Undifferentiated Embryonal Sarcoma of Liver- A Rare Case Entity

CASE REPORT
An 11-year-old male child presented with complaints of right upper quadrant pain, loss of appetite for the past month, and a high-grade fever for the past three days. The pain had an insidious onset, was gradually progressive, and described as a dull, aching pain without any specific aggravating or relieving factors. The child had a history of blunt abdominal trauma due to a handlebar injury during bicycle riding six months ago. However, there was no subsequent bleeding or swelling, so the child was not hospitalised for treatment at that time. There was no reported history of liver disease, drug allergies, or food allergies.

Laboratory findings have been summarised in [Table/Fig-1]. Serological studies for hepatitis B surface antigen and Hepatitis C virus antibody were negative. Ultrasonography of the abdomen and pelvis revealed hepatomegaly, with the liver measuring 16.2 cm and showing multiple solid and cystic areas. The impression given was a hydatid cyst. Plain X-rays of the chest and abdomen showed normal bilateral lung fields and cardiac shadow. A soft-tissue shadow was noted on the right side of the abdomen, displacing the bowel gas shadow to the left, with no visible calcification; the soft tissue appeared normal. A plain CT scan of the abdomen in the axial section displayed a large hypodense lesion in the right lobe of the liver, measuring 10x9 cm, with calcifications within it and no free fluid, as shown in [Table/Fig-2]. The contrast-enhanced CT scan revealed a heterogeneous lesion measuring 10x9 cm with peripheral enhancement, displacing the portal vein and biliary tract to the left, as depicted in [Table/Fig-3]. The contrast-enhanced CT scan in the coronal section displayed similar findings as in the axial section, with the splenic shadow and bilateral kidney appearing normal, as seen in [Table/Fig-4]. The final impression was a large hepatic space-occupying lesion, and the following differential diagnoses were considered: 1) Embryonal sarcoma of the liver; 2) Hepatoblastoma. The clinical diagnosis was a hepatic hydatid cyst, and the patient underwent the Percutaneous Aspiration, Irrigation and Resepiration (PAIR) procedure.

During the gross examination of the specimen received, multiple grey-brown and grey-white soft-tissue fragments were observed, with the largest measuring 7×4×2 cm and the smallest measuring 2×1×0.5 cm, as shown in [Table/Fig-5]. The external surface

<table>
<thead>
<tr>
<th>S. no</th>
<th>Biochemistry</th>
<th>Units</th>
<th>Patient values</th>
<th>Normal values (in range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Total bilirubin</td>
<td>mg/dL</td>
<td>0.6</td>
<td>(0.1-0.2)</td>
</tr>
<tr>
<td>2.</td>
<td>Direct bilirubin</td>
<td>mg/dL</td>
<td>0.3</td>
<td>Less than 0.3</td>
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<tr>
<td>3.</td>
<td>Aspartate aminotransferase</td>
<td>IU/L</td>
<td>18</td>
<td>(12-35)</td>
</tr>
<tr>
<td>4.</td>
<td>Alanine aminotransferase</td>
<td>IU/L</td>
<td>15</td>
<td>(6-40)</td>
</tr>
<tr>
<td>5.</td>
<td>Gamma-glutamyl transpeptidase</td>
<td>IU/L</td>
<td>60</td>
<td>(0-48)</td>
</tr>
<tr>
<td>6.</td>
<td>Alkaline phosphatase</td>
<td>IU/L</td>
<td>38</td>
<td>(115-359)</td>
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<tr>
<td>7.</td>
<td>Total protein</td>
<td>g/dL</td>
<td>6.5</td>
<td>(6.4-8.3)</td>
</tr>
<tr>
<td>8.</td>
<td>Albumin</td>
<td>g/dL</td>
<td>3.8</td>
<td>(3.8-5.2)</td>
</tr>
<tr>
<td>9.</td>
<td>Alpha-fetoprotein</td>
<td>ng/mL</td>
<td>5</td>
<td>(0-10)</td>
</tr>
</tbody>
</table>

[Table/Fig-1]: Summary of laboratory data.

[Table/Fig-2]: Plain CT abdomen shows a hypodense lesion in right lobe of liver measuring 10x9 cm with calcification within it; no free fluid detected.

[Table/Fig-3]: Contrast-enhanced CT scan revealed a heterogeneous lesion measuring 10×9 cm with peripheral enhancement, displacing the portal vein and biliary tract to the left.

[Table/Fig-4]: The final impression was a large hepatic space-occupying lesion.

[Table/Fig-5]: The external surface
appeared grey-brown and congested, while the cut-surface displayed a variegated appearance with areas of necrosis and haemorrhage. Microscopic examination revealed a malignant neoplasm composed of spindle-shaped and stellate cells, along with pleomorphic multinucleated giant cells arranged in a myxoid stroma. The cells exhibited moderate cyttoplasm and pleomorphic nuclei, with many atypical mitotic figures present, along with extensive areas of haemorrhage and necrosis, as depicted in [Table/Fig-6,7a]. Eosinophilic PAS positive hyaline globules were observed in the cytoplasm of tumour cells, as seen in [Table/Fig-7b]. To confirm the diagnosis, additional sections were taken, and a panel of IHC markers was utilised. Cluster Differentiation 10 (CD10) exhibited strong membranous positivity in 60-70% of tumour cells, as shown in [Table/Fig-8a]. Glypican displayed cytoplasmic positivity in 30-40% of tumour cells, as seen in [Table/Fig-8b]. Desmin showed cytoplasmic positivity in 50-60% of tumour cells, depicted in [Table/Fig-8c]. Ki67 demonstrated strong nuclear positivity in 70-80% of tumour cells, as seen in [Table/Fig-8d]. Vimentin exhibited positivity in 50-60% of tumour cells, as shown in [Table/Fig-8e]. Markers such as Smooth Muscle Actin (SMA),

- [Table/Fig-3]: Contrast enhanced CT scan-Axial section shows a heterogeneous lesion measuring 10x9 cm with peripheral enhancement present, pushing biliary tract.

- [Table/Fig-4]: Contrast enhanced CT scan coronal section shows a hypodense lesion measuring 10x9 cm with calcification in right lobe of liver, spleen and bilateral kidneys appear normal.

- [Table/Fig-5]: Gross specimen showing multiple grey white-grey brown fragments with variegated appearance on cut surface.

- [Table/Fig-6]: Microphotograph showing spindle-shaped cells and stellate cells in myxoid background (H&E, 40x).

- [Table/Fig-7a]: Microphotograph showing extensive areas of haemorrhage and necrosis along with pleomorphic cells and multinucleated giant cells (H&E, 10x).

- [Table/Fig-7b]: Shows PAS positive eosinophilic hyaline globules within tumour cell cytoplasm (PAS, 40x).

- [Table/Fig-8a]: CD10 showed strong membranous positivity in 60-70% of tumour cells.

- [Table/Fig-8b]: Glypican showed cytoplasmic positivity in 30-40% of tumour cells.
**DISCUSSION**

Willis first described the pathology of UESL in 1962 as a rhabdomyoblastic mixed tumour. In 1973, Stanley classified it as a malignant mesenchymoma due to the presence of focal chondroid-appearing cells. In 1978, Stocker and Ishak definitively described the pathology and adopted the term “undifferentiated embryonal sarcoma of the liver” to describe a mesenchymal hepatic tumour without any sign of specific differentiation based on the Armed Forces of Pathology (AFIP) series [1,2]. There were only 26 reported adult cases in the literature from 1977 to 2015, with sarcomas accounting for less than 1% of primary liver tumours and 13% of primary hepatic malignancies. It has non-specific clinical features with varied symptoms ranging from sharp abdominal pain, fever, anorexia, diarrhoea, or a solitary liver cyst, resulting in a diagnostic dilemma [1]. Only 150 to 200 cases were reported in the literature, with an annual incidence of one per million cases. The prognosis is significantly worse in adult patients compared to paediatric cases [3-5].

It is the first case reported in the present Institution. Jaundice is usually absent. Typical ultrasound findings show a large mass with solid and cystic components, mostly mistaken for an abscess or an echinococcal cyst [5]. Usually, there are no abnormal liver function tests, normal alpha fetoprotein levels, non-specific laboratory findings, and no specific serum markers. Increased C-reactive protein, erythrocyte sedimentation rate, and leucocytosis are usually seen in cases of haemorrhage or necrosis in the tumour [3,6]. Metastasis sites include the lung, pleura and peritoneum [6]. UESL is a malignant mesenchymal neoplasm and the third most common type of liver malignancy in the paediatric population, following hepatoblastoma and hepatocellular carcinoma, accounting for 16% of primary hepatic sarcoma [7,8].

Computed tomography usually shows a well-circumscribed huge cystic/solid mass with few internal septations and a dense peripheral rim corresponding to the fibrous pseudocapsule, which is hypodense in the pre-contrast phase and slightly enhanced in the contrast phase. Central foci of high attenuation representing acute haemorrhage may be present. The presence of serpiginous vessels within the tumour has been recently reported in the literature as an important finding for diagnosis [6,9].

The prognosis is generally poor due to delayed diagnosis caused by the lack of initial symptoms, rapid tumour growth and early invasion of adjacent tissue. However, the outcome of treatment has improved with primary surgical resection followed by chemotherapy [9]. Macroscopically, usually large, unencapsulated well-circumscribed tumours are commonly seen in the right lobe of the liver, with an average diameter of 10-30 cm and a variegated appearance: cystic and solid components of grey-white gelatinous areas with or without red and yellow haemorrhagic and necrotic parts [6,9].

Microscopically, UES is composed of primitive, high-grade undifferentiated spindle cells, with numerous mitotic figures and myxoid stroma with varying degrees of spindling and myxoid change. It is histologically heterogeneous with a variable but distinctively sarcomatous appearance [10,11]. The morphology will vary considerably depending on the area of examination. Some areas may appear to be composed of a relatively uniform sheet of undifferentiated cells, while other areas demonstrate wildly pleomorphic anaplastic cells, some with multinucleation and a myxosarcomatous background. Considerable areas of necrosis with abundant mitoses are easily identified. Areas of cystic change can often be seen histologically corresponding to this tumour’s cystic appearance on both gross and radiology.

Despite the presence of a pseudocapsule, cords of normal hepatocytes and bile ducts are commonly entrapped along the
Clinical history

11.5×8.3×6.7 cm

Mesenchymal

immunohistochemistry

Hepatoblastoma

Gastrointestinal

Right hypochondriac pain,

age/Sex
diagnosis

age and sex

CD34, c-KIT, DOG1

M:F=3:2, age

Present case

Clinical features

Myogenin, desmin, Myo-D1

Hepatocellular

immunohistochemistry

CD31, CD34, S100, SMA-negative

Iqbal K et al.,

radiology findings

defined [1], UESL is considered the malignant counterpart of the precise histogenesis and its cell of origin are still to be

losses in chromosomes 14, 9p, and 11p [1,13]. Even though 19q13 [1]. There are gains in chromosomes 1q, 5p, 6q, and

cases harbour recurring chromosomal rearrangements involving mechanism of tumourigenesis has not been identified, MHL

Pathogenesis

Comparative Genomic Hybridisation (CGH) studies suggest a role for chromosomal instability and show that copy number alterations are common in UESL [1]. Although the exact mechanism of tumourigenesis has not been identified, MHL cases harbour recurring chromosomal rearrangements involving 19q13 [1]. There are gains in chromosomes 1q, 5p, 6q, and losses in chromosomes 14, 9p, and 11p [1,13]. Even though the precise histogenesis and its cell of origin are still to be defined [1], UESL is considered the malignant counterpart of mesenchymal hamartoma, so the mesenchymal origin of this tumour is accepted by many authors [2,6]. A translocation of the long arm of chromosome 19 has been reported (19q13.4) [13]. The synchronous or metachronous occurrence of mesenchymal hamartoma and UES suggests they share a common genetic link.

Based on imaging, the differential diagnoses include abscess, mesenchymal hamartoma of the liver, hydatid cyst, cystic degeneration in hepatoblastoma, or hepatocellular carcinoma, and cystic metastasis in adults. Published cases are tabulated in [Table/Fig-10] [1,6,7,12,14]. Various differential diagnoses have been documented in the literature based on the overlapping clinical and histopathological features, so it is important to rule out those tumours [Table/Fig-10].

CONCLUSION(S)

Undifferentiated embryonal sarcoma is a diagnosis of exclusion in paediatric liver tumours. Usually, in imaging, it shows a paradoxical appearance of solid and cystic features on ultrasound and CT scans, which is peculiar due to the high water content of the myxoid stroma. This can lead to confusion with cystic liver lesions. The present case is presented here for its rarity and diagnostic challenge, as the patient was clinically diagnosed and imaged as having a hydatid cyst, which was then curedtted, and the specimen was sent for histopathological examination. It was only discovered to be a malignant neoplasm on microscopic examination by pathologists. A high index of clinical suspicion, along with a panel of immunohistochemical markers, can enable a peroperative frozen section, which can help in the diagnosis and early initiation of treatment.

S. no | Diagnosis | Age and sex | Clinical history | Microscopy | Immunohistochemistry
--- | --- | --- | --- | --- | ---
1. | Hepatoblastoma | M:F=3:2, age 0-19 months | Hepatomegaly elevated alpha-fetoprotein levels with thrombocytosis | Different subtypes resembles various stages of liver development | Beta catenin, glypican 3, Hep par-1 (variable in different subtypes)
2. | Embryonal rhabdomyosarcoma | F>M, age <5 years | Fever, icterus | Small round blue cells underneath cambium | Myogenin, desmin, Myo-D1
3. | Mesenchymal hamartoma | M:F, age <2 years | Enlarged liver mass, respiratory distress | Clustered hepatocytes, lobular growth, elongated branched bile ducts with stromal component | Non contributory
4. | Hepatocellular carcinoma | M:F, history of chronic liver injury, Adults | Abdominal mass mostly in the setting of chronic liver disease | Pleomorphic hepatocytes arranged as thickened trabeculacae | Hep par-1, glypican 3, agrinase, alpha-fetoprotein, CD110, pCEA
5. | Gastrointestinal stromal tumour | M:F, Adults | Intra-abdominal mass | Spindle cells with eosinophilic fibrillary cytoplasm | CD34, c-KIT, DOG1

[Table/Fig-9]: Differential diagnoses [1].

Hep par-1: Hepatocyte paraffin-1; Myo-D1: Myogenic regulatory protein; pCEA: Polyclonal carcinoembryonic antigen; C-kit: A type of receptor tyrosine kinase; DGS1: Discovered on gastrointestinal stromal tumours (a transmembrane protein)

S. no | Articles | Age/Sex | Clinical features | Size and site of lesion | Radiology findings | Immunohistochemistry
--- | --- | --- | --- | --- | --- | ---
1. | Manabe Y et al., 2020 [1] | 50-year-old male | Incidental cystic liver lesion | 5.4x4.6x5.37 cm in liver | Cystic lesion without solid lesion | CD31, CD34, S100, SMA-negative
2. | Gomes F et al., 2021 [8] | Six-year-old female | Recurrent urinary tract infection incidental finding | 8.2x7.3x7.3 cm in right lobe of liver | Complex hypechoic mass with solid isoechoic mass | -
4. | He B et al., 2014 [12] | 9-year-old female | Abdominal pain, fever | 11.5x8.3x6.7 cm | Cystic and solid mass with well-defined border | Caldesmon, CD68, K67, Vimentin-positive; Cytokeratin, Desmin, Myo-D1, SMA, Alpha-fetoprotein-negative
5. | Iqbal K et al., 2008 [14] | 14-year-old boy | Five day history of non specific right hypochondriac pain | 14x15x15 cm in right lobe of liver | Large hypodense mass | Positive for phosphoenolpyruvate carboxykinase, vimentin, alpha 1 antitrypsin . Negative for Ephelial Membrane Antigen (EMA)
6. | Present case | 11-year-old boy | Right hypochondriac pain, loss of appetite and fever | 10x9 cm involving right lobe of liver | Large heterogenous lesion with peripheral enhancement | Positive for CD10, glypican, desmin, vimentin, K67. Negative for SMA, PanCK, BCI-2, myogenin

[Table/Fig-10]: Comparison of published literature with present case [1,6,7,12,14].
REFERENCES


