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Treatment of undifferentiated embryonal sarcoma of the liver in children—single center experience

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Abstract

Background: Undifferentiated embryonal sarcoma of the liver (UESL) represents less than 5% of all malignant hepatic tumors in childhood. It is considered an aggressive neoplasm with an unfavorable prognosis. The aim of this paper is to present a single center experience in the treatment of children with UESL.

Materials and methods: Ten children with UESL were treated between 1981 and 2012. Age at diagnosis ranged from 4 months to 17 years (median age, 6 years and 9 months). Surgery after neoadjuvant chemotherapy (CHT) was performed in 7 patients, and in 3 patients primary surgery was done. Adjuvant chemotherapy was administered in all 10 patients (CYVADIC, CAV, CAV/ETIF/IF + ADM, CDDP/PLADO). Right hemihepatectomy was performed in 1 patient, extended right hemihepatectomy in 6, and partial resection of the right lobe (segments V-VI, segment V) in 2 patients. One patient with unresectable tumor affecting both lobes was listed for liver transplantation (LTx).

Results: Follow-up from diagnosis ranged from 50 to 222 months (mean 138 months). Among 9 patients treated with partial liver resection, distant metastases/local recurrence was not observed in any, and disease-free survival in this group is 100% (9 patients alive). The patient that underwent liver transplantation died of multiorgan failure 4 months postoperatively.

However, this patient was misdiagnosed as having hepatoblastoma (HBL) and received PLADO chemotherapy. The overall survival rate is 90%.

Conclusion: Excellent results with long-term survival can be achieved in children with UESL with conventional therapy, including a combination of neoadjuvant and adjuvant chemotherapy and surgery, even in large extensively growing tumors.

Undifferentiated embryonal sarcoma of the liver (UESL) is a rare mesenchymal tumor that typically presents in late childhood. UESL constitutes less than 5% of all childhood

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malignant hepatic tumors. The peak age at presentation is between 6 and 10 years of life. However, it can present in younger patients as well as in adults [1,2]. UESL was described first by Stocker and Ishak in 1978 and then by Horowitz as a malignant tumor with a very unfavorable prognosis and high mortality rate [1,3–5]. Since the introduction of chemotherapy in an neoadjuvant or post surgical, adjuvant setting UESL has become a highly curable disease [4,6].

The aim of our paper is to present a single center experience in the treatment of children with UESL.

1. Materials and methods

During last 30 years 103 children with malignant liver tumors were treated in our department. There were 65 children with hepatoblastoma, 26 with hepatocellular carcinoma, 1 patient with angiosarcoma, 1 child with intrahepatic cholangiocarcinoma and 10 children diagnosed with UESL (10%).

Of the 10 children with undifferentiated sarcoma 8 were boys. The patient's age ranged from 4 months to 17 years (median age, 6 years and 9 months). Table 1 presents the patients characteristics.

Retrospective analysis included: clinical symptoms, tumor location and extension, chemotherapy details, response to chemotherapy using RECIST criteria (Response Evaluation Criteria In Solid Tumors), surgical treatment, histological tumor response to chemotherapy and final outcome.

All pathology slides were reviewed to confirm the diagnosis.

2. Results

2.1. Symptoms and diagnosis

All patients presented with abdominal pain, 8 with a palpable liver mass, 2 with persistent fever and 2 with significant weight loss. In one patient, an elevated serum AFP (alpha-protein) level was observed on diagnostic workup – 3410 IU/ml (N < 5 IU/ml).

The tumor was limited to the right lobe in 8 patients and in 2 it extended to the left lobe. The tumor diameter ranged from 4.5 to 21 cm, with a median size 11 cm. None of the patients had extra-hepatic involvement.

In 7 patients the diagnosis was based on histological examination from diagnostic biopsy (surgical in 2 and needle biopsy in 5 patients). In the remaining 3 children pathomorphologic diagnosis was made from the tumor specimen after primary resection.

2.2. Treatment

Treatment consisted of surgery followed by chemotherapy in 3 patients and neodjuvant chemotherapy followed by tumor resection and postoperative chemotherapy in 7.

Primary right extended hemihepatectomy was performed in 2 and partial right lobe resection in 1 patient (segment V). Neoadjuvant chemotherapy was administered in 7 patients. In 4 it was CAV/ETIF/IF + ADM and in 2 CYVADIC protocol.

Six patients had a partial response (PR) to chemotherapy. One patient received PLADO chemotherapy because she was misdiagnosed as having hepatoblastoma. Progressive disease was observed after initial chemotherapy in this patient.

Delayed surgery was performed in 7 patients. In 1 patient right hemihepatectomy was performed, 4 had extended right hemihepatectomy and 1 patient had partial resection of right lobe (segments V–VI). Hepatectomy and liver transplantation were performed in 1 patient with bilobar involvement.

Histopathology of the resected tumors revealed total necrosis (no viable tumor cells) in 1 patient and partially necrotic tumors in 5. In the patient misdiagnosed as HBL foci of necrosis in the explanted liver were noted. Resections were microscopically tumor free at the margins in all 10 patients. All patients received adjuvant chemotherapy (Table 1).

The misdiagnosis of hepatoblastoma in one of our patients was based on pathological examination from a tumor biopsy performed in another center and elevated serum AFP levels. She had an unresectable, bilobar tumor that did not respond to preoperative chemotherapy consisting of two courses of cisplatin and doxorubicin. The child was listed for liver transplantation as an unresectable HBL. The histological examination of explanted liver again was interpreted by pathologist as HBL and patient received adjuvant chemotherapy according to a SIOPEL protocol. Four months after transplantation the patient presented with mediastinal tumor. Biopsy of the tumor was performed and UESL diagnosed. All biopsy specimens were re-reviewed and acknowledged as a misdiagnosis.

Nine children are alive and disease free with follow up from 50 to 222 months (mean 138 months). The only death occurred in the patient with misdiagnosis of HBL. This girl died of disease progression 8 months from diagnosis and 4 months after liver transplantation.

3. Discussion

Undifferentiated embryonal sarcoma of liver (UESL) is a rare mesenchymal tumor. Numerous cases have been described in the literature but there are only few reports on larger series of patients with this entity [1–7]. Epidemiological data from various studies indicate that UESL represents about 5% of all malignant primary liver tumors occurring in childhood. The observation that UESL is a liver tumor with a low incidence was also confirmed in our series, where it represented 10% of children with primary liver malignancies treated in our institution. No gender predilection is reported for this tumor, although in the study by Bisogno, boys represented 70% of the tumor population as in our series in which males represented 80% of the group [4]. The tumor