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CASE REPORT
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# Prenatal Diagnosis of Fetal Hepatoblastoma with a Good Neonatal Outcome: Case Report and Narrative Literature Review

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The authors report a case of congenital hepatoblastoma that was diagnosed in the antenatal period at 39 weeks' gestation. The infant was delivered vaginally without rupture of the tumor. The neonate then received chemotherapy and underwent surgical excision of the tumor. After 1 year, no tumor recurrence has been noted.

**Keywords** congenital hepatoblastoma, fetal tumor, prenatal diagnosis, timely treatment



Hepatoblastoma is a rare tumor of childhood with a reported incidence in the first year of life of 1 per million [1]. Antenatal diagnosis of hepatoblastomas is uncommon, and of the 42 congenital hepatoblastoma cases reported in the literature, only 1 was diagnosed in the prenatal period [1]. Congenital hepatic tumors can be diagnosed prenatally by ultrasound, and the differential diagnosis of intrahepatic tumors includes hemangioma, mesenchymal hamartoma, hepatoblastoma, and metastatic neuroblastoma [2]. When a hepatoblastoma is detected antenatally, cesarean delivery is considered due to the concern of tumor rupture during vaginal delivery; however, there are too few cases to provide definitive guidance. We herein report a case of congenital hepatoblastoma that was diagnosed in the antenatal period at 39 weeks' gestation. The infant was delivered vaginally without rupture of the tumor. After delivery, the neonate received chemotherapy, surgical excision of the tumor was performed, and at 1 year of age no tumor recurrence has been noted. This case illustrates the importance of prenatal diagnosis and subsequent timely treatment that can lead to good outcomes in cases such as this one.

## CASE REPORT

A 28-year-old gravida 1 was referred to our hospital at 39 weeks' gestation due to the detection of an intra-abdominal fetal mass during an ultrasonographic examination. The mass was described as hypoechoic, 3.0 cm in diameter, and located in the right

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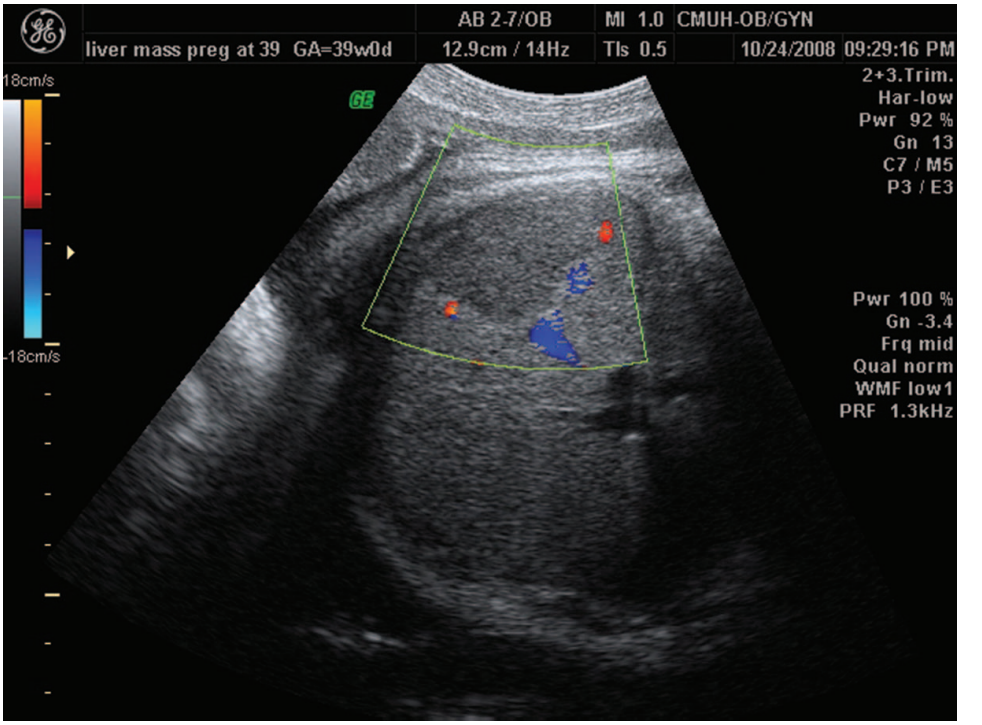


**FIGURE 1** Ultrasound at 39 weeks' gestation revealed a well-defined hypoechoic mass in the right posterior lobe of the fetal liver.

posterior aspect of fetal liver. Biophysical assessment at that time was within normal limits. The patient had received regular prenatal care and her prenatal course was unremarkable. Maternal alpha-fetoprotein (AFP) at 17 weeks' gestation was normal (AFP, 74 ng/dL [1.4 Multiples of the Median (MoM)];. Down syndrome risk, 1/7056), and a second trimester ultrasound performed at 26 weeks' gestation revealed no abnormalities and normal growth.

Ultrasound at our hospital revealed a well-defined hypoechoic intrahepatic mass in the right posterior lobe of the fetal liver (Figure 1). Both fetal kidneys appeared normal. Color Doppler imaging revealed abundant peripheral vascularization of the mass, different than that seen in a hemangioma. Hepatoblastoma was considered likely because of the apparent rapid growth of the mass (no mass was detected during the ultrasound at 26 weeks' gestation), and by exclusion of other possibilities. Approximately 3 days after the ultrasound, the patient arrived at our hospital with ruptured amniotic membranes and delivered a 3410-g male infant via normal spontaneous vaginal delivery. The labor and delivery were without complications, and the Apgar scores were 9 and 10, at 1 minute and 5 minutes, respectively.

Abdominal ultrasound of the neonate revealed a well-defined heteroechogenic mass in the right posterior lobe of the liver, compatible with the prenatal ultrasound. Abdominal computed tomography (CT) revealed a heterogeneous enhancing mass ($3.0 \times 2.1$ cm) in S7–6 of the liver, and another small lesion ($0.6 \times 0.6$ cm) in S4 (Figure 2). The infant's AFP level was 29,123 ng/mL at birth, and maternal hepatitis B was excluded by laboratory testing.

A wedge biopsy of the larger mass was performed 15 days after delivery. Histopathological examination revealed the lesion to be a pure epithelial type hepatoblastoma. Because of the presence of multiple lesions, chemotherapy consisting of cisplatin

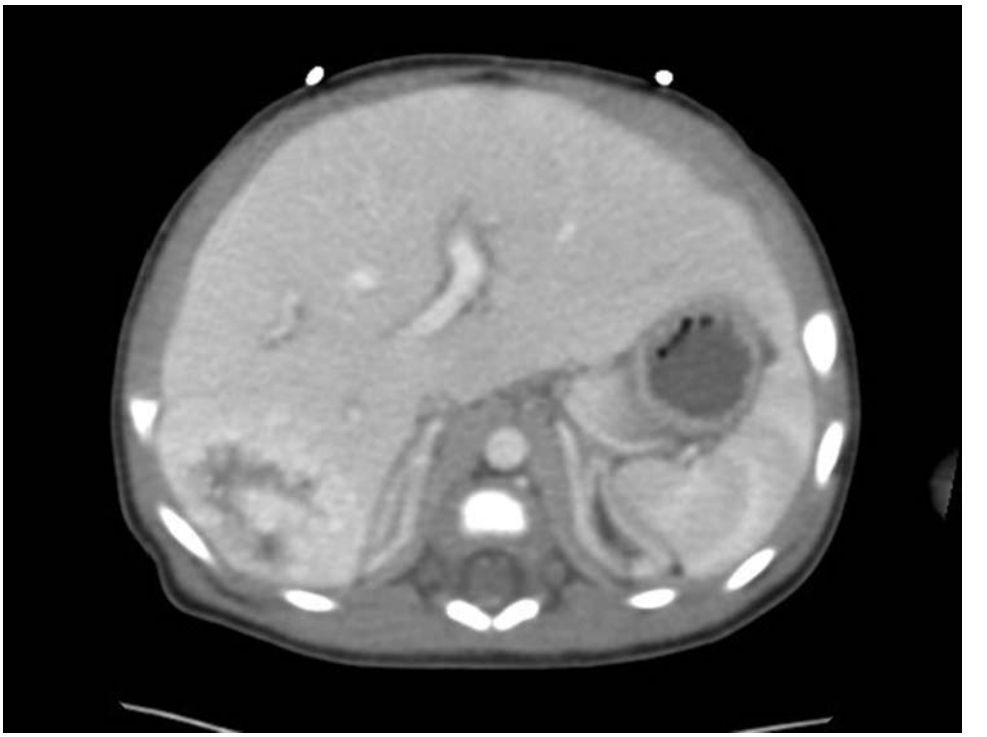

**FIGURE 2** Abdominal computed tomography revealed a heterogeneous enhancing mass in right posterior lobe of the fetal liver.



80 mg/m$^2$, doxorubicin 60 mg/m$^2$, and carboplatin 500 mg/m$^2$ administered every 3 to 4 weeks was begun. At 3.5 months of age, after 3 courses of chemotherapy, tumor resection (trisegmentectomy) and cholecystectomy were performed. Postoperatively, the AFP level decreased to 54 ng/mL.

Postoperatively, adjuvant chemotherapy consisting vincristine, cyclophosphamide, and 5-fluorouracil was administered. CT at 5 months of age (1.5 months postoperatively) showed no evidence of residual tumor, metastases, or lymphadenopathy. At 1 year of age, no evidence of recurrence has been detected.

## DISCUSSION

Hepatoblastoma is a rare tumor of childhood, with a reported incidence in the first year of life of 1 per million [1]. A search of PubMed revealed only 42 reported cases of congenital hepatoblastomas, which were summarized by Ergin et al in 2008, and antenatal diagnosis was rare [1]. Of these 42 cases, 7 were diagnosed as a "liver tumor" prenatally; only 1 of the 7 was diagnosed as a hepatoblastoma prenatally. In the other 6 cases, definitive diagnosis was not made until after birth. All 7 infants died in the postnatal period, with or without surgery and/or chemotherapy [1]. When detected antenatally, cesarean delivery is considered because of the concern of tumor rupture during vaginal delivery; however, there are too few cases to provide definitive guidance.

Tumors detected antenatally or after birth up to 3 months of age are considered congenital fetal tumors. The lesions can be benign or malignant, and early detection of the tumor can significantly affect neonatal care [2]. Congenital hepatic

tumors, although uncommon, can be diagnosed prenatally by routine ultrasound. The differential diagnosis of intrahepatic tumors includes hemangioma, mesenchymal hamartoma, hepatoblastoma, and metastatic neuroblastoma [2]. Congenital hemangiomas can be detected prenatally with color Doppler ultrasound, and the presence of abundant vessels can differentiate hemagiomas from less vascularized tumors [3, 4]. Mesenchymal hamartomas are a developmental malformation consisting of a tumor-like overgrowth of tissue or tissues inherent to an organ or area [5]. Metastatic neuroblastomas are associated with primary adrenal tumors, and may present as single or multiple hypoechoic nodules [2, 3]. Though uncommonly detected in the antenatal period, hepatoblastomas are the most common liver malignancy in childhood [3, 4].

Congenital hepatoblastomas exhibit some important distinctive features when compared to hepatoblastomas diagnosed in children beyond the neonatal period [6]. These are a different clinical presentation, a higher incidence of pure fetal histology, a significant risk for systemic metastases, and a worse outcome. Systemic metastases without lung involvement is frequent with congenital hepatoblastomas, thus a bone scan and CT or magnetic resonance imaging (MRI) of the brain should complete the usual staging procedures. Short follow-up intervals are recommended [6].

Histologically, hepatoblastoma can be classified into pure epithelial (~56%) and mixed epithelial/mesenchymal (~44%) types, and the pure epithelial type can be divided into 4 subtypes (pure fetal, embryonal, macrotrabecular, small cell undifferentiated) [2, 3]. The pure fetal subtype and the presence of mesenchymal elements have been associated with better outcomes [2, 3]. Though the pathogenesis of hepatoblastomas remains unclear, evidence suggests that the Wnt signaling pathway plays an important role in their development [7]. Hepatoblastomas occur more commonly in the right lobe than the left [8]. The left lobe of the fetal liver is supplied with oxygenated blood from the umbilical vein, whereas the right lobe is supplied with portal vein blood, which has an lower oxygen saturation. Presumably, the lower oxygen tension impedes the embryonic differentiation of hepatoblasts, thus predisposing to the development of hepatoblastomas in the right lobe [8]. Hepatoblastomas have been associated with Beckwith-Wiedemann syndrome, hemihypertrophy, familial adenomatous polyposis, hepatitis B, low birth weight, prematurity, polyhydramnios, and fetal hydrops [9–12].

Benign and malignant fetal tumors have similar ultrasonographic appearances, and usually appear as a heterogeneous solid or cystic mass that distorts the surrounding tissues [13]. The characteristic sonographic findings of hepatoblastomas are a large, echogenic to hypoechoic solid lesion in the right lobe of the liver with focal hemorrhage, necrosis, and calcification [13]. Most cases that have been detected prenatally have been diagnosed in the third trimester [14]. Gray-scale, color, and power Doppler ultrasonography have all been used to differentiate hepatoblastomas from other conditions; however, definitive diagnosis requires histopathological examination of a tissue specimen [1, 2, 14]. In one reported case, 3-dimensional power Doppler ultrasonography was used to visual the vascular anatomy of a right-sided fetal hepatic tumor, and this lead to the diagnosis of a hepatoblastoma, which was confirmed after birth [8]. AFP is a sensitive marker of hepatoblastomas, and is elevated in approximately half of neonates with hepatoblastomas, thus helping to establish the diagnosis [13].

When a fetal liver mass suspicious for a hepatoblastoma is diagnosed, close fetal monitoring is required due to the possibility of nonimmune hydrops and obstruction of venous return [14]. Management of hepatoblastomas after birth includes lobar resection, chemotherapy, and liver transplantation, depending on whether the tumor can be resected or not [9, 15, 16]. The role of chemotherapy is to reduce the size of tumors that are unresectable at presentation, and to control microscopic residual

disease after definitive resection [9]. The chemotherapy regimen used for the patient presented herein was based on that of the SIOPEL-3HR study [17]. The authors found that a preoperative regimen of cisplatin, carboplatin, and doxorubicin rendered a significant portion of the tumors resectable, and improved survival in comparison to previous reports. Long-term survival rates from 80% to 100% have been reported; however, prognosis is related to the presence of metastases at the time of diagnosis [15, 16]. AFP levels correlate with the extent of disease and a decline of AFP levels during treatment is prognostic of better outcomes [9].

In summary, diagnosis of fetal abdominal tumors in the antenatal period is possible with available imaging modalities. Early detection of hepatoblastomas allows for consideration of the mode of delivery, prompt treatment, and may lead to better outcomes. This report highlights the importance of prenatal diagnosis for the achievement of good outcomes.

**Declaration of Interest**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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