A RARE CASE OF HEPATOCELLULAR CARCINOMA IN A 6-YEAR-OLD FEMALE

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Introduction

Hepatocellular carcinoma (HCC) is quite rare in children. Hepatoblastoma is the most common liver malignancy in pediatric patients and should always be considered as a differential diagnosis in a case such as this. While the etiology of HCC in adults is generally secondary to chronic disease, the etiology in children is typically related to Hepatitis B or cirrhosis. HCC is generally diagnosed between age 12 and 14 in pediatric patients, and rarely is it diagnosed in those younger than 5.

The symptoms of hepatocellular carcinoma are quite non-specific and include abdominal pain and distension, nausea, vomiting, weight loss, and fever. This leads to a diagnostic delay as well as a delay in treatment. Only those who have advanced disease have symptoms such as jaundice and cachexia. Ultrasound can be used initially, however further analysis requires the use of CT or MRI. Elevated levels of serum AFP are specific but not very sensitive for detecting hepatocellular carcinoma in those who are at increased risk. For lesions without known cirrhosis, biopsy is recommended to confirm the diagnosis. There are no specific recommendations in children about when to biopsy, however it is recommended that in children without cirrhosis, histological evaluation be done, due to the implication of different histological subtypes on the prognosis and response to treatment.

When deciding treatment for pediatric patients with HCC it is important to consider four factors: 1) Liver function status including aspartate aminotransferase, alkaline phosphatase, bilirubin, portal vein thrombosis, and Child-Turcotte-Pugh scores; 2) tumor characteristics – including size, number of nodules, vascular invasion, TNM staging, distant metastasis, and AFP levels; 3) presence of portal hypertension; and 4) the overall status of the patient. The option that provides the highest success rate is complete resection for non-metastatic HCC or liver transplantation. It should be noted that there has been a dramatic improvement in the 5-year survival rates of children with HCC. This is likely attributed to improvement in surveillance and surgical techniques, specifically liver resection. For children in whom liver transplantation or resection is not an option, systemic neoadjuvant chemotherapy – specifically, and include – Sorafenib and cisplatin. The combination of PLADO – cisplatin and doxorubicin or super-PLADO – cisplatin, carboplatin, and doxorubicin can be used and can serve as a bridge to transplantation re-evaluation at a later time. Other treatment options include targeted therapies based on certain pathological mechanisms of cell proliferation involved in the oncological process.

Sorafenib is a novel multikinase inhibitor against RAF kinase and VEGF along with anti-proliferative and anti-angiogenic properties. Many trials have shown that use of sorafenib, in combination to placebo has improved time to tumor progression and overall survival. Additionally, the combination of doxorubicin with sorafenib has shown better outcomes than either agent alone. From the German GPOH group, sorafenib when used in combination with PLADO in children with hepatocellular carcinoma showed tumor regression in 4 out of 7 unresectable tumors.

Case Presentation

A 6-year-old female patient with past medical history of seasonal allergies presented to the primary care with the chief complaint of abdominal pain and diarrhea for about 2 weeks. The patient was otherwise healthy, very active, a diligent student with minimal absences and good grades, no recent travel history, and no sick contacts. No family history of liver diseases, cancers, or autoimmune diseases. The following sequence of events are mentioned with dates for proper orientation.

Timeline

Incident/Results

Day 1

- Patient complaints of “increased abdominal pain, decreased intake and increased lethargy” has fevers, vomiting, diaphoresis, cough, nasal congestion, or bleeding.
- White blood cell count (WBC) at the time patient complained of “her heart beating fast

Day 14

- Follow up with CT and again patient had a “stomach bug”.
- No vomiting, fever, or diarrhea. Only symptoms were ongoing abdominal pain and distension.
- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 24

- Follow up with FU, unremarkable for July 4th.
- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 26

- Patient taken to the ED for hypoglycemia
- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 28

- Follow up with FU, CT scan ordered for July 4th.
- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 34

- Follow up with FU, unremarkable for July 4th.
- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 51

- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 54

- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 56

- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 70

- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 88

- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 106

- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 135

- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 164

- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 215

- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 243

- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Day 269

- labs showed elevated liver enzymes (ALT 114 & AST 47) but normal bilirubin at this time.

Figure 1: MRI Abdomen-MP with and without contrast – Initial Evaluation (Day 24)

The liver is markedly abnormal and enlarged with the horizontal dimension of the right lobe reaching almost 18 cm. There are intratumoral lesions throughout the liver, that are nodular. There are large conglomerate areas of indeterminate lesions rather than a large single mass, involving the right and left lobes. This area is difficult to measure precisely but is set at the order of 7.6 x 12.7 x 12.2 cm. There are scattered innumerable other lesions throughout all hepatic segments.

There is a large portal vein involvement with separated irregular margin and left and right lobes segments of the portal vein of abdominal high signal material showing some enhancement. There is a high suspicion that this is very likely a tumor thrombus. Some changes shown are compatible with continuous transformation near the main portal vein where it becomes occluded. There is no evidence of obstruction or thrombosis of the IVC of the right, left or hepatic vein. These veins are in an anteroposterior contact with the tumor and in place are suspected to be encased by tumor. The IVC is compromised and quite narrow but is not occluded. The lesions in question enhance less so than the liver. Tumor enhancement occurs on the laterportals venous phases. There is some atypical phase enhancement in the periphery of the main lesion right lobe.

Hepatocellular carcinoma has a varied extent of metastasis. One example lymph node enlargement, in front of the aorta displacing the vena cava to the left measuring 1.5 x 2.3 x 2.1 cm. The kidneys, adrenal glands, and pancreas appear normal. The splenic is enlarged without focal lesions. The craniodorsal dimension of the spleen measures 14 cm. The gallbladder wall appears thickened and abnormal. There are multiple small peritoneal fluid collections. There appears to be no discernible bilateral diaphragm. There is mild to moderate splenic enlargement and the splenic bed and adjacent to the spleen. No organized fluid collection is evident. There is some bilateral pleural effusion.

Final Impression:

Overall the findings are that of metastasis with evidence of multi nodal. There is evidence of Portal vein tumor thrombus and Hepatic vein pseudo disease. The present aperioptic and sepsis are likely related to portal vein hypertension.

Radiology/Imaging

HCC is a rare diagnosis in the pediatric population. There was 4 weeks delay between the initial presentation seen by PCP and definitive diagnosis in our patient. This case highlights the challenge of the PCP not keeping cancer in their differential diagnosis in children because of its rarity, and rather attributing symptoms and even physical findings to more benign diagnosis such as constipation. In this case, this occurred even at the subspecialist levels (GI and oncology).

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References


