

Undifferentiated embryonal sarcoma of liver in an old female: Case report and review of the literature

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Abstract

The clinical characteristics of undifferentiated (embryonal) sarcoma of the liver (UESL) were investigated and the best treatment modalities were recommended. Both histology and immuno-histochemistry demonstrated the cellular features of this peculiar tumor. The tumor size was 12 cm × 9 cm × 8 cm in the right liver lobe. The patient underwent surgical resection of the tumor. The postoperative recovery was uneventful and she died eight months after diagnosis. The tumor showed mixed spindle and polygonal cells within the myxoid matrix. Some tumor cells contained eosinophilic hyaline globules that were positive for resistant diastase. Immunohistochemistry showed positive vimentin. Stellate and spindle cells were positively stained with alpha-1-antichymotrypsin (AACT) and CD68. This case indicates that UESL is not obviously differentiated in old-aged adults.

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Key words: Undifferentiated (embryonal) sarcoma; Old-aged adult; Immunohistochemistry; Liver tumor

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INTRODUCTION

Undifferentiated (embryonal) sarcoma of the liver (UESL), first documented in 1978, is a rare and highly malignant hepatic neoplasm of mesenchymal origin and shows a divergent differentiation^[1,2]. Although UESL is considered a relatively major entity in pediatric liver malignancies, its frequency in the adult population is extremely low. In fact, few reports have focused on the general features of adult cases^[3]. Given that the majority of the populations are under the age of 30 years, adult cases over the age of 40 years are quite exceptional. Furthermore, the detailed pathological characteristics of adult cases based on particular immunohistochemistry are not yet clear. To our knowledge, no study has described the systemic pathology features of UESL. In the present study, we describe a UESL patient at the age of 61 years with no obvious mesenchymal differentiation such as smooth muscle phenotype.

CASE REPORT

A 61-year-old woman was admitted in November 2007 to the Department of Hepatobiliary Surgery because of a huge abdominal mass, located in the right hypochondrium. Her major complaint was abdominal pain. An abdominal ultrasound showed a lesion in the right liver lobe, which was avascular on angiographic examination, and subsequently confirmed by CT scan (Figure 1). However, her serum alpha-fetoprotein (AFP) level was normal. No pulmonary metastases were detected by chest X-ray examination. Medical and family histories were unremarkable, and the patient reported

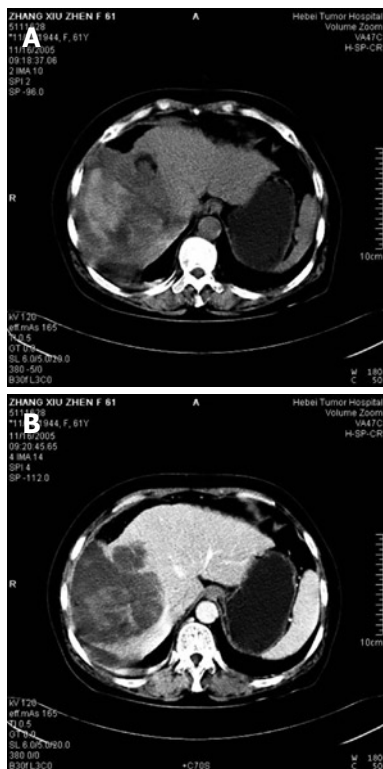


Figure 1 CT scan before surgery showing a large mass (A) and a well-circumscribed and lowly-attenuated mass (B) in the right liver lobe.

no contact with any hepatitis virus carrier. Right hepatic lobectomy and cholecystectomy were performed at a laparotomy. The postoperative period was uneventful, no adjuvant irradiation or chemotherapy was administered. The patient died after 8 mo.

A mass measuring 12 cm × 9 cm × 8 cm was found in the right liver lobe. The tumor was well circumscribed and demarcated from the normal liver tissue. The cut surface revealed a white or yellowish soft mass with massive necrosis, hemorrhage and degeneration.

For light microscopy, fresh tissue was fixed in 10% formalin and embedded in paraffin. The tissue was cut into 4- μ m thick sections which were stained with hematoxylin and eosin and periodic acid-Schiff (PAS) with and without diastase. The histopathological features of the neoplasm are presented in Figures 2 and 3. The primary tumor showed proliferation of atypical spindle cells mixed with stellated cells. These cells had obvious heteromorphism and were irregularly arranged. In some areas, the cells were differentiated into epithelium and had light eosinophilic cytoplasm. Cell membrane was fuzzy (Figure 2A). Some tumor cells contained eosinophilic hyaline globules, which were resistant to diastase and positive for PAS (Figure 2D, Figure 3B). Some ducts lined by a single layer of cuboidal cells resembling normal bile ducts were found in the tumor periphery (Figure 2B and C). Lymphocytes and plasma cells infiltrated around many thin-walled vessels in the background component of the tumor.

Immunohistochemical and alkaline phosphatase staining was performed using a labeled streptavidin biotin system. Primary antibodies such as broad-

Table 1 The immunohistochemical findings

Antibody	Expression
Vimentin	4+
AACT	1+
CD68	2+
Lysozyme	1+
α -sarcomeric actin	-
Myoglobin	-
SMA	-
NSE	-
Factor VIII	-
EMA	-
AE1/AE3	-
AFP	-
HMB-45	-
S-100	-
CD34	-

spectrum vimentin, desmin, alpha-smooth muscle actin (SMA), muscle-specific actin, neuronspecific enolase (NSE), HMB-45, CD68, CD34, factor VIII, epithelial membrane antigen (EMA) and cytokeratins AE1/AE3 (Dako, Kyoto, Japan) were used. Immunostained sections were graded using a sliding scale of 1+ to 4+ according to the percentage of reactive cells (-: negative; 1+: < 10%; 2+: 10%-25%; 3+: > 25%-50%; 4+: > 50%). The immunohistochemical findings are summarized in Table 1. Most tumor cells were strongly reactive with vimentin (Figure 3A). Some stellate and spindle cells showed a granular cytoplasmic positivity for AACT and CD68. Lysozyme, alpha-sarcomeric actin, myoglobin, SMA, NSE, neurofilament, S-100 protein, HMB-45, CD34, factor VIII, EMA, AE1/AE3 and AFP were negatively stained. The tumor was diagnosed as an undifferentiated embryonal sarcoma (malignant mesenchymoma).

DISCUSSION

UESL has a predilection for children and young adults in the first 2 decades of their life. To our knowledge, few cases have been reported in patients over the age of 40 years^[3]. The overall clinical outcome is poor with a long-term disease-free survival rate of less than 30% in all series. In 2 other series, the outcome was better^[4]. In the first series of 9 patients, 4 were alive with no evidence of disease, whereas in the second series, 3 out of 4 patients were alive with no evidence of disease^[4]. In all series, the long-term survival was achieved only in those whose tumors could be resected completely.

According to the literature, the principal pathological features of UESL in children include an expansive intrahepatic growth with massive necrosis, hemorrhage, and occasional gelatinous appearance^[1,2]. Laboratory evaluations including alpha-fetoprotein showed no specific abnormality. Radiologic characteristics of USL are characterized by enhanced peripheral rim, some solid portions at the periphery or adjacent to the septa, and discrepancy in internal architecture between computed tomography (CT) and ultrasound scan^[5].

UESL is histologically surrounded by a fibrous

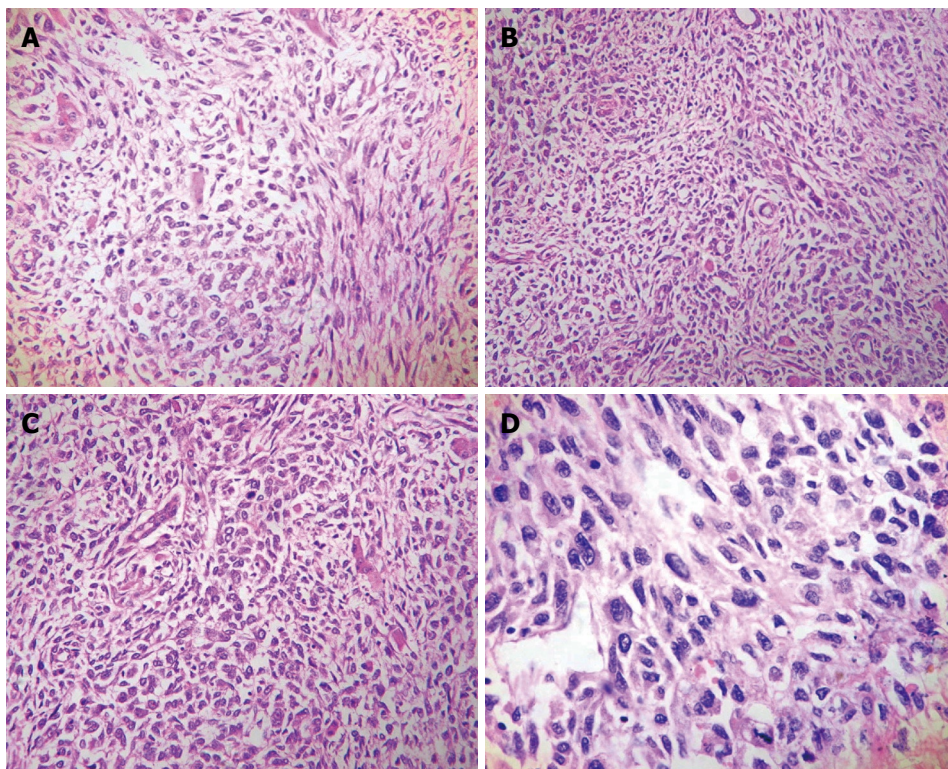


Figure 2 UESL. A: Atypical spindle cells mixed with stellated cells (HE, x 200); B: Normal bile ducts in the tumor (HE, x 200); C: Normal hepatic cells in the tumor (HE, x 200); D: Giant cells containing eosinophilic hyaline globules in the cytoplasm (HE, x 400).

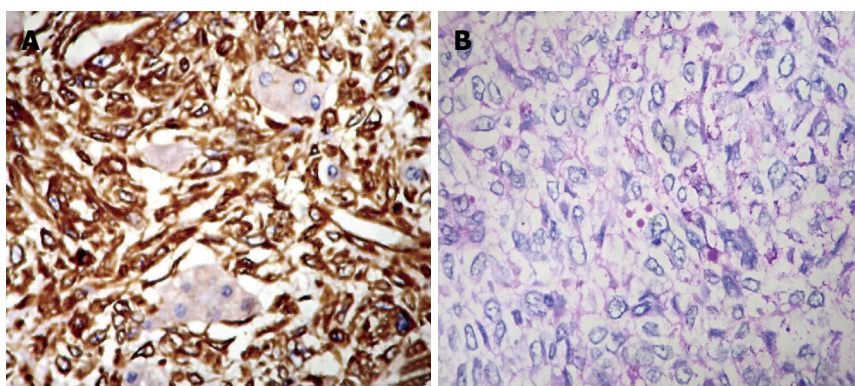


Figure 3 Immunohistochemical expression of UESL. A: Strong reactivity for vimentin in spindle and polygonal or round cells (streptavidin-biotin method, x 200); B: Tumor cells containing eosinophilic hyaline globules with positive PAS.

pseudocapsule with a slightly direct invasion of the adjacent hepatic parenchyma. The cellular component is composed of medium-large spindle or satellite cells with marked nuclear pleomorphism. At the periphery, trapped hepatocytes and abnormal bile duct cells are apparent^[6]. In addition, there are prominent eosinophilic, PAS-positive, and diastase-resistant globules in the cytoplasm of tumor cells^[1,7]. Generally, immunohistochemistry using various cell-specific markers reveals that UESL is highly positive for histiocytic markers such as AACT and CD68, and vimentin is commonly positive. A few case reports demonstrate that tumor cells are reactive to cytokeratin, S-100 protein, and NSE^[1,7,8-11]. In our case, both vimentin and histiocytic markers were positive, whereas cytokeratins, S-100 protein, and NSE were negative. In some cases, the smooth muscle differentiation was confirmed by the positivity of desmin and alpha-SMA. However, our case did not exhibit any myogenic features. The differential diagnosis of UESL in old-aged adults includes malignant fibrous histiocytoma (MFH), leiomyosarcoma, liposarcoma,

and angiomyolipoma (AML). MFH is characterized by fibroblastic, histiocytic, and pleomorphic tumor cells forming a storiform pattern. In the present study, the tumor was basically composed of primitive mesenchymal cells with a divergent differentiation toward fibroblastic, histiocytic lines. Although these cellular compositions are quite similar to those of MFH^[7,12], it is possible to distinguish UESL from MFH on the basis of tissue pattern^[13]. In our case, the diagnosis of leiomyosarcoma was inappropriate, because the tumor did not show any variable size of the foci and any fascicular pattern of the brightly eosinophilic spindle cells in hematoxylin, and SMA was negative. Lipoblastic differentiation has been suggested by some investigators on the basis of oil red O staining, and cells resembling lipoblasts seen at light microscopy^[14]. However, no multivacuolated lipoblasts were observed in our case under light microscope, and the tumor cells were negative for S-100 protein. AML is characteristically composed of a varying heterogeneous mixture of 3 tissue components: blood vessels, smooth muscle cells, and adipose cells. However, the proportions

of the 3 tissue components vary markedly from case to case and from area to area within the same tumor^[15]. AML with spindle cells and pleomorphic features may be misdiagnosed as various sarcomas, including MFH, leiomyosarcoma, dedifferentiated liposarcoma, and undifferentiated sarcoma^[16-20]. Recent studies indicate that HMB-45 is a promising marker for AML and can facilitate differentiation of this tumor from other lesions^[20-22]. In our case, the tumor cells were negative for HMB-45. Whenever pathologists encounter spindle cell tumors in the liver, immunostaining with HMB-45 should be performed to distinguish AML from other neoplasms.

The prognosis of UESL is poor. Even after complete resection of the tumor, few UESL patients can achieve a long-term, disease-free survival. Our patient died 8 mo after the tumor resection. Since 1990, long-term survivors after multiagent chemotherapy have been reported and their outcome appears to have improved substantially over the last decades^[23,24]. The chance of cure depends on radical resection and vigorous multiple approaches including chemotherapy^[23,24]. We hold that multiagent chemotherapy after resection can significantly improve the survival and the identified pathologic changes may offer important clues to the pathogenesis and development of UESL and other pediatric mesenchymal tumors.

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