Acta Scientific Gastrointestinal Disorders (ISSN: 2582-1091)

Volume 6 Issue 9 September 2023

Research Article

Undifferentiated Embryonal Sarcoma of the Liver. Clinical Features and Outcomes in 5 Cases of Pediatric and Adult Patients

Carlos Florez-Zorrilla[1,2]*, Karina Mendoza-Gallo[2,3] and Josue Olivares-Del Moral[1,2]

[1]Hepatopancreatobiliary and Liver Transplant Surgery, Hospital Regional Valentín Gómez Farías-ISSSTE, Zapopan, México

[2]Hepatopancreatobiliary and Liver Transplant Surgery, Centro Médico Puerta de Hierro Andares, Zapópan, México

[3]Department of Pediatrics, Hospital General de Zona 89-IMSS, Guadalajara, México

***Corresponding Author:** Carlos Florez-Zorrilla, Hepatopancreatobiliary and Liver Transplant Surgery, Hospital Regional Valentín Gómez Farías-ISSSTE, Zapopan, México.

Received: July 10, 2023

Published: August 23, 2023

Abstract

Undifferentiated embryonal sarcoma of the liver (UESL) is a very rare and uncommon liver malignancy from primary mesenchymal-derived cells. This malignancy is mostly diagnosed in the childhood and being exceptional in adults over 40 years. 5 cases of UESL were collected from 2016 to 2023, the patients were 9 to 65 years old and included 2 children and 3 adults. Tumor size ranged between 17 to 24 cm in diameter and predominantly showed fibrous pseudocapsule, mixoid matrix, spindle and polygonal cells and scarce eosinophilic cytoplasm. 4 patients underwent surgical resection and 1 was considered for chemotherapy. Although UESL has poor prognosis early diagnosis and complete tumor resection are the most important variables for long term survival.

Keywords: Undifferentiated Embryonal Sarcoma; Liver; Hepatectomy; Pediatric; Adult

Introduction

Undifferentiated embryonal sarcoma of the liver is an extremely rare malignant mesenchymal tumor mostly diagnosed in pediatric population, in adults few cases are reported in literature. These tumors were frequently known as mesenchymoma, rhabdomyosarcoma, fibrosarcoma, embryonal sarcoma or just sarcoma [1]. The first report of a malignant mesenchymoma was done by Donovan in 1946 [1] and the first series of three patients were published by Andersen in 1951 [3], but Stocker and Ishak in 1978 did an extensive review of 31 cases and proposed the term of undifferentiated embryonal sarcoma of the liver (UESL) [1]. Although UESL is a childhood predominant disease it also happens in adults. UESL is the third more common malignant tumor in pediatric population [4] with a peak incidence of age between 6-10 years [5], on the contrary primary liver sarcomas in adults accounts for 0.2% of all primary liver tumors.

We present our experience with 5 cases: 2 children and 3 adults, describing their clinical and immunohistochemical features, treatment and outcomes.

In the last 20 years liver cancer mortality increased about 50% years despite the recent advances in medical technology and new treatments available for hepatitis C-virus (HCV) and hepatocellular carcinoma [4]. In 2000 the mortality rate was 4.16 per 100,000 and

by 2015 mortality rate raised to 5.2 per 100,000. In our experience at three medical centers, two thirds of the patients with liver cancer were related to HCV and the mortality rate was higher in patients over 65 years and in males over 45 years [4,5].

Patients and methods

We collected patients with confirmed pathologic diagnosis of UESL, all of them treated by our group. Patient data included clinical and histological features, management, and outcomes. From January 2016 to January 2023, 5 cases of UESL were retrieved from our records.

Clinical and pathological analysis

Clinical data and diagnostic studies were analyzed from the medical files. Tissue stains and immunohistochemical characteristics were reviewed by the same pathologist.

Outcome analysis

Clinical data were obtained from the medical files. Overall survival (OS) was calculated from the time of diagnosis to the last follow up available or death. Complications were classified according to Clavien-Dindo scale.

Statistical analysis

Survival analysis was calculated using the non-parametric method of Kaplan-Meier (Statistics Kingdom).

Results

We collected 5 patients including 3 females and 2 males, mean age at the time of diagnosis was 32 years (range 9-65 years), 2 patients were children and 3 adults. All the patients showed giant liver tumors (> 10 cm), 3 patients (60%) complained of right upper quadrant (RUQ) pain, 4 patients (80%) presented with right liver location and 1 patient with multifocal tumor (Figure 1).

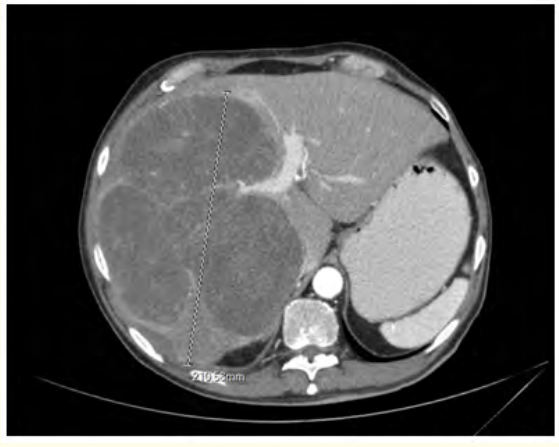

Figure 1: Triphasic CT-scan showing a right liver with a 21 cm-sized hypodense predominant lobulated cystic lesion with peripheral and septal reinforcement.

Immunohistochemistry analysis showed 100% positivity to vimentin, cytokeratin AE1/AE3, CD 10 and α1-antitrypsin. Epithelial membrane antigen (EMA) was 100% positive in the 3 adult patients but none in children, in the same way mean proliferation index Ki-67 were notably higher in adults than in children, 68.3% and 47.5% respectively (Table 1).

	Case 1	Case 2	Case 3	Case 4	Case 5
Age (yr)	9	11	18	57	65
Sex	F	F	F	M	M
Antibody					
Vimentin	+	+	+	+	+
Epithelial Membrane Antigen (EMA)	-	-	+	+	+
Hepar-1	-	-	-	-	-
CK AE1/AE3	+	+	+	+	+
CD 10	+	+	+	+	+
Alpha 1-antitrypsin	+	+	+	+	+
Alpha fetoprotein (AFP)	-	-	-	-	-
Ki-67	40%	45%	60%	75%	70%

Table 1: Immunohistochemical features of undifferentiated liver embryonal sarcoma.

Surgical management were done to 4 patients (80%): Extended right hepatectomy in 3 patients (60%), extended right hepatectomy plus pancreatoduodenectomy in 1 patient (20%) and only liver tumor biopsy in 1 patient (Figure 2). The 4 patients with liver resection (100%) received adjuvant chemotherapy. Perioperative complications were grade II in 2 patients (40%), mean survival was better in children and younger adults than elderly ones; 64.3 and 7 months respectively. (Table 2). The overall survival was 41.4 month and the 5-year survival was 60% (Figure 3).

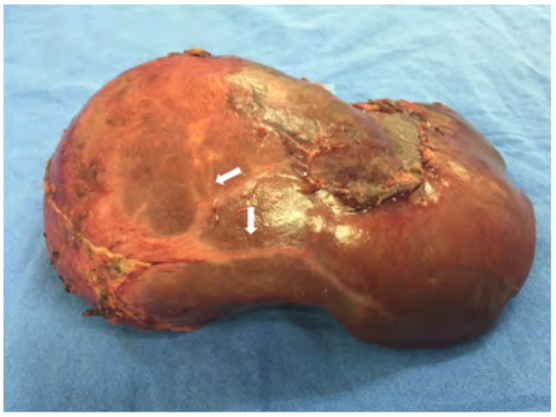

Figure 2: Extended right hepatectomy with fibrous pseudocapsule surrounding liver tumor (white arrows) in a 11 year-old patient.

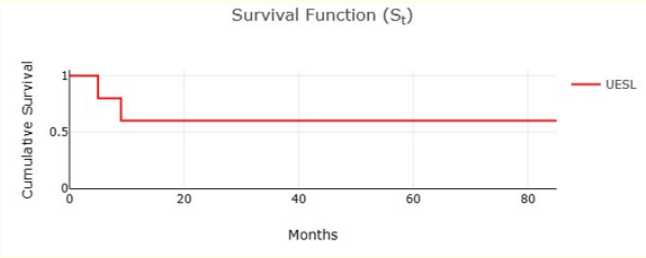

Figure 3: Kaplan-Meier survival analysis.

	Case 1	Case 2	Case 3	Case 4	Case 5
Age (yr)	9	11	18	57	65
Sex	F	F	F	M	M
Location	RL	RL	RL	Multifocal	RL
Signs and symptoms	Liver mass, pain	Liver mass, pain	Liver mass, pain	Liver mass, liver failure	Liver mass, jaundice
Size	17 x 16 x 10	20 x 18 x 17	21 x 18 x 10	24 x 22 x 20	22 x 21 x 22
Surgery	ERH	ERH	ERH	Biopsy	ERH + PD
Complications (Clavien-Dindo)	-	-	-	II	II
Adjuvant chemotherapy	+	+	+	NA	-
Recurrence	-	-	-	NA	+
Alive	+	+	+	-	-
Overall Survival	62	85	46	9	6

Table 2: Clinical characteristics and outcomes.

RL: Right liver; ERH: Extended right hepatectomy; PD: Pancreatoduodenectomy; PO: perioperative; NA: Not applicable

Discussion

Undifferentiated embryonal sarcoma of the liver is the third most frequent pediatric primary malignant tumor of the liver only after hepatoblastoma and hepatocarcinoma [4]. Although it is commonly believed as a children's malignancy, adults can also develop UESL and it is associated with poorer prognosis comparing with child [4-6]. Clinical features in all ages are predominantly abdominal mass and pain, maybe related to the large size of the tumor usually found at the time of diagnosis [7], some other patients may present with nausea, jaundice, and liver failure as in one of our patients. UESL is usually reported in literature as a solitary solid-cystic mass with fibrotic pseudocapsule and extensive areas of necrosis and hemorrhage [8,9], in our series only 1 patient (20%) presented as multifocal disease. Differential diagnosis is mesenchymal hamartoma, liver abscess, hemangioma, hemangioendothelioma, intrahepatic cholangiocarcinoma, hepatocarcinoma, biliary adenoma, angiosarcoma and paraneoplastic syndromes [9-13].

Histologically it has a sarcomatous appearance with spindle and pleomorphic cells, sometimes with giant cells, scarce eosinophilic cytoplasm [3,4]. At immunohistochemistry usually expresses vimentin, cytokeratin, α1-antitrypsin, epithelial membrane antigen, CD 10, CD34, CD 68, actin and desmin, among others [4,8]. In our series, all patients expressed vimentin, CK AE1/AE3, EMA and α1-antitrypsin. Complete surgical resection of the tumor plus adjuvant chemotherapy has demonstrated the best chance of survival and liver transplantation is reserved only in those patients with unresectable disease or recurrence with no extrahepatic spread [5,9,14,15]. Neoadjuvant and adjuvant chemotherapy, radiotherapy and peripheral blood stem cells are also being advocated in some patients [4,15,17].

In most of the literature the survival of UESL is < 35.6% at 5 years, with recurrence and metastatic disease within the first 2 years from surgical resection [6,8], in our series only 1 patient developed recurrence at 6 months and our overall survival (OS) is 41.6 months, but when only pediatric patients are analyzed, the mean OS was 64.3 months.

Primary liver cancer is the fifth most common cancer worldwide [18,19], hepatocarcinoma (HCC) represents around 90% and Mexico is one of the Latin-American countries with the highest mortality due to HCC [18-20]. Other primary liver tumors like UESL are extremely rare in our country to define precisely the clinical features and outcomes, but it seems that UESL in adults have a very poor prognosis compared with children, especially when recurrence and metastatic disease occurs.

Conclusion

Although Mexico is one of the Latin American countries with the highest mortality rate due to hepatocellular carcinoma, epidemiological data on primary liver sarcoma is lacking. Undifferentiated embryonal liver sarcoma is extremely rare even so, our surgical group collected 5 cases in few years. The clinical presentation commonly is abdominal mass and abdominal pain. All our patients showed very large tumors at the time of diagnosis, mostly in the right liver.

It seems that pediatric patients did better in terms of overall survival than adults but maybe it is because an early diagnosis in childhood and the comorbidities usually found in adults. In our experience females are predominant in children and males in adults but this is only an observation in this small series of patients. Although UESL is a malignant disease with poor prognosis, it seems that in pediatric population long term survival can be achieved.

Availability of Data and Materials

Not applicable.

Financial Support and Sponsorship

None.

Conflicts of Interest

All authors declared that there are no conflicts of interest.

Ethical Approval and Consent to Participate

Not applicable

Consent for Publication

Not applicable.

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