Hepatic Embryonal Sarcoma

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Definition

Hepatic embryonal sarcoma (HES) is a malignancy classified among soft tissue tumors of uncertain differentiation. It is also known as liver embryonal sarcoma, embryonal sarcoma of the liver, undifferentiated embryonal sarcoma, malignant mesenchymoma of the liver, and mesenchymal sarcoma of the liver.

Epidemiology and Presentation

HES occurs mainly in children (usually between ages of 6 and 10 years, without gender preference), representing 10–15% of pediatric hepatic tumors (in this population it is the third malignancy after hepatoblastoma and hepatocellular carcinoma). Rare cases have been described in adults.

In children, HES has been associated with mesenchymal hamartoma of the liver (→ see dedicated section); some investigators believe that HES might be an evolution of mesenchymal hamartoma (mainly based on cytogenetics similarities).

It typically presents with pain, fever, abdominal mass, and normal serum levels of alpha-fetoprotein (AFP).

Magnetic resonance imaging is helpful in the surgical planning because it may detect vascular invasion, biliary obstruction, and hilar lymphadenopathy.

Pathology

Macroscopically it presents as a solitary, well-demarcated mass (usually 10–30 cm in diameter) with cystic, gelatinous, hemorrhagic, and necrotic foci.

Microscopically the tumor shows a pseudocapsule and is variably cellular with anaplastic, spindled-to-oval cells with prominent PAS-positive diastase-resistant

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hyaline globules and frequent mitotic activity. Multinucleated cells and bizarre cells with hyperchromatic nuclei can often be observed between the sarcomatoid cells. The stroma is variably myxoid, with numerous thin-walled veins. Extramedullary hematopoiesis is common. Areas of myogenic, lipoblastic, or endothelial differentiation can be found (hence the name "mesenchymoma").

Biomarkers

HES cells are characterized by PAS-positive diastase-resistant hyaline globules and often stain positive for vimentin and desmin.

Glypican 3 (GPC3), known to be a diagnostic marker for hepatoblastoma and hepatocellular carcinoma, can be positive in a subset of HES and thus is not a reliable biomarker to differentiate HES from these neoplasms. HES is usually negative for AFP, hepatocyte paraffin 1 (HepPar1), myogenin, CD34, c-Kit (CD117), anaplastic lymphoma kinase 1 (ALK1), cytokeratins, and S100.

Differential diagnosis may be needed with the following: embryonal rhabdomyosarcoma (usually 2–6 years old, myxoid mass extending into bile duct, rhabdomyoblastic differentiation with cytoplasmic cross striations, cambium layer present, no diffuse anaplasia or hyaline globules, myogenin and MyoD1 positive); gastrointestinal stromal tumor (adults, CD117, DOG1, and CD34 positive); hepatoblastoma (cytokeratin and AFP positive); mesenchymal hamartoma (the second most common benign hepatic tumor in the pediatric population after infantile hemangioma, usually <1 year old, cystic, bland tumor cells and no giant cells); sarcomatoid hepatocellular carcinoma (variably positive to cytokeratin); and sclerosing variant of hepatocellular carcinoma (rare in children, has intracellular bile, Mallory-Denk bodies, HepPar1 positive).

Prognosis

HES is an aggressive malignancy. Before the introduction of multimodality approach, the prognosis was dismal, whereas the current 5-year overall survival rate is approximately 80%. Large tumors can undergo rupture and cause (even fatal) hemoperitoneum.

Therapy

Surgery remains the treatment of choice, if feasible. Neoadjuvant chemotherapy is often helpful in initially unresectable cases. In addition, postoperative (adjuvant) chemotherapy and radiation therapy are often reasonable options, particularly in surgical cases with positive margins.

For unresectable, refractory, or recurrent HES, liver transplantation is an option.

Suggested Readings

Chavhan (2019) Rare malignant liver tumors in children. Pediatr Radiol 49(11):1404–1421
Pandit (2019) Undifferentiated embryonal sarcoma of liver in an adult with spontaneous rupture and tumour thrombus in the right atrium. ANZ J Surg 89(9):E396–E397
Perl (2020) Paraneoplastic syndrome in undifferentiated embryonic sarcoma of the liver. EJNMMI Res 10(1):11
Putra (2015) Undifferentiated embryonal sarcoma of the liver: a concise review. Arch Pathol Lab Med 139(2):269–273
Saeed (2017) Primary mesenchymal liver tumors of childhood. Semin Diagn Pathol 34(2):201–207
Shi (2017) Characteristics and outcomes in children with undifferentiated embryonal sarcoma of the liver: a report from the National Cancer Database. Pediatr Blood Cancer 64:4. https://doi.org/10.1002/pbc.26272
Techavichit (2016) Undifferentiated Embryonal Sarcoma of the Liver (UESL): a single-center experience and review of the literature. J Pediatr Hematol Oncol 38(4):261–268