Both of the presented cases are currently in postoperative month 11 without any complication.

In conclusion, treatment of the disease, which may rapidly progress, without delay, with LDLT provided an uneventful 11-month survival. Randomized controlled studies are required to determine the most effective treatment option.

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