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Case Report

Living Donor Liver Transplantation for Adult Hepatic Undifferentiated Embryonal Sarcoma: A Case Report

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Abstract

Introduction: Undifferentiated embryonal sarcoma of the liver (UESL) is an aggressive tumor. There is no established treatment, and it is an uncommon tumor in adults. Treatment usually involves a combination of surgery, chemotherapy, and occasionally liver transplantation (LT). The role of LT in patients with irresectable UESL merits exploration. **Case Description:** A 20-year-old boy with a large palpable abdominal mass, shortness of breath, and weight loss presented to our clinic. His computed tomography scan showed showed a large cystic lesion measuring 11.5 × 22.7 × 23 cm, predominantly involving the left lobe and right anterior sector, with a biopsy consistent with UESL. The tumor was abutting to the right hepatic vein, with bland main portal vein thrombosis. Due to an irresectable tumor and deteriorating clinical condition, living donor LT was performed. The patient remains in good health at 16 months of follow-up. **Practical Implication:** In carefully selected patients with UESL, when other options are not feasible, LT might prolong survival and improve quality of life.

Keywords: Chemotherapy, liver transplantation, survival, undifferentiated embryonal sarcoma

Introduction

Undifferentiated embryonal sarcoma of the liver (UESL) is a rare neoplasm with a predilection for the pediatric age group.[1] It is composed of primitive parenchymal cells without histological differentiation and has been associated with hepatic mesenchymal hamartoma. There is no established treatment for UESL, and chemotherapy, radiotherapy, partial hepatectomy, and liver transplantation (LT) have been tried with variable

results.[2] Based on a recent review, only seven adult patients (age >12 years) with UESL underwent LT. The authors proposed that LT and adjuvant chemotherapy might be an acceptable option for UESL.[1] However, in patients with resectable disease, neoadjuvant chemotherapy followed by liver resection was considered more appropriate. Hepatic embryonal sarcoma might be considered irresectable due to multifocality, major vascular involvement, and unacceptable future liver remnant in patients without extrahepatic disease.[3] Due to its rarity, post-transplant outcomes in patients with UESL are not well described. Here, we share our experience of living donor LT (LDLT) with large irresectable UESL.

Case Description

A 20-year-old boy presented to the clinic with complaints of pain in the right hypochondrium, right lower chest pain, low-grade fever, and weight loss over 3 months. He had shortness of breath and was not able to sit or lie flat. On examination, there was a palpable mass in the upper abdomen extending to the pelvis. At presentation, his hemoglobin was 9.7 g/dL, white blood cell count was 11790/uL, and platelet count was 534000/uL. His liver function, renal function, and coagulation profile were normal. Tumor markers, including alpha-fetoprotein (AFP), cancer antigens (CA) 19-9, CA-125, protein induced by vitamin K absence-II, and carcinoembryonic antigen, were within normal range, and his viral markers were also negative. There was a history of exploratory laparotomy 1 month back for a presumed diagnosis of a hydatid cyst of the liver. A large cystic mass was noted involving the whole left lobe extended into the right lobe. An incisional biopsy was performed, which was reported as poorly differentiated hepatocellular carcinoma (HCC).

Diagnosis and Management

We performed a computed tomography (CT) scan which showed a large solid/cystic mass involving segments 2, 3, 4, and 8, measuring approximately 11.5 × 22.7 × 23 cm. There was no evidence of arterial phase enhancement with venous washout to suggest HCC. The tumor was closely applied to the right hepatic vein [Figure 1] and there was bland main portal vein thrombosis [Figure 2]. There was no evidence of extrahepatic disease. The histopathology was reviewed and was confirmed as UESL. After evaluation in the multidisciplinary team meeting, LT was offered as the most suitable treatment option.

The patient underwent LDLT in October 2021. On exploration, there was no extrahepatic disease. A large left lobe mass involving segments 2, 3, 4, and 8 was noted [Figure 3]. It extended into the pelvis and was adherent to the anterior abdominal wall and surrounding tissues by thick and thin adhesions. The patient received a right lobe graft without a middle hepatic vein from his brother [Figure 4]. The explanted liver weighed more than 6 kg. After a prolonged stay in the hospital, he was discharged on the 33rd post-operative day in stable condition. On explant histopathology, there was a large lobulated tan-yellow solid tumor with anaplastic, spindled/oval cells in a myxoid stroma [Figure 5]. Immunohistochemistry (IHC) showed high Ki-67 activity and glypican positivity, but was negative for hepatocyte paraffin1, AFP, cytokeratin AE1/AE3. myogenin and desmin. He received six cycles of adjuvant chemotherapy, including ifosfamide and doxorubicin. He remained well until 12 months after the transplant when he developed abdominal pain. On dynamic CT scan of the liver, a lobulated heterogeneous centrally enhancing necrotic lesion measuring 47 × 43 mm was noted. A smaller similar lesion was noted inferiorly. Positron emission tomography scan showed a hypermetabolic well-defined, rounded, heterogeneous density lesion in the right midabdomen (SUVmax 15.2) measuring 47 mm × 43 mm × 51 mm. A heterogeneous density metabolically active lesion (SUVmax 7.7) measuring 33 mm × 21 mm was identified in the epigastric region to the left of the midline. Based on the multidisciplinary team's recommendation, laparotomy with surgical excision of abdominal nodules was performed. The histopathology was

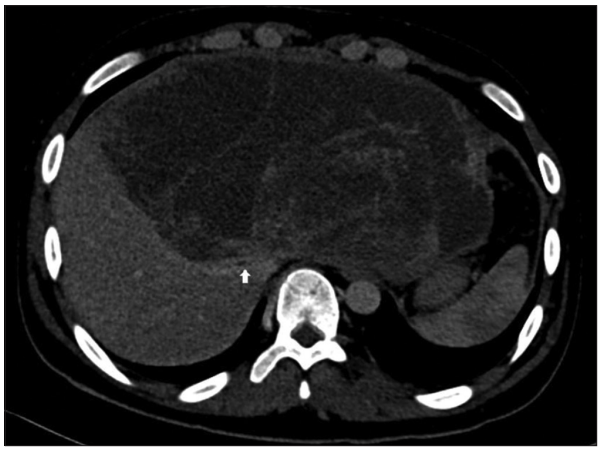

Figure 1: Large solid-cystic tumor predominantly involving the left lobe and right anterior sector closely applied to the right hepatic vein (white arrow)

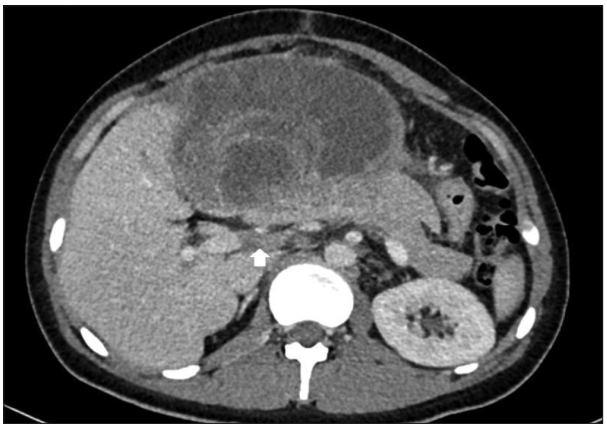

Figure 2: Large solid-cystic tumor with bland thrombus in the main portal vein (white arrow)

consistent with UESL. The patient is alive and remains in follow-up.

Discussion

Primary liver sarcomas are uncommon and usually occur in children. The more common varieties include angiosarcoma, leiomyosarcoma, and fibrosarcoma. The UESL is relatively rare and was first described in 1978.[3]

Symptoms are directly related to the mass effect and consist of abdominal pain and swelling, anorexia, weight loss, and other constitutional symptoms. There are no specific laboratory

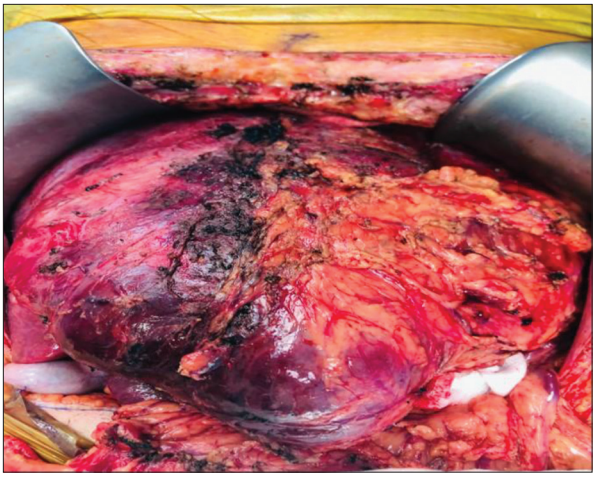

Figure 3: Intraoperative photo showing large hepatic tumor involving the left lobe and right anterior sector (Segment 8) of the liver

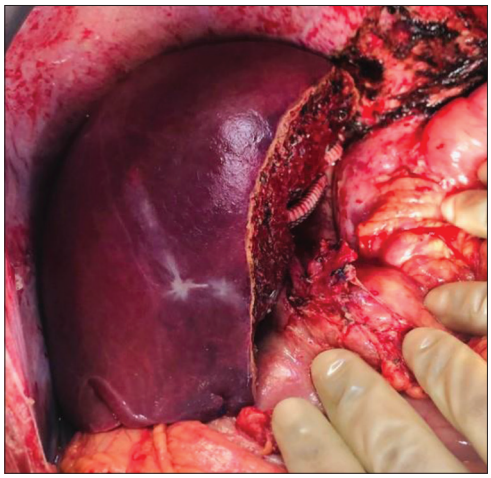

Figure 4: Right lobe graft with Segment 5 and 8 veins reconstructed using DACRON grafts

markers. UESL might appear as a hypoechoic solid mass on ultrasound. On CT, the tumor exhibits solid portions with a predominantly cystic appearance. This can be confused with a liver abscess or hydatid cyst.[4,5] We performed a liver dynamic CT scan, which showed a large inhomogeneous mass with eccentric abnormal contrast uptake and portal vein thrombosis. Magnetic resonance imaging (MRI) usually confirms CT findings and is more useful for the identification of vascular invasion, biliary obstruction, and hilar lymphadenopathy. Precise localization of the tumor and its relationship with the

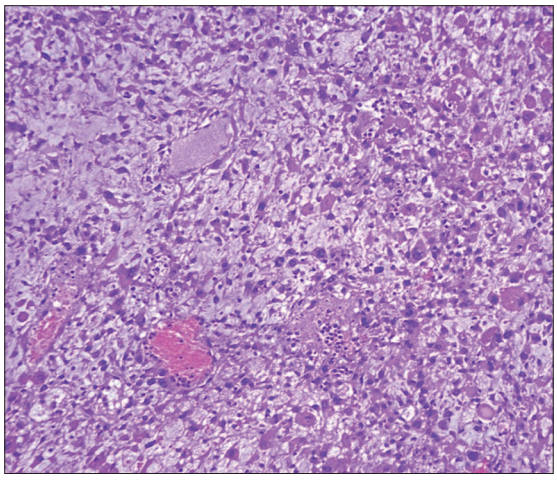

Figure 5: Explant histopathology showing variably cellular tumor with anaplastic, spindled/oval cells in myxoid stroma (H/E ×200)

major vessels are crucial in defining resectability, which represents the most important prognostic factor in patients with UESL.[6] We could not perform an MRI in our patient due to shortness of breath and inability to lie flat. IHC is generally required to rule out other mimickers. A specific immunophenotype has not been associated with UESL.[5]

UESL is an aggressive tumor and usually presents at an advanced stage. With regard to treatment, there is no standard of care for UESL. Multimodal treatment can improve outcomes, and survival rates of 70–100% have been documented. In general, it is accepted that neoadjuvant chemotherapy followed by surgical resection is the most suitable management for resectable UESL. For unresectable UESL, neoadjuvant chemotherapy followed by LT or LT followed by adjuvant chemotherapy can be considered.[1] Surgical resection with negative margins is considered one of the most important prognostic factors in resectable tumors.[6,7] Neoadjuvant chemotherapy was not an option in our patient due to poor quality of life and constitutional symptoms due to large tumor size. With regards to surgical resection, an extended left hepatectomy with portal vein thrombectomy and PTFE or DACRON graft reconstruction would be needed. Despite this extensive surgery, a positive margin on the right hepatic vein was a very likely possibility. The patient received six cycles of doxorubicin and ifosfamide as an adjuvant chemotherapy, which is in line with previously published reports.[6,7]

In a recent systematic review of literature, Babu *et al*. have shown that only seven adult patients underwent LT for UESL. Out of these, two had salvage LT after surgical resection, while five underwent primary LT.[1] Overall, UESL in adults is associated with inferior outcomes when compared with children.[7,8] Due to their internal myxoid nature with cystic and solid components, UESL is prone to rupture on biopsy.[9] Unfortunately, our patient had an open biopsy elsewhere due to a presumed diagnosis of hepatic hydatid cyst. We believe that this led to peritoneal spillage, which was not evident at the time of the transplant. The abdominal recurrence without the involvement of a transplanted liver or any other extra-abdominal site raises the suspicion of peritoneal contamination during the open biopsy. We suggest that in such patients, when possible, a period of watchful waiting or neoadjuvant chemotherapy should be considered to allow tumor biology to declare itself. Unfortunately, this was not possible for this patient due to his deteriorating condition.

We would also like to highlight the ethical dilemmas when considering LDLT for patients with such aggressive tumors. Upfront LT in patients with large, aggressive tumors is associated with high recurrence, and the double equipoise associated with a voluntary donation should not be jeopardized.[10] LT was carefully considered in this particular patient due to young age and lack of alternative treatment options. The family was counseled in detail regarding the potential risk of early recurrence and failure to achieve long-term survival. The patient and the family understood the risk and, due to the deteriorating condition, wanted to proceed with LT.

There is no established treatment for UESL in adults. History of surgery or open biopsy increases the risk of peritoneal dissemination due to tumor rupture and should be ruled out before contemplating

curative surgery. LT might be an acceptable option for unresectable UESL confined to the liver, and long-term survival is occasionally possible.

Acknowledgment

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Author Contributions

Conceived and designed the analysis: US and ABHB; Collected the data: AS, ZA, and BYF; Contributed data or analysis tools: AS, ZA, BYF, and ABHB; Performed the analysis: US and ABHB; Wrote the paper: US and ABHB.