Report of seven children with undifferentiated embryonal sarcoma of the liver

Hui-Min Hu, Wei-Ling Zhang, Jing Li, Yuan Wen, Fan Li, Tian Zhi, Dong-Sheng Huang

Department of Pediatrics, Beijing Tongren Hospital, Capital Medical University, Beijing 100176, China.

Undifferentiated embryonal sarcoma of the liver (UESL) very rarely presents clinically. Approximately 1% to 4% of all solid tumors in children are malignant liver tumors, and UESL accounts for 9% to 15% of the liver tumor. The onset of UESL usually occurs at 6 to 10 years of age and there is no obvious difference based on sex. The first symptoms of UESL are abdominal distention and abdominal pain without jaundice, while a physical examination commonly reveals no positive vital signs except the palpable liver tumor. The serum alphafetoprotein (AFP) test is not sensitive for UESL. Preoperative diagnosis of UESL is very difficult. A definitive diagnosis depends on histopathologic examinations including immunohistochemical analysis. Patients with UESL usually have positive for vimentin, antitypspin (AAT), desmin, and smooth muscle actin and have foci positive for cytokeratin (CK8/18) but negative for AFP and S-100 protein. Complete tumor resection is still a key factor that affects the prognosis of UESL. UESL is an aggressive liver tumor with a poor prognosis. The previously reported long-term disease-free survival rate of UESL was less than 37%. In recent years, the prognosis of UESL has improved as treatment has changed to the use of surgery combined with chemotherapy. A recent article reported that the total 5-year survival rate was as high as 92% to 100%. However, the recurrence rate of UESL is high, and the overall prognosis is still not optimistic. Because of its low incidence, the recurrence features and high-risk factors affecting prognosis are seldom reported upon. Therefore, in this report we summarize the characteristics of recurrence and the risk factors affecting prognosis of UESL.

We retrospectively analyzed the medical data of seven cases of UESL that were treated with chemotherapy at our hospital between October 1, 2005 and December 31, 2016. This study was approved by the Ethics Committee of the Beijing Tongren Hospital, Capital Medical University, and was performed in accordance with the Declaration of Helsinki. All patients and their parents gave written informed consent for treatment and testing.

Of the seven patients with UESL, five were girls and two were boys. The age of onset was 5.0 to 15.3 years, with a median onset age of 9.3 years. Five patients presented with abdominal pain as their first clinical symptom, and one patient presented with abdominal distension as their first symptom, and one patient presented with poor appetite and irritability. AFP was normal in all seven cases. All cases were diagnosed pathologically as UESL. The UESL originated in the right hepatic lobe in five cases and in the left hepatic lobe in two cases. Distant metastases were not observed in any of the cases at diagnosis.

Pathologic analysis confirmed that all cases showed positive for vimentin, whereas most cases showed positive for AAT and ACT. The ki67 index was higher than 50% in all cases. However, all cases showed negative for AFP, S-100 protein, and CEA.

All seven patients were treated with combined modality therapy, including surgery and chemotherapy. Because of a ruptured tumor, one patient (case 3) underwent emergency surgery for embolization of the right branch of the hepatic artery, followed by an extended right hepatectomy while the patient’s condition had stabilized. Five patients received postoperative direct chemotherapy, two patients received combined chemotherapy after the first recurrence of the tumor, and one patient received combined treatment with radiotherapy because of multiple recurrences. Chemotherapy mainly involved administration of cyclophosphamide, vincristine, pirarubicin, cisplatin or ifosfamide, and etoposide. The number of chemotherapy cycles ranged from 6 to 42. The main adverse reactions to chemotherapy were bone marrow suppression and gastrointestinal symptoms. The gastrointestinal symptoms were completely alleviated with symptomatic treatment.

Access this article online

Quick Response Code: 
Website: www.cmj.org
DOI: 10.1097/CM9.0000000000000429

Correspondence to: Dr. Dong-Sheng Huang, Department of Pediatrics, Beijing Tongren Hospital, Capital Medical University, Beijing 100176, China. E-Mail: dongshenghuang@126.com Copyright © 2019 The Chinese Medical Association, produced by Wolters Kluwer, Inc. under the CC-BY-NC-ND license. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Chinese Medical Journal 2019;132(18)

Received: 19-04-2019 Edited by: Li-Min Chen
The treatment of all cases is shown in Supplementary Table 1, http://links.lww.com/CM9/A88.

In one case (case 3), the tumor ruptured and the disease progressed, leading to the patient’s death. In another case (case 6), the patient was followed up for 12 months without recurrence. UESL recurred in the other five cases (71.43%). Three recurrence cases had received postoperative chemotherapy directly, just one case showed progression after the recurrence. The remaining two recurrence cases (case 2 and case 7) had not received chemotherapy after surgery directly. The tumors relapsed in multiple sites in case 2 (twice) and case 7 (three times). The recurrence sites included the liver, pelvis, hepatonephric gap, and lung. The first recurrence of all cases occurred 0.33 to 6.67 (median 0.50) years after the patient’s first surgery. Computed tomography images of case 7 are shown in Supplementary Figure 1, http://links.lww.com/CM9/A88.

Follow-up ended on December 31, 2017. The median follow-up time was 4.25 (range: 1–15) years. Three patients died, and four patients achieved complete remission (CR). The median survival time of the four alive patients was 4.29 (range: 1–15) years, whereas that of the three died patients was 2.16 (range: 1.83–4.56) years. The 5-year disease-free survival rate was 33.3%. The prognosis of all cases is shown in Supplementary Table 1, http://links.lww.com/CM9/A88.

In four cases with tumor diameter >15 cm, three patients died, and one case achieved CR. In the remaining three cases with tumor diameter <15 cm, all achieved CR. Three of the seven cases showed tumor breakage, among which one (case 3) progressed to death, one relapsed and achieved remission, and one relapsed and progressed to death. In the four cases without tumor rupture, all survived, showing a significant difference from patients with tumor rupture (P = 0.029). The prognosis of the patients with huge tumor size and tumor breakage was poor. The three patients with positive margins and the one patient with a negative margin all survived (P = 1.000), indicating that the condition of the tumor margin was not related to the prognosis of these patients with UESL.

According to our results, for the old children with the liver tumor and normal AFP, those might be UESL possibly. The common symptoms of UESL might be abdominal pain. The diagnosis of UESL depends on pathologic examination.

The prognosis of UESL has improved by surgery combined with chemotherapy, but the recurrence rate remains very high (71.43%). Two patients with relapse did not receive direct combined chemotherapy after surgery, and both patients experienced repeated recurrences and metastization to multiple sites with a recurrence frequency of two and three in cases 2 and 7, respectively. The other three recurrences occurred just once and in the liver. Therefore, postoperative direct combined chemotherapy can reduce the frequency of relapse and prevent repeated recurrence and metastatization of cancer to multiple sites.

In our report, the most common recurrence site was the liver, although the pelvic cavity, hepatonephric gap, and lung were also sites of recurrence and metastasis. Once a relapse has occurred in the liver or lung, re-resection of the tumor and treatment with chemotherapy can still improve the prognosis. This was seen in case 7, in which CR was achieved after three relapses and four resections.

A tumor diameter >15 cm or tumor breakage was a risk factor for a poor prognosis in our patients. Conversely, the tumor margin was not related to the prognosis of our patients with UESL. The results are consistent with those reported in the literature.[2]

In this report, the 5-year disease-free survival rate was only 33.3%, which is significantly different from the long-term survival rate reported in the literature.[2] This may be attributed to the three cases of tumor breakage and two cases of recurrence in which the patients’ parents chose to end treatment.

To summarize, tumor resection combined with chemotherapy is the first choice for the clinical treatment of pediatric UESL, but patients should be closely observed during follow-up because of the high recurrence rate. Tumor size and tumor breakage significantly affect the prognosis. For cases of relapse and with distant metastasis, CR can be achieved with combined treatment that includes surgery, chemotherapy, and radiotherapy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients and their parents understand that the names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Funding

This study was supported by a grant from the “Climbing the Peak” Talent Plan of the Beijing Municipal Administration of Hospitals (No. DFL20180201).

Conflicts of interest

None.

References

1. Stocker JT, Ishak KG. Undifferentiated (embryonal) sarcoma of the liver: report of 31 cases. Cancer 1978;42:336–348. doi: 10.1002/1097-0142(197807)42:1<336::aid-cncr2820420151>3.0.co;2-v.
2. Shi Y, Rojas Y, Zhang W, Beerele EA, Doski JF, Goldberg M, et al. Characteristics and outcomes in children with undifferentiated embryonal sarcoma of the liver: a report from the National Cancer Database. Pediatr Blood Cancer 2017;64:26272. doi: 10.1002/pbc.26272.
3. Putra J, Ornvold K. Undifferentiated embryonal sarcoma of the liver: a report from the National Cancer Database. Pediatr Blood Cancer 2017;64:26272. doi: 10.1002/pbc.26272.
4. Mathias MD, Ambati SR, Chou AJ, Slotkin EK, Wexler LH, Meyers PA, et al. A single-center experience with undifferentiated embryonal sarcoma of the liver. Pediatr Blood Cancer 2016;63:2246–2248. doi: 10.1002/pbc.26154.

How to cite this article: Hu HM, Zhang WL, Li J, Wen Y, Li F, Zhi T, Huang DS. Report of seven children with undifferentiated embryonal sarcoma of the liver. Chin Med J 2019;132:2244–2245. doi: 10.1097/CM9.0000000000000429