CASE REPORT

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Undifferentiated embryonal sarcoma of the liver in an adult patient: Case report

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Undifferentiated embryonal sarcoma of the liver is a rare and aggressive tumor in adults, with an unfavorable prognosis. We present a 33-year-old female patient who was admitted with fatigue, weight loss and right upper abdominal pain. Magnetic resonance imaging of the liver revealed a bulky malignant mass with necrotic and cystic center, which nearly occupied the left lobe and invaded the middle-left hepatic vein and left portal vein. The patient was evaluated as inoperable, and in order to determine the histologic diagnosis, a Tru-cut biopsy was performed. Both histopathologic features and the immunocytochemical stainings revealed the diagnosis of hepatic embryonal sarcoma. Since the patient had no chance of surgery due to the advanced stage of the tumor and progressive hepatic failure, a combination chemotherapy was applied. Unfortunately, the patient did not respond to treatment at all and died in the second post-therapy week. Undifferentiated embryonal sarcoma of the liver is a highly chemo-sensitive tumor. Radical resection may be possible after combination chemotherapy in the childhood period, but since the disease is extremely rare in adults, an optimal treatment approach is still unknown.

Key words: Embryonal sarcoma, hepatic neoplasm, mesenchymal origin

Erişkin hastada karaciğerin diferansiye olmamış embriyonel sarkomu: Olgu sunumu

Karaciğerin diferansiye olmamış embriyoner sarkomu, erişkinlerde nadir görülen ve kötü prognozla seyreden agresif bir tümördür. Bu vaka ile halsizlik, kilo kaybı ve sağ üst kadran ağrısı şikayetleriyle hastane yatırılan bir hastayı sunmaktayız. Karaciğerin manyetik rezonans görüntülemesinde sol portal ve orta-sol hepatik venleri tutan, karaciğerin sol lobunu tama yakın kaplayan merkezi kistik ve nekrotik, büyük habis bir kitle saptanmıştır. Bu bulgularla hasta ameliyat edilemeyeceğinden histolojik tanıyı koyabilmek için hastaya biyopsi yapılmıştır. Hem histopatolojik bulgulara hem de immünositokimyasal boyanmaya dayanarak hastaya embriyonel sarkom tanısı konmuştur. Hastanın cerrahi şansı olmamasından ve karaciğer yetmezliğinin ilerlemiş olmasından yalnız kombinasyon kemoterapisi uygulanabilmiştir. Fakat hasta tedaviye cevap vermemiş ve tedaviyi takip eden ikinci haftada exitus olmuştur. Karaciğerin embriyoner sarkomu kemoterapiye duyarlı bir tümördür ve çocuklarda kombinasyon kemoterapisi sonrası radikal rezeksiyon mümkün olabilmektedir. Fakat erişkinlerde nadir görünmesi nedeniyle ideal bir tedavi yaklaşımı henüz bilinmemektedir.

Anahtar kelimeler: Embriyoner sarkom, karaciğer kanseri, mezenkimal orijin

INTRODUCTION

Undifferentiated embryonal sarcoma (UES) of the liver is a rare, highly malignant hepatic neoplasm of mesenchymal origin, which is almost exclusively seen in the pediatric population (1). Its frequency in the adult population is extremely rare, affecting mostly adults under the age of 30 years. Although the disease has a poor prognosis, recent trials have shown that long-term survival may be achieved in patients who have the opportunity for complete resection plus adjuvant chemotherapy (2). Therefore, UES is a chemosensitive and potentially treatable tumor.

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Owing to its rarity in adults, it may sometimes be difficult to keep this disease in mind as a differential diagnosis of a hepatic tumor. Here, we report our experience of treating a female patient with UES of the liver.

CASE REPORT

A 33-year-old female was admitted to a government hospital in February 2010 with fatigue, weight loss and right upper abdominal pain. The physical examination revealed abdominal tenderness and giant hepatomegaly. She had no comorbidities. During admission, her blood pressure was 130/90 mmHg and heart rate was 96/min. No pathologic finding was detected in the cardiopulmonary examination. A huge, tender and smooth-faced liver was palpable from right side of the abdomen towards the midepigastric region. At the time of diagnosis, laboratory data showed normal liver function tests, normal tumor markers including carcinoembryonic antigen (CEA), carbohydrate antigen (CA)125, CA19-9, and alpha-fetoprotein (AFP) and negative hepatitis markers.

Abdominal ultrasound (US) demonstrated a large solid mass with heterogeneous inner aspect located in the left segment of the liver. Gallbladder and intra- and extrahepatic biliary tracts were all normal. Minimal perihepatic and intraperitoneal ascites collection was observed. For further evaluation, a dynamic contrast magnetic resonance imaging (MRI) was performed, which showed a gross (12 x 8 cm), hypervascular lesion with diffuse infiltrating character and not well-defined borders (Figure 1). This lesion showed low signal intensity on T2-weighted images and high congestion in the arterial phase. Both middle-left hepatic vein and left portal vein were invaded by the lesion. Contiguous to this lesion, there were also satellite nodules with hypervascular appearance.

The differential diagnosis by MRI findings was hepatocellular carcinoma, cholangiocarcinoma or neuroendocrine tumor metastasis. For the possibility of metastasis, the patient underwent both colonoscopy and gastroscopy. No abnormality was seen in these endoscopic evaluations. US of bilateral breasts was also normal.

An urgent biopsy of the liver was performed. Histological examination showed the tumor was composed of atypical spindle cells mixed with anaplastic giant cells (Figure 2). A myxoid background and rare mitotic figures were observed in the tumor. No necrosis or hemorrhage was observed. Immunocytochemically, the tumor cells were positive for cytokeratin (Figure 3), vimentin (Figure 4), S-100 (Figure 5), and alpha 1-antitrypsin (Figure 6) and negative for desmin, CD34, CD117 (c-kit), ALK-1, HMB45, and HepPar1. The tumor was diagnosed as undifferentiated (embryonal) sarcoma of the liver.

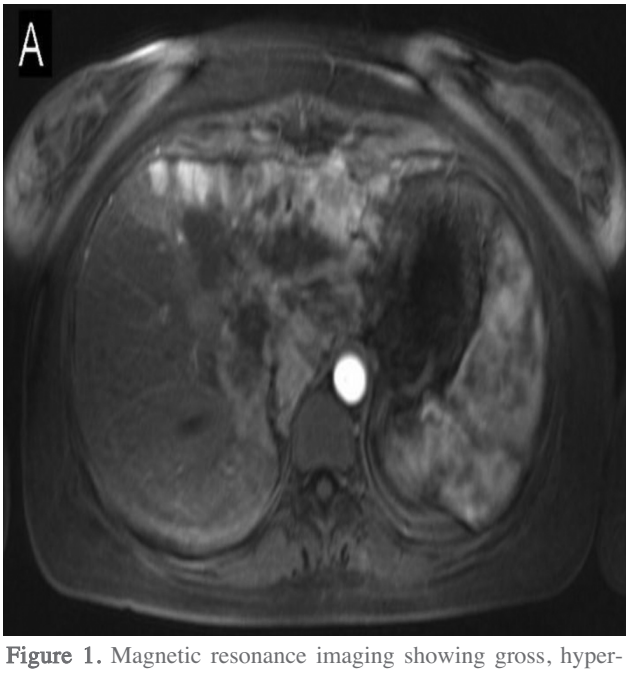

Figure 1. Magnetic resonance imaging showing gross, hypervascular lesion with diffuse infiltrating character and not well-defined borders.

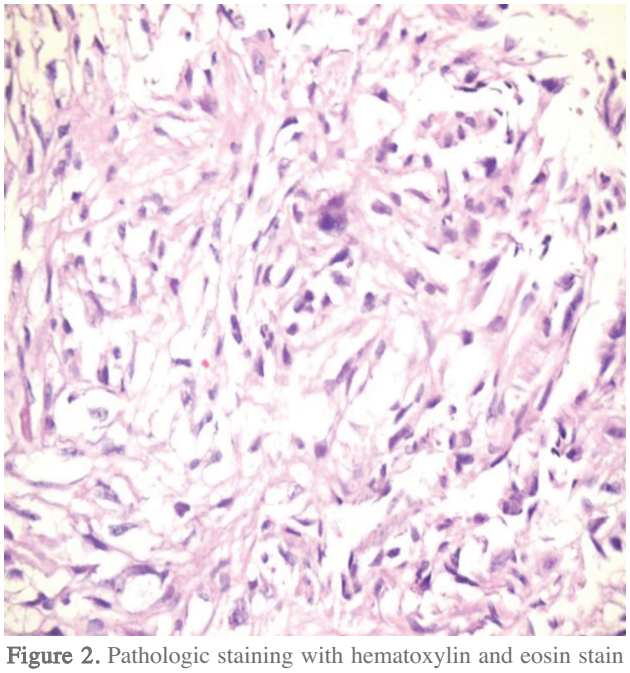

Figure 2. Pathologic staining with hematoxylin and eosin stain (x400), imaging atypical spindle cells mixed with anaplastic giant cells found in the embryonal sarcoma.

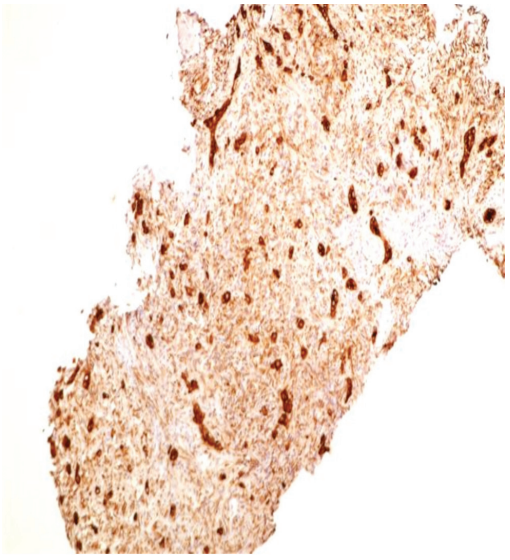

Figure 3. Immunohistochemical staining of tumor cells with cytokeratin (x100).

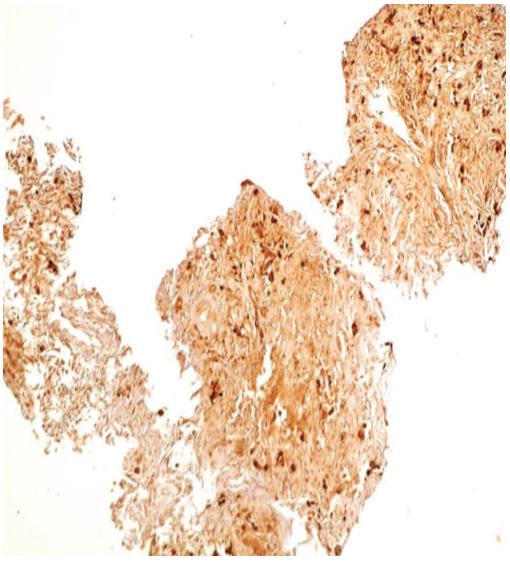

Figure 5. Immunohistochemical staining of tumor cells with S-100 (x40).

Figure 4. Immunohistochemical staining of tumor cells with vimentin (x100).

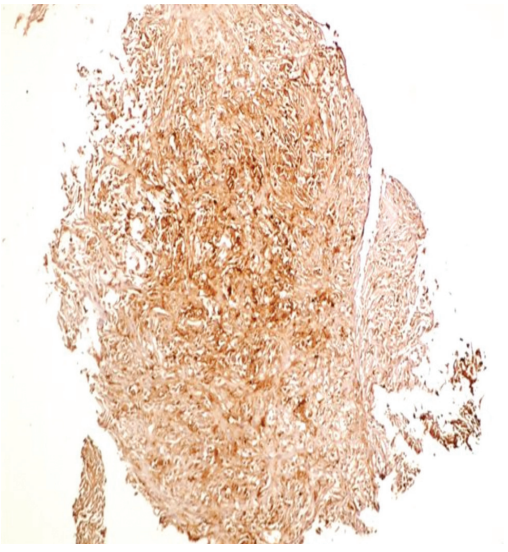

Figure 6. Immunohistochemical staining of tumor cells with alpha 1-antitrypsin (x40).

Since the lesion was too large and invaded large vessels, it was accepted as inoperable by the hepatic surgeons. As the differential diagnosis of UES is very rare in this age group, the pathologists worked intensely on the biopsy by applying a wide range of different dyes to the specimens. Unfortunately, the patient developed jaundice within this 10-day period. Considering progressive hepatic failure and chemo-responsiveness of the histological type of the tumor, we decided to apply chemotherapy to the patient promptly. She was treated with chemotherapy including vincristine at 1.4 mg/m^2, doxorubicin at 75 mg/m^2 and cyclophosphamide at 1400 mg/m^2. Nevertheless, during the follow-up, the patient's hepatic functions worsened and she died within the second post-therapy week.

DISCUSSION

Undifferentiated embryonal sarcoma (UES) of the liver is a typical pediatric neoplasm with a decline in incidence after 10 years of age, and it has been diagnosed rarely over the age of 30 years (2). Malignant mesenchymal tumors of the liver are the fourth most common malignant hepatic tumors in

children (3). However, in contrast, about 50 cases of hepatic UES in adults have been reported in the literature. Owing to its rarity in adults, the differential diagnosis of this mesenchymal tumor from hepatocellular carcinoma and other hepatic neoplasms is troublesome.

In the cases of UES, clinical symptoms are not pathognomonic. Various nonspecific tumor-related symptoms such as abdominal pain, nausea, vomiting, weight loss, fatigue, and jaundice are found in the majority of the tumors, just as in our patient (4). Occasionally, as it is a rapidly growing tumor, intraperitoneal rupture and hemorrhage can be seen (5). In general, no elevation in tumor markers is observed, but in a small proportion of the cases, elevation in AFP is exceptional (2,6).

Tumor size often exceeds 10 cm in greatest dimension when it becomes symptomatic. It is usually not hard to detect the tumor using different imaging modalities (3,7). However, MRI defines the lesion more accurately than the others, with better resectability information, as it gives more details about the vascular, biliary and hilar lymphous structures (2,3,8).

The ultimate diagnosis of hepatic UES depends on liver biopsy evaluated by an experienced pathologist. Under the microscope, the tumor cells have ill-defined borders and are either stellate, oval or spindle-shaped, with marked nuclear pleomorphism (3). They may be compactly or loosely arranged and embedded in a myxoid stroma that contains many thin-walled veins. The peripheral areas of the tumor are composed of abnormal bile ducts, multinucleated giant cells and trapped hepatocytes (1,9). Although immunocytochemical staining is not specific for UES, it may be helpful to distinguish this type of sarcoma from other malignancies of the liver (10). Variable immunoreactivity with antibodies to desmin, vimentin, cytokeratin, alpha 1-antitrypsin, muscle-specific actin, alpha 1-antichymotrypsin, S-100, and CD34 has been reported. In our case, the biopsy specimen was positive for cytokeratin, vimentin, S-100, and alpha 1-antitrypsin (1,2,9).

Undifferentiated embryonal sarcoma (UES) is an aggressive type of tumor with recurrences even after complete resection. Radical resection of the tumor should be done if possible (11,12). In addition, recent data have shown that adjuvant chemotherapy and/or radiotherapy in addition to surgery should be performed to improve patient survival (2,13). A neoadjuvant treatment approach may be an option for the patients with initial unresectable tumors (2,14). Although most of the patients were treated by adjuvant chemotherapy, the role of neoadjuvant treatment is being evaluated, and may become an option for treating UES patients, especially when they have been diagnosed preoperatively. This approach is supported by the pediatric oncologists as a result of their experiences in treating children with UES of the liver (15).

Combination chemotherapy regimens may be effective, including cisplatin with cyclophosphamide or ifosfamide, doxorubicin or actinomycin D and/or vincristine (2). Different combination schedules have been tried for the treatment of UES. Radiotherapy is used rarely and is preferred only for incomplete resection or inoperable lesions. Multidisciplinary treatment seemed to provide superior local control and better clinical outcome (1,3). If there is any evidence of recurrence in the upper abdomen, radical excision of the tumor, whenever feasible, should be considered (2,10).

In our case, the patient had no chance of surgery due to the advanced stage of the tumor and high bilirubin levels. Therefore, there was no option for the treatment except chemotherapy. Unfortunately, the chemotherapy did not work in our patient, and she died within the second post-therapy week.

In conclusion, the optimal therapy of UES of the liver is still under debate. However, we know exactly that it is a chemo-sensitive tumor and that radical surgery should be combined with multiagent chemotherapy either as an adjuvant or neoadjuvant approach. It is important to implement the differential diagnosis of this mesenchymal tumor in time and accurately, keeping this rare entity in mind in case of hepatic masses, regardless of the patient's age.

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