

Hepatoblastoma and Immunohistochemistry (IHC) Indicators

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Background

Hepatoblastoma (HBL) is the most common malignant liver tumor in children. With a high correlation between premature birth and birth weight under 1000g, incidence of HBL has doubled in the last 40 years from 0.8 per 1 million children (1975-1983) to 1.6 per 1 million children (2002-2009) [1,2]. Most are diagnosed in children under 3 years old. Traditional tumor staging criteria as well as pre-treatment extent of disease (PRETEXT) data are used to give a better indication of prognosis [3]. Additionally, use of IHC can provide additional information regarding efficacy of certain treatment therapies and future risks for development of malignancy.

Case Information

History of Present Illness

Now 5-year-old patient presented 6 months prior to surgery with abdominal pain. Parents note new abdominal swelling beginning one-month prior. Also note fatigue and easily tiring, with no other symptoms.

Past Medical History

Still's murmur as an infant

Physical Exam

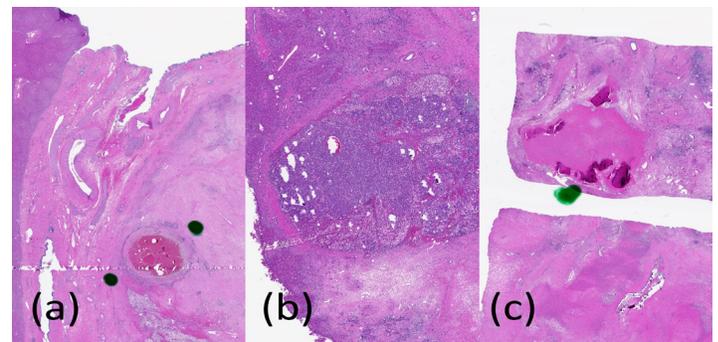
RUQ and RLQ distension, liver extending into pelvic cavity. U/S revealed 18x15x13.5 cm unilocular liver mass involving the right liver (segments V-VIII) with a second unilocular mass described in segment IVb with involvement of the portal vein. α -Feto protein (α FP) at time of exam was >187500 IU/mL.

Images



Photo by Naomi Grimminck, at Children's National Hospital.

Figure 1: Right hepatectomy with mass, gross.



Slide images scanned by Naomi Grimminck and Angela DiPoto, MD at Children's National Hospital.

Figure 2: Micrographs; (a) mass to resection margin with vessel (b) mass to liver capsule with caseous induration (c) mass with bone nodule

Case Information

Gross

A right hepatectomy was performed after chemotherapy treatment, which although mentioned in the patient's history was not further elaborated in the clinical history available. A discrete, partially encapsulated mass was present in liver segments V-VIII measuring 10.5x8x5 cm, and abutting the liver capsule, resection margin, and vascular structures. The cut surfaces of the mass had multifocal areas of hemorrhage and caseous-like necrotic material. No additional lesions were identified in the specimen, and the remaining parenchyma appeared unremarkable. The gallbladder was also removed, which was uninvolved and unremarkable.

Micro

The mass was assessed to be 90% necrotic due to the prior chemotherapy treatment. The cellular type was determined to be a combination of mitotically active fetal epithelial, and embryonal types.

A nodule of bone was also present. Additionally, the vascular resection margin contained an adjacent microscopic focus of tumor with cautery, rendering the resection margin positive for tumor (Figure 2a). IHC was performed for beta-catenin and SALL4, which both were positive.

Implications/Discussion

While premature delivery is unconfirmed, a number of factors indicate poor prognostic outcome. A second lesion was reported by the physician with involvement of the portal vein, but was not received with the surgical specimen. This would indicate that the patient was in PRETEXT III. While the age range is prognostically poor only for PRETEXT group 4, the positive IHC for beta-catenin and SALL4 is associated with poor prognosis. There were determined to be no distant metastases, and true lymphovascular invasion could not be assessed due to post-treatment necrosis. With consideration to the patient's age, two concurrent lesions, reported involvement of the portal vein, and measured α FP levels at time of diagnosis, the patient meets criteria for being in a high risk category by SIOPEL and GPOH classifications, due primarily to the reported involvement of the portal vein. Positive IHC staining of beta-catenin is significant for being present in 80-84% of

HBL cases, and has high association with downregulation of the WNT/beta-catenin cellular differentiation pathways [4]. Overall, at the present time chemotherapy targeting defective beta-catenin receptors are deemed highly effective when the tumor is assessed to have necrosis of >30%. Some studies indicated defective microRNA which appeared causative of the malfunctioning WNT/beta-catenin complexes, and chemotherapies to target these microRNAs are being investigated. However, these studies include small experimental in vivo samples of patient tissue and further research is needed to evaluate efficacy [5]. While the amount of necrosis in this case is promising, these findings are contraindicated by the positive IHC staining for SALL4, which responds poorly to chemotherapies. SALL4 has a high association with all embryonal and 41% of fetal epithelial subtypes, and high expression is strongly associated with poor long term survivorship [6].

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