

Early Diagnosis, Team Approach and Individualized Treatment Plan Key to Successful Treatment of Hepatoblastoma

This case study was written in collaboration with:

John Bucuvalas, MD

*Associate Medical Director
Pediatric Liver Care Center
Associate Medical Director
Liver Transplant Program*

Kathleen Campbell, MD

*Medical Director
Liver Transplant Program*

James Geller, MD

*Director
Liver Tumor Program*

Greg Tiao, MD

*Surgical Director
Liver and Intestinal Transplantation*

Clinical History and Presentation

During a well-child visit with her local pediatrician, a 3-year-old girl was noted to have an abdominal mass. A follow-up CT scan showed a large mass in the left lateral segment of her liver. Her previous medical history included a patent ductus arteriosus (PDA), a ventricular septal defect and an atrial septal defect, which had been surgically closed prior to this specific well-child visit. She also had persistent ductus arteriosus but no symptoms of cardiac insufficiency. Once the hepatic mass was discovered, she was referred to oncologists at Cincinnati Children's Hospital Medical Center for further evaluation and treatment.

Our Approach

During her initial evaluation at Cincinnati Children's, the patient underwent an MRI exam, which showed the left lobe mass but also revealed a mass in the right lobe, as well as a previously undiagnosed patent sinus venosus. An open liver biopsy was conducted to determine the histologic subtype of her tumor. The biopsy and additional imaging confirmed Stage III hepatoblastoma. Due to the multifocality of the disease, as well as the aberrant vascular anatomy, physicians involved in her care decided that gross resection of the cancer by conventional means was not possible. The decision was made to proceed with chemotherapy and transplantation.

Pre-Transplant Chemotherapy Treatment

One week after the liver biopsy, she received the first of four rounds of chemotherapy using cisplatin, 5-fluorouracil and vincristine. Two weeks later, she underwent a comprehensive transplant evaluation by pediatric subspecialists from hepatology (John Bucuvalas, MD), oncology (James Geller, MD) and transplant surgery (Greg Tiao, MD). The medical team determined that closure of the PDA was not necessary prior to transplantation. Following the evaluation, the child was deemed a viable transplant candidate and was listed for transplant.

While awaiting liver transplantation, she experienced an initial response to chemotherapy as demonstrated by imaging and alpha-fetoprotein levels (a marker of tumor activity). However, following the fourth round of chemotherapy her alpha-fetoprotein began to rise to levels above 100,000, suggesting the development of front-line chemotherapy resistance.

Liver Transplantation and Post-Transplant Chemotherapy

After a two-month wait on the transplant list, the patient received a whole liver transplant. When resected and examined, the tumors were found to be more than 95 percent viable with small cell anaplastic features; however, there was no evidence of venous invasion. To lower her risk of hepatoblastoma recurrence, she received three rounds of post-transplant chemotherapy using ifosfamide and doxorubicin at Cincinnati Children's.

Clinical Outcome and Follow Up

Eight months post-transplant, the patient's PDA was closed at Cincinnati Children's. At one year post-transplant, she experienced a case of moderate acute cellular rejection—a typical transplant-related complication—which was easily managed with standard therapy. Now more than five years from her initial diagnosis of hepatoblastoma and her subsequent liver transplantation, she has excellent graft function with no other long-term complications and is cancer free.

Patient Survival Pediatric Liver Transplantation for Hepatoblastoma

Transplants performed Jan. 1, 1999 – Jun. 30, 2009*



■ Cincinnati Children's
(n=19 since 1999)

■ National Average
(n=225 since 1999)

The patient continues to be followed by our liver transplant team, which provides coordinated long-term care across distance and inpatient/outpatient care for transplant recipients, to optimize graft survival and function and minimize complications of immunosuppressive therapy. She also is followed by our Cancer Survivor Center, which provides specialized medical care and psychosocial support to childhood cancer survivors through adulthood.

Discussion and Lessons Learned

The standard management for a patient with hepatoblastoma is a combination of chemotherapy and surgery. Increasingly, liver transplantation has been employed in the treatment of children with lesions unresectable by conventional surgery. Our care model involves creating an individualized pre- and post-transplant

chemotherapy protocol, taking into account each patient's unique needs, risk factors and morbidities. In customizing the post-transplant treatment plan, physicians consider the patient's pre-transplant course of therapy and response, the appearance of the transplant and the tumor once it is removed, as well as post-transplant markers. The importance of providing long-term, follow-up care to support these patients cannot be underestimated. This decision-making process requires a cooperative mindset and fluid communication among all caregivers.

Our team approach extends beyond treatment provided at Cincinnati Children's. From the beginning of a child's care, our team confers with a patient's hometown care team on acute management decisions, providing a level of comfort and confidence to physicians who may not be as familiar with hepatoblastoma and pre- and post-transplant chemotherapy.

Expedited Process for Transplant Evaluation and Placement

Early assessment, diagnosis and decision-making in the course of this disease are critical for good outcomes. We prefer to consult early in a patient's treatment course; however, we will provide a comprehensive consultation at anytime. Because we don't always see children until they are further along in their therapy, our liver transplant and oncology teams developed an expedited process for placing qualified children on the transplant list. Within a week of their initial visit at Cincinnati Children's, patients undergo a comprehensive evaluation by all involved specialists. Our goal is to place qualified patients on the transplant list within seven days of the transplant evaluation. This allows less time for the cancer to spread and minimizes the long-term consequences of delay in terms of chemotherapy side effects and immunosuppression issues.

Cincinnati Children's is ranked #1 for Digestive Disorders and #5 for Cancer Care by *U.S. News & World Report*. We are one of only 10 pediatric hospitals in the United States included on the Honor Roll in *U.S. News'* 2009 edition of *America's Best Children's Hospitals*.

Call 1-888-346-5124 to speak with a member of our hepatoblastoma team.