case report

Undifferentiated sarcoma of the liver: a rare pediatric tumor

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Ann Saudi Med 2012; 32(2): 203-205

DOI: 10.5144/0256-4947.2012.203

Undifferentiated embryonal sarcoma of the liver (UESL) is an uncommon hepatic tumor of mesenchymal origin recognized as a unique clinicopathologic entity since 1978. UESL has historically been considered an aggressive neoplasm with an unfavorable prognosis. Survival has improved using recent multimodal approaches, designed for patients with soft tissue sarcomas at other sites. Several small series have reported survival of up to 70% of children. We report a case of a 12-year-old boy from the United Arab Emirates who relapsed after complete surgical resection and was then successfully treated with re-resection followed by chemotherapy and radiotherapy. With a follow-up of 5 years, he is well and asymptomatic, and is leading a healthy life. This case emphasizes the fact that these poorly prognostic tumors may benefit from post-surgery chemotherapy. This case illustrates the improved survival of UESL patients following the multimodality therapy with a relatively long follow-up. This is the first case of UESL reported in this region of the world.

Primary neoplasms of the liver are rare during childhood, accounting for 0.5% to 2% of all tumors in the pediatric age group, and are mostly represented by epithelial malignancies such as hepatoblastoma and hepatocellular carcinoma.[1] Undifferentiated embryonal sarcoma (UESL) is a rare malignant hepatic neoplasm of mesenchymal origin, first described by Stocker and Ishak in 1978, that accounts for 9% to 13% of pediatric hepatic tumors in various series.[2,3] In the past, this tumor was described as embryonal sarcoma, mesenchymoma, primary sarcoma, fibromyxosarcoma, or malignant mesenchymoma.[2-4] UESL occurs mainly between 5 and 10 years of age, without gender predilection.[1,4] Clinical presentation is typically an abdominal mass, which may be accompanied by pain and, in some cases, by systemic symptoms such as fever, weight loss, or vomiting.[1,2] Malignant mesenchymal elements without any evidence of specific differentiation are observed on histology.[2-4] Evidence from previous reports revealed UESL to be an aggressive neoplasm,[5,6] but more recently, there have been long-term survivors after complete surgical excision with or without postoperative chemotherapy.[1,7,8]

CASE

We report a case of a 12-year-old boy who presented with a 6-month history of increasing right upper quadrant pain and fullness. Examination confirmed a nontender palpable epigastric mass. The child otherwise appeared well. His hemoglobin level was 12 mg/dL; bilirubin, 7 μmol/L; alkaline phosphatase, 201 U/L (normal range, 35-115 U/L); lactate dehydrogenase, 274 U/L (normal range, 120-250 U/L); aspartate aminotransferase, 31 U/L (normal range, 0-30 U/L); gamma-glutamyl transferase 40 U/L (normal range, 0-60 U/L); and α-fetoprotein, 5.0 μg/L (normal, 0-9.0 μg/L). The ultrasonography provided abdominal results showing a cystic lesion, and the computed tomographic (CT) scan confirmed the presence of a 5-cm cystic lesion in liver segments 6 and 7, for which a wide excision with clear surgical margins was done. Undifferentiated sarcoma was histologically diagnosed without any further treatment. However, 8 months later, the follow-up magnetic resonance imaging (MRI) showed a radiological recurrence measuring 5×6 cm, for which the patient underwent a second radical excision with clear surgical margins.

Histopathology confirmed the same diagnosis, an undifferentiated sarcoma (**Figure 1**). Thereafter, the treatment of the patient was started with an adjuvant sarcoma-like multiagent chemotherapy consisting of vincristine, actinomycin, and cyclophosphamide every 3 weeks along with vincristine weekly for 9 doses, a proposed total treatment of 4 such cycles over 45 weeks. After 25 weeks of chemotherapy, a follow-up MRI revealed an increased T2 single uptake in the tumor bed, suggesting a strong possibility of residual disease. The patient was referred for adjuvant radiotherapy, and received 40 Gy radiation in 20 fractions to the tumor bed in the right liver lobe, with a 2-cm margin to cover the possible microscopic extension, following which he completed chemotherapy as mentioned. With a follow-up of 5 years off therapy, he was well and asymptomatic, and in remission as evidenced by the follow-up CT scan (**Figure 2**).

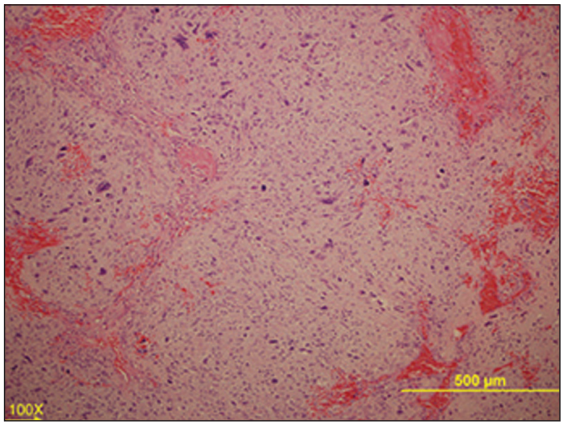

Figure 1. Histopathologic features of undifferentiated sarcoma of the liver (100×).

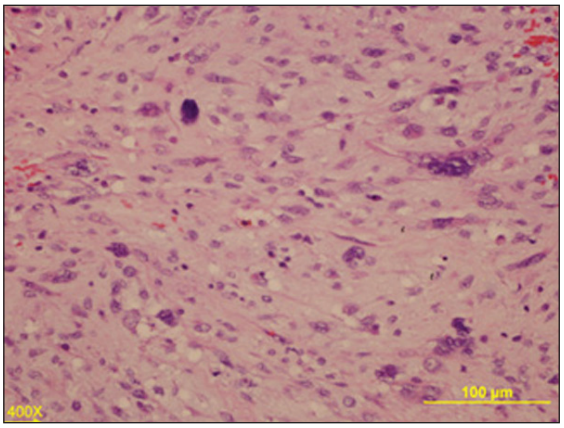

Figure 2. Undifferentiated sarcoma of the liver with a large amount of multinucleated large tumor cells of giant cell type (400×).

DISCUSSION

Various terms such as malignant mesenchymoma, embryonal sarcoma, and fibromyosarcoma were unified under the term UESL after Stocker and Ishak published a series of 31 cases in 1978.[2] The peculiar age of the children, a normal level of α-fetoprotein, and the radiological appearance of the tumor should alert the clinician to consider UESL in the differential diagnosis of a liver mass.[1] Histological studies are mandatory to distinguish UESL from other hepatic malignancies of mesenchymal origin, such as rhabdomyosarcoma, leiomyosarcoma, and fibrosarcomas, but differential diagnosis may be difficult because of some overlapping features (e.g., focal rhabdomyoblastic differentiation in UESL).[1-4] In the original report published by Stocker and Ishak, the majority of patients died within 12 months of the diagnosis and resection of the tumor. Despite the use of radiotherapy and/or chemotherapy, only 6 of the 31 patients reported were alive with no evidence of disease.[2] Since then, the prognosis of UESL has generally been considered poor.[1,3] According to a more recent published reports review spanning from 1950 to 1988, by Leuschner et al, only 37% of the patients were reported to be alive.[4] In previous studies, the treatment was reported to be based mainly on tumor resection, with radiotherapy and chemotherapy used only occasionally. Despite its reported poor prognosis, UESL appears to be a chemo-sensitive tumor. The outcome of patients in whom radical resection is not possible is dismal,[6,9] and no evidence is available that chemotherapy alone or in combination with radiotherapy can cure these patients. A few reports confirm that patients can be cured with surgery alone,[7] but most studies report disappointing results.[9] It appears that the best chance of cure is to achieve complete surgical resection; however, recurrences suffered by patients after apparently complete resections support the need for a more systemic approach for treating these tumors.[10,11] It is only in the late 1980s that the first evidence of long-term survival after multiagent chemotherapy was reported.[10,11] Prognosis of UESL has improved over time.[1] Other than the progress in supportive therapy and diagnostic tools in recent years, we believe this improvement is also because of the better use of a defined multimodal treatment including surgery and effective sarcoma-like multi-agent chemotherapy. Several small series have reported survival of up to 70% of children because of these techniques.[1,12,13] As seen in our report, aggressive surgery is mandatory but not enough, and it should be followed by chemotherapy.[1,5,8] If radical resection is anticipated to be difficult at diagnosis, in our opinion a

more definite surgery should be planned after an initial course of chemotherapy. Our case also opens the door for further studies looking at adding radiotherapy as an additional treatment modality, especially if there is a question of positive margins or recurrence. In only a few studies has the use of radiotherapy been reported.[1,6] Therefore, the role of irradiation is still unknown in undifferentiated sarcoma of the liver.

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