Imaging Findings of Hepatic Ewing’s Sarcoma on Computed Tomography and Gadobenate Dimeglumine-enhanced Magnetic Resonance Imaging: A Case Report and Literature Review

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Abstract

Ewing’s sarcoma (ES) is a tumor that often occurs in the long bones and rarely arises from visceral organs primarily. Here, we report a case of primary hepatic ES, discuss its computed tomography (CT) and gadobenate dimeglumine-enhanced magnetic resonance (MRI) features. This is the first Chinese and fifth primary hepatic ES case reported, based on a literature review. Imaging examinations showed that the tumor was solid, with necrosis and hemorrhage. Contrast-enhanced images showed that the tumor was hypervascular and especially had heterogeneous signal intensity on hepatobiliary phase MRI images. Intratumoral vessels and vascular invasion were also present.

Keywords: Ewing’s sarcoma; Primitive neuroectodermal tumor; CT; MRI; Literature review.

Abbreviations: AFP, alpha-fetoprotein; ALT, glutamic oxaloacetic transaminase; AST, glutamic pyruvic transaminase; CA125, cancer antigen 125; CA19-9, cancer antigen 19-9; CEA, carcinoembryonic antigen; CT, computed tomography; DWI, diffusion-weighted imaging; ES, Ewing’s sarcoma; EWSR1, Ewing sarcoma breakpoint region 1; FISH, fluorescence in situ hybridization; FLI-1, friend leukemia virus integration 1; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HE, hematoxylin and eosin; ICC, intrahepatic cholangiocellular carcinoma; IVC, inferior vena cava; LHV, left hepatic vein; MHV, middle hepatic vein; MRI, magnetic resonance imaging; PANS, periodic acid-Schiff; PCR, polymerase chain reaction; PECT, positron emission computed tomography; PET, positron emission tomography; PNET, primitive neuroectodermal tumor; PV, portal vein; RHV, right hepatic vein; SI, signal intensity; Syn, synuclein; T1WI, T1 weighted image; T2WI, T2 weighted image.

Introduction

Ewing’s sarcoma (ES) is also known as primitive neuroectodermal tumor (PNET) because of the overlap of their genetic abnormalities. ES/PNET, together with skin tumors and atypical ES, are members of the ES tumor family.1,2 ES usually occurs in the long bones of the extremities and in the pelvic bones, and extraosseous ES can occur in the deep soft tissue around the extremities, chest wall, retroperitoneum, and solid organs, including the pancreas, kidney, uterus, ovary, gastrointestinal tract, and other visceral organs.3–8 Primary hepatic ES is uncommon, and only four cases of this disease have been reported.9,7,9,10 Herein, we present a case of primary hepatic ES/PNET and describe the computed tomography (CT) and gadobenate dimeglumine-enhanced magnetic resonance imaging (MRI) features of the tumor, with an accompanying review of the literature.

Case report

Patient information

A 27-year-old woman presented with severe epigastric pain for 20 days. The patient had an unremarkable medical and family history, and the physical examination was normal. After admission, routine laboratory examinations, including serum glutamic oxaloacetic transaminase (ALT), glutamic pyruvic transaminase (AST), and bilirubin index, were normal. However, serum lactate dehydrogenase was 320 U/L (normal range: 120–250 U/L). Viral serology tests for hepatitis B virus (HBV)/hepatitis C virus (HCV) were negative. The serum tumor biomarker test revealed that the cancer antigen 125 (CA125) level was 44.5 U/mL (normal range: 0–35 U/mL), while alpha-fetoprotein (AFP) and carcinoembryonic antigen (CA19-9) levels were normal. Further laboratory investigations showed slightly increased monocytes (0.650 10^9/L), a slightly decreased lymphocyte rate (18.1%; normal range: 20–50%), and decreased albumin (3.67 g/dL; normal range: 3.5–4.5 g/dL) and prealbumin (14.9 mg/dL; normal range: 16–45 mg/dL).

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The imaging examination, including contrast-enhanced CT, indicated a heterogeneous, solid mass with areas of necrosis measuring 9.6×9.1×10 cm in the hepatic caudate lobe. The mass showed obvious heterogeneous enhancement with multiple tortuous vessels in the arterial phase and persistent enhancement with mild dilation of distal hepatic ducts in the portal venous phase (Fig. 1). The mass extended to the portacaval space and upward to invade the second porta hepatis, including the inferior vena cava (IVC) and the roots of the right hepatic vein (RHV), the middle hepatic vein (MHV), and the left hepatic vein (LHV). The left branch of the portal vein (PV) was also possibly invaded. On MRI, the tumor was hypointense on the T1 weighted image (T1WI) and heterogeneously hyperintense on the T2 weighted image (T2WI), showing areas of hemorrhage and necrosis. Diffusion-weighted imaging (DWI) also showed hyperintensity. After injection of gadobenate dimeglumine, the mass showed obvious heterogeneous enhancement in the arterial phase and persistent enhancement in the portal venous and delayed phases. In the hepatobiliary phase (HBP), the tumor showed heterogeneous signal intensity (SI) (Fig. 2). Both CT and MRI prompted suspicion of mesenchymal neoplasm, such as sarcoma, in the caudate lobe of the liver. A search for any other sites of involvement of the tumor using whole-body bone scan and positron emission tomography (PET) showed no abnormality.

**Surgical procedure**

A laparoscopic exploration was performed and showed the mass located in the caudate lobe, 10×11 cm in size and involving segments 2/3/5/8 of the liver, the diaphragm, second porta hepatis, RHV, MHV, and IVC (Fig. 3). On the cut surface, the tumor was grayish red and hard, with necrosis. On microscopic examination, the tumor was composed of small blue tumor cells with necrosis. Immunohistochemical examination revealed positive expression for CD99 and NKX2.2 and weak positivity for synuclein (Syn) and Ki-67 (the positive rate was approximately 20%) (Fig. 4). Dual-color, break-apart probe fluorescence in situ hybridization (FISH) examination revealed that more than 30% of the cells (200 counted cells per slide) exhibited one yellow and one red signal, which indicated a break of the Ewing sarcoma breakpoint region 1 (EWSR1) locus (Fig. 4). These findings supported a diagnosis of localized ES arising from the liver. However, the patient refused standard postoperative chemotherapy and/or radiotherapy as adjuvant treatments.

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**Fig. 1.** Contrast-enhanced CT scans of the hepatic ES. (A–B) Obvious heterogeneous enhancement with multiple serpentine neovascular (axial arterial phase). (C) Persistent enhancement with mild dilation of distal hepatic ducts (portal venous phase). (D) IVC involvement (coronal portal venous phase image). IVC, inferior vena cava.
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Fig. 2. Gadobenate dimeglumine-enhanced MRI of the hepatic ES. (A) Hypointense (axial T1WI) image. (B) Heterogeneous hyperintense (axial T2WI) image. (C) Diffusion restriction in DWI. (D) IVC involvement (coronal image). T1WI, T1 weighted image; T2WI, T2 weighted image; DWI, diffusion-weighted imaging; IVC, inferior vena cava.

Fig. 3. Intraoperative findings. (A) The tumor originated from the hepatic caudate lobe. (B) The tumor was greyish red and hard, with necrosis.
She is currently alive (3 months postoperatively) without any signs of recurrence.

**Literature review**

A literature search was initiated to review cases of primary hepatic ES. Based on the literature review, only four prior cases of primary hepatic ES have been reported. Following the previous reports and our case presented herein, 80% of patients with ES were younger than 20 years, and all patients with hepatic ES were younger than 30 years. The clinical symptoms of ES in the liver are nonspecific, with abdominal pain being the most common. Uncommon symptoms include abdominal distention, nausea, emesis, and diarrhea (Table 1).

**Discussion and conclusions**

Due to the rarity of the tumor, little information on the imaging features of hepatic ES is available. Relying on CT and ultrasound findings, two previous reports only described the tumor as solid, with one report using CT to describe the tumor as a multilocular cystic mass with enhanced septa, and the other to describe an enlarged liver without a mass lesion.9–12 To the best of our knowledge, this is the first case of both CT and gadobenate dimeglumine-enhanced MRI features of ES in the liver.

In the present case, the tumor was solid, with necrosis and hemorrhage, as shown by CT and MRI imaging. The tumor also showed diffusion restriction in DWI. After enhancement, the tumor was hyper vascular, with prominent intratumoral vessels in the arterial phase and persistent enhancement to the portal venous phase and delayed phase from dynamic MRI scans. The tumor was aggressive, based on vascular invasion demonstrated by CT and MRI. On HBP, the tumor showed heterogeneous SI, which was only partly due to intratumoral hyperintensity representing intralesional hemorrhage. These findings suggested the tumor to be non-HCC or –ICC but raised a suspicion of sarcoma.

With similar clinical, immunohistochemical and cytogenetic profiles, ES and PNET are regarded as two extremes of a morphologic spectrum of the same tumor entity. ES/PNETs are divided into two main categories, according to the cell origin and location. Central PNETs are derived from the neural tube, mainly involving the brain and spinal cord. Peripheral PNETs are derived from the neural crest and occur outside the central nervous system, often involving the sympathetic nervous system or soft tissue and bones.4,13–16 In children, approximately 80% of ES are found in bones and <20% in soft tissues, while in adults, >50% of ES occur in soft tissues but ES rarely affects visceral organs. When
visceral involvement does occur, the most common affected organ is the kidney.\textsuperscript{18–20} The liver is a rather rare organ of involvement. The gross appearance of the tumor is usually multilobulated, soft, and friable, and it usually exceeds 10 cm in its largest dimension.\textsuperscript{11} The tumors could be solid, cystic, or diffusely enlarged to involve the entire liver, but most of the tumors reported have been solid, with or without areas of necrosis and hemorrhage. Histologically, ES is composed of poorly differentiated small round cells containing dark staining and round or oval nuclei.\textsuperscript{9} Special stains, such as periodic acid-Schiff (PAS), usually show positivity for cytoplasmic glycogen,\textsuperscript{10} and immunostains usually show positivity for CD99, vimentin and NKX2.2.\textsuperscript{21} However, these findings are not specific to ES, so molecular biological examination is recommended to confirm the disease. FISH or real-time polymerase chain reaction (PCR) tests have demonstrated that most ES's harbor the EWSR1-ETS fusion protein, which results in a chromosomal translocation t (11:22) between the EWS (22q12) and friend leukemia virus integration 1 (FLI-1) (11q24) genes.\textsuperscript{3–5}

The major differential diagnosis for hepatic ES includes carcinosarcoma, angiosarcoma, leiomyosarcoma, and undifferentiated embryonal sarcoma. Carcinosarcoma is a rare malignant tumor containing both carcinomatous and sarcomatous components. It is more common in elderly males, and most patients have elevated tumor markers, including CEA, AFP, and CA19-9. Tumors usually show heterogeneous density/intensity accompanied by vast cystic changes and necrosis with moderate to clearly-irregular marginal enhancement.\textsuperscript{22,23} Angiosarcoma is the most common malignant mesenchymal tumor of the liver, accounting for <2% of primary hepatic tumors.\textsuperscript{24,25} It typically occurs in males in the fifth to seventh decade of life. Tumors are multifocal and have heterogeneous signals on T2WI and HBP images with intralesional hemorrhage. On dynamic scans, angiosarcoma demonstrates at least some extent of progressive enhancement with enhancing foci of irregular or rim-like nodular/linear shape, or bizarre shapes.\textsuperscript{26,27} Hepatic leiomyosarcoma derives from smooth muscle cells in hepatic vessels, bile ducts, or ligaments.\textsuperscript{28} The patient ages at the time of tumor detection ranged from 5 months to 86 years, with no obvious sex difference.\textsuperscript{29–32} On CT, the tumors are hypodense, with necrosis or bleeding, and heterogeneous enhancement. On MRI, the tumors are hypointense on T1WI and heterogeneous hyperintense on T2WI with heterogeneous enhancement. On MRI, the tumors are hypointense on T1WI and heterogeneous hyperintense on T2WI with heterogeneous enhancement.\textsuperscript{29,31,34} Undifferentiated embryonal sarcoma of the liver occurs mostly in children aged 6 to 10 years and rarely in adults.\textsuperscript{35,36} On CT scan, the tumor appears as a solitary, well-defined cystic mass with solid nodules and septations, showing progressive enhancement. Tortuous vessels within the tumor may be observed.\textsuperscript{35,37,38}

The standard treatment plan for extraosseous ES has not been established and should correspond to the treatment method for all sarcomas in the Ewing family.\textsuperscript{39} ES/PNET is highly sensitive to chemotherapy and radiotherapy; however, surgical resection should also be considered for patients with localized extraosseous ES. In line with this, systemic multiagent chemotherapy combined with surgery and/or radiotherapy is recommended.\textsuperscript{40} Previous studies have shown a 5-year survival of 58–61%, with a median survival of 120 months for patients with PNETs.\textsuperscript{51,42} Finally, age and surgical treatment are recognized as important prognostic variables in the treatment of extraosseous ES, in particular.\textsuperscript{10}

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Conflict of interest
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Author contributions
Design of the study (TL, WY), collection of the patient’s clinical data (WY, XY, CY), analysis of the patient’s clinical data and of the literature data (XY, WD, XL), and writing of the paper (TL, CY).

Ethical approval and consent for publication
The hospital board committee provided approval for the procedural application in clinic and case report publication. Written informed consent for publication was obtained from the patient.

Data sharing statement
All data generated or analyzed during this study are included in this published article.

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