

Primary hepatic Ewing sarcoma: a very infrequent case report

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ABSTRACT

Ewing sarcoma (ES) is a member of small round cell tumors of which contains Wilms' tumor, neuroblastoma, rhabdomyosarcoma and lymphoblastic lymphoma. ES occurs most commonly in the bone but infrequently occurs in the soft tissues without involvement of the bones. Primary involvement of the liver is even rarer. We report the case of 24-year-old female patient with abdominal pain. Abdominal computed tomography scan showed hepatic large cystic lesion. Liver biopsy showed tumoral cells with small narrow stoplasmic and hyper chromatic nucleus evaluated as small round cell tumor. Immunohistochemical study of the lesion revealed CD99 and bcl-2 positive, cytokeratin, LCA, CD138, chromogranin, synaptophysin, myoD1, terminal deoxynucleotidyl transferase and myoglobin negative the diagnosis primary hepatic ES. A research for any other tumor involvement by using positron emission tomography yielded only hepatic involvement revealed. The patient treated with vincristine-cyclophosphamide-adriamycin and ifosfamide-etoposide alternately chemotherapy then hepatic tumor regressed. Patient operated on hepatic wedge resection. She has continued on chemotherapy and she has been doing well at the sixth month of diagnosis.

Introduction

Ewing sarcoma (ES) is a member of small round cell tumors of which contains Wilms' tumor, neuroblastoma, rhabdomyosarcoma and lymphoblastic lymphoma. Ewing's sarcoma family of tumors not only includes ES, but also primitive neuroectodermal tumor

(PNET) and Askin's tumor. ES occurs most commonly in the bone but infrequently occurs in the soft tissues without involvement of the bones. Primary ES has been described very rarely in the pancreas, pulmonary, stomach, small bowel, kidney and ovaries.¹⁻³ Primary involvement of the liver is even rarer.

In this presented case, primary liver ES in a young female patient who was treated with hepatic wedge resection and chemotherapy.

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Case Report

A 24-year-old Syrian female (refugee) patient was admitted with the complaints of right upper abdominal pain and fatigue. She did not have a history of previous illness or any medication. Physical examination revealed palpable liver at 3 cm below the costal margin. Abdominal scans revealed 120×100 mm with cystic mass lesion on the right hepatic lobe (Figure 1). Computed tomography (CT) of the thorax was normal. Pathological examination of liver biopsy revealed as diffuse narrow cytoplasmic and hyper chromatic nucleus small round tumor cells. Immunohistochemical (IHC) study of the lesion showed CD99 and fli-1 (*friend leukemia virus integration*) positive (Figure 2), cytokeratin (CK), LCA, CD138, chromogranin, synaptophysin, myoD1, terminal deoxynucleotidyl transferase (Tdt), myoglobin and reticulin negative. The morphology of the hepatic lesion and findings of IHC study was consistent with ES. A research for any other tumor involvement by using positron emission tomography yielded only hepatic involvement (SU-

Vmax: 15). Bone marrow aspiration had not any pathological infiltration. NCI VAC (vincristine 2 mg, cyclophosphamide 900 mg/m², adriamycin 45 mg/m² first 12 week then 35 mg/m²) and IE (ifosfamide 1800 mg/m², etoposide 100 mg/m²) chemotherapy was started alternately every 3 weeks. At the 9th week, abdominal CT scan revealed a regression in hepatic lesion size 120 mm to 90 mm. She was operated due to the risk of perforation. Then encapsulated tumor was seen in the exploration. The right liver lobe segments of 4-6 and gallbladder were resected. On cut surface and the hepatic parenchyma was replaced by capsular white mass lesion (Figure 3), which was measured 7.5×6×5 cm. Pathological examination consisted in 95% of necrosis. She continued on chemotherapy and received 52th NCI chemotherapy without recurrence. She was doing well at the twelfth month of diagnosis.

Discussion

ES and PNET are the same group tumors but ES has been used for tumors that lack in the evidence of neuroectodermal differentiation. Both of them are being evaluated within two categories; central and peripheral ES/PNET. Peripheral ES/PNET which occurs in bones and/or extra osseous sites was introduced initially by Arthur Purdy Stout in 1918.⁴ ES has been described in the kidney, parotid gland, chest wall, ovary, rectum or retroperitoneal cavity. The kidney is the most commonly involved visceral organ site however involvement of the liver is very rare. Children and young adults are most commonly affected and the presented patient was under 30 years of age. Patients including ours usually have the complaints of localized pain and swelling. Gross appearance of the ES tumor is multilobulated, soft, friable and rarely cystic formation. It rarely exceeds 10 cm. In the presented case, hepatic cyst formation size is 12×10 cm.

Herein we have presented the case of a patient with primary hepatic Ewing sarcoma. To the best of our knowledge there were four hepatic ES cases in English literature.⁵⁻⁸ In our case she had multiloculated cystic liver lesion and diagnosed by CT scan and biopsy. In the English literature this was the second case of primary hepatic ES, which was presented with multiloculated liver cystic lesion. Ozaki *et al.* reported the first hepatic multiloculated cystic lesion diagnosed with hepatic ES.⁷ In that case a 27-year-old Japanese woman was admitted with abdominal pain. Multiloculated cystic lesion on liver was revealed with clinical examination. Before patient was operated; mucinous hepatic cyst adenoma had been diagnosed by liver biopsy. But after operation, primary hepatic ES was diagnosed. Differential diagnosis of hepatic cystic lesion comprises simple solitary cystic lesion, poly cystic liver disease and neoplastic lesions such as

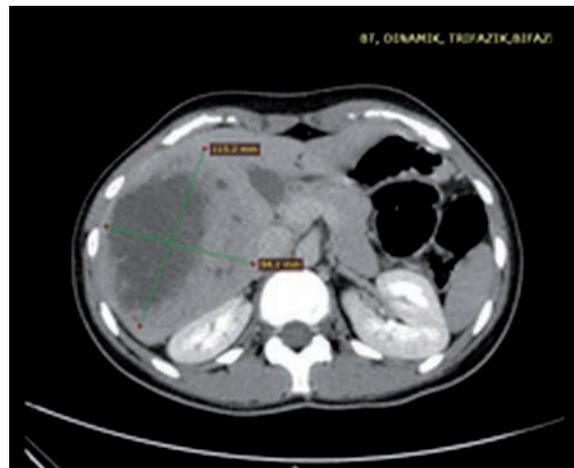


Figure 1. Abdominal computed tomography showed hepatic centrally necrotic cystic lesion.

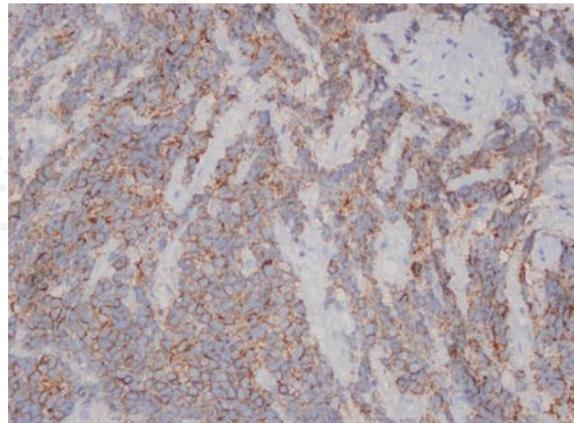


Figure 2. Liver biopsy tumor cells immunoreactivity flil-1 (200x).



Figure 3. Hepatic wedge resection showing capsular white mass lesion.

mucinous cystadenomas, mucinous cystadenocarcinoma, hepatocellular carcinoma and metastasis from other diseases.

There were two cases of hepatic ES in the literature which were presented with hepatic solid mass lesion.^{6,8} The case reported by Cambruzzi *et al.* was an 18-year-old male showing solid hepatic mass with the complaints of abdominal pain. Preoperative hepatic artery embolization was performed and then the patient was operated for hepatic resection. One month after the surgery, the patient died with pulmonary embolization.⁶

Mani *et al.* reported a 20-year-old female patient with massive hepatomegaly without mass lesion and bulky renal involvement. The patient was diagnosed with hepatic ES with core biopsy and treated with combined chemotherapy (VAC/IE alternatively).⁵ Over 43 weeks she has been doing well.⁵

Several steps are required for the diagnosis of ES/PNET. ES has specific histological and phenotypic features. The first approach is using light microscopic examination. Histological ES/PNET is composed by monomorphic small blue round cell that reacts positively to glycoprotein p30/32 MIC2 (CD99). The second approach is immunohistochemical consideration. Pathological specimen should be evaluated with immunohistochemical markers including, CK, CD138, a WT1, synaptophysin, muscle specific actin, desmin, myogenin, LCA and leukocyte common antigen (CD45) to exclude other small round cell tumors including neuroblastoma, myeloma, desmoplastic small round cell tumor, mesenchymal chondrosarcoma, alveolar rhabdomyosarcoma, non-Hodgkin's lymphoma and small cell osteosarcoma.⁸⁻¹⁰ Neuroblastoma shows immunoreactivity to NSE, S-100 and Leu-7 like ES, but negative for vimentin. Lymphoblastic lymphoma is immunoreactive to CD99 but different in that it tests positive to CD45 and Tdt. Rhabdomyosarcoma is immunoreactive to myogenin, myo-D1, desmin and actin differs from Ewing sarcoma. In our patient, IHC showed CD99 and bcl-2 positive, CK, LCA, CD138, chromogranin, synaptophysin, myoD1, Tdt and myoglobin negative.

The translocation t(11, 22)(q24; q12) is specific of Ewing sarcoma and resulting in the production of the *EWS/Flt-1* fusion gene. This fusion gene expresses CD 99 antigen (MIC 2) and occurs in 85% of patients with ES/PNET. The remaining of patients have variant of this translocation.^{11,12} In our case liver biopsy is strongly positive for CD99 but we were unable to work the t(11:22)(q24;q12) translocation due to our genetic laboratory having no special based translocation assay kits.

Treatment of ES needs multidisciplinary approach. A high initial complete response of 94% was observed in patients of PNET treated with VAC chemotherapy

plus local radiation therapy.¹³ The best response was reported with combinations based on anthracyclines (doxorubicin) and high doses of alkylation agents (cyclophosphamide or ifosfamide).^{14,15} Despite high responses with multimodal therapy, most patients have a rapid progression. For the presented case, VAC/IE chemotherapy alternatively was started. After 9 cycles of chemotherapy tumor was regressed and the patient was operated. After 52 weeks of treatment, the patient was in good condition.

The prognosis of patients with hepatic ES is very poor especially in the metastatic stage and standard therapy approach is still unclear. But multimodal therapy may improve clinical symptoms. Prognostic factors of ES are the presence of metastatic disease at the time of initial diagnosis, large tumor size, extensive necrosis and poor response of initial chemotherapy.

Conclusions

As conclusion clinicians should carefully evaluate young patients who have cystic and necrotic hepatic lesions to exclude hepatic ES.

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