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Primary Malignant Rhabdoid Tumor of the Liver in a 5-Month-Old Female Who Presented with Abdominal Distension

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 Hanood Basam Abu Rass
ABEF 1 Moutaz W. Sweileh
ADEF 2 Mohammad Abuawad

1 Department of Pathology, An-Najah National University Hospital, Nablus, Palestine
2 Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine

Corresponding Authors: Mohammad Abuawad, e-mail: m.abuawad@najah.edu, Hanood Abu Rass, e-mail: h.rass@najah.edu
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Patient: Female, 5-month-old
Final Diagnosis: Hepatic primary malignant rhabdoid tumour
Symptoms: Abdomen distension
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology • Oncology

Objective: Rare disease

Background: Malignant rhabdoid tumors are rare and aggressive pediatric tumors that usually arise in the kidney and have a characteristic appearance on histology. Extrarenal malignant rhabdoid tumors originating in the liver are extremely rare. This report is of a 5-month-old girl who presented with a rapidly enlarging abdominal mass due to a malignant rhabdoid tumor of the liver.

Case Report: A 5-month-old female patient with no known medical history had been experiencing increasing abdomen distention and less overall activity for 1 month, according to her parents. Abdominal ultrasonography was used for diagnostic purposes, and the results showed the presence of a mass with a solid and cystic appearance in the upper left quadrant of the abdomen. The patient was transferred to a tertiary care hospital for further investigations. The laboratory test results indicated a hemoglobin level of 8.2 g/dL, and the liver function tests were within the reference range. However, the serum tumor marker alpha-fetoprotein level was 1310 ng/mL, while the β-human chorionic gonadotropin was within range. Computed tomography detected a nonspecific heterogeneous mass of the liver. Histopathology revealed discohesive cells with rich eosinophilic cytoplasm, eccentric nuclei, and large central nucleoli (rhabdoid appearance). Immunohistochemistry showed negative integrase interactor 1 protein expression. The diagnosis was a primary malignant rhabdoid tumor located in the liver.

Conclusions: This report shows the importance of combined diagnostic imaging and histopathology analysis to confirm the diagnosis of rare pediatric tumors, including malignant rhabdoid tumor, to ensure early diagnosis and appropriate treatment.

Keywords: Rhabdoid Tumor • Infant • Liver

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/941968

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Background

Malignant liver tumors account for approximately 3% of all childhood tumors [1]. Mesenchymal harmatoma, infantile hemangioma, and hepatoblastoma are the most common primary liver tumors diagnosed in the majority of these patients [2-4]. In addition, malignant rhabdoid tumor (MRT) is a rare, very aggressive tumor of childhood, mainly arising from the kidney and the central nervous system, and is characterized by the presence of rhabdoid cells that resemble rhabdomyoblasts, which are distinctive in having eosinophilic perinuclear inclusion bodies [5-8]. SMARCB1 is a member of the SWI/SNF chromatin-remodeling complex. Rhabdoid tumors develop when both copies of the SMARCB1/INI1/hSNF5/BAF47 gene are inactivated. In 5% to 30% of cases, individuals have a genetic change in SMARCB1 present in their germline [8,9]. Extra-renal rhabdoid tumors are extremely rare and have been reported in the liver, brain, neck, esophagus, mediastinum, tongue, and other sites [10-14]. Rhabdoid tumors of the liver present with abdominal mass in 35.8% of cases in the right upper quadrant, abdominal distention in 17.0% of cases, and usually with symptoms such as fever, vomiting, and loss of appetite. A notable finding is that 17% of patients experience a spontaneous rupture of the tumor [15]. Extrarenal rhabdoid tumors are malignant tumors that have a poor prognosis; the 3-year survival rate for patients with this condition is only 9% [16]. It may be difficult to distinguish from hepatoblastoma, although the poorer prognosis and differing treatment approaches make early differentiation important. Typically, hepatoblastoma is diagnosed at a later age (around 16 months compared with 8 months for other types of liver cancers), and it is less prone to spontaneous rupture. Moreover, about 90% of hepatoblastoma cases exhibit elevated levels of alpha-fetoprotein [15].

In addition, MRT in the liver must be distinguished from other mesenchymal liver tumors, such as embryonic sarcoma and mesenchymal harmatoma, as they have different clinical and pathological features than MRT. Owing to the rarity of MRT, histopathology along with special immunohistochemical stains can aid in the early diagnosis of this aggressive tumor [17,18]. The standard chemotherapy approach for treating MRTs involves a combination of carboplatin and etoposide, alternating with cyclophosphamide. However, this treatment strategy has not shown significant improvement in outcomes for patients. Various attempts with different chemotherapy combinations, such as ifosfamide-carboplatin and etoposide or ifosfamide-etoposide alternating with vincristine-doxorubicin-cyclophosphamide and ifosfamide, vincristine, and actinomycin have been made, but the average survival rates for affected children have ranged from just 5 days to 5 months. Only a few individuals have achieved long-term survival with these diverse therapeutic approaches [8]. Here, we report the presentation and laboratory and imaging data of a 5-month-old female patient who presented with a rapidly enlarging abdominal mass due to a primary MRT in the liver, which was first diagnosed as hepatoblastoma on imaging and required surgical biopsy, pathology, and immunohistochemical staining for the final diagnosis.

Case Report

A 5-month-old female patient with a free past medical history was transferred from an outside hospital for investigation of an abdominal mass. She had a 1-month history of progressively increasing abdominal distention, decreased activity, and decreased oral intake, as noticed by her parents. At an outpatient clinic, a diagnosis of abdominal colic was made, and the patient was prescribed anti-colic medication; however, no improvement was noted. Abdominal ultrasound revealed a large solid and cystic heterogenous echotexture mass in the left upper quadrant, with lobulated margins and increased vascularity. She was then referred to an outside hospital, where she underwent laboratory, imaging, and histopathology studies. At admission, initial laboratory test results revealed anemia, with a hemoglobin level of 8.2 g/dL (reference value: 10-17 g/dL), normal liver function test results, elevated serum tumor marker alpha-fetoprotein of 1310 ng/mL (reference value: < 20 ng/mL), and normal beta-human chorionic gonadotropin (reference value: less than 5 mIU/mL). An abdominal computed tomography (CT) scan revealed a large heterogeneous enhancing soft tissue mass of the liver, with central necrosis and lobulated outlines located in the left upper quadrant (**Figure 1**). A CT scan of the lung showed multiple lung nodules (**Figure 2**). At that time, it was difficult to diagnose those nodules as metastatic lesions.

Based on the clinical, laboratory, and imaging data, the differential diagnosis included hepatoblastoma, yolk sac tumor, and neuroblastoma. A surgical biopsy of the mass was performed, and histopathology results showed a hypercellular mass of loosely cohesive neoplastic cells, with abundant cytoplasm, eccentric vesicular nuclei, and centrally located prominent nucleoli giving the characteristic appearance of a rhabdoid mass (**Figure 3**). Neoplastic cells were seen within a background of myxoid stroma. A focal area of necrosis was noted. Tumor cells showed periodic acid-Schiff reagent-positive eosinophilic intracytoplasmic inclusions. On immunohistochemical staining, the tumor cells were diffusely positive for cytokeratin and SALL-4, focally positive for glypican 3 and EMA, and had negative expression for INI-1 (BAF47). Immunohistochemistry markers, including Hepbar-1, CD34, synaptophysin, CD99, CD56, S100, chromogranin, desmin, and myogenin, were done and were negative, excluding the possibility of hepatoblastoma, germ cell tumor, Ewing sarcoma/PNET, and rhabdomyosracoma (**Figure 4**). Therefore, the histology result was consistent with an MRT.

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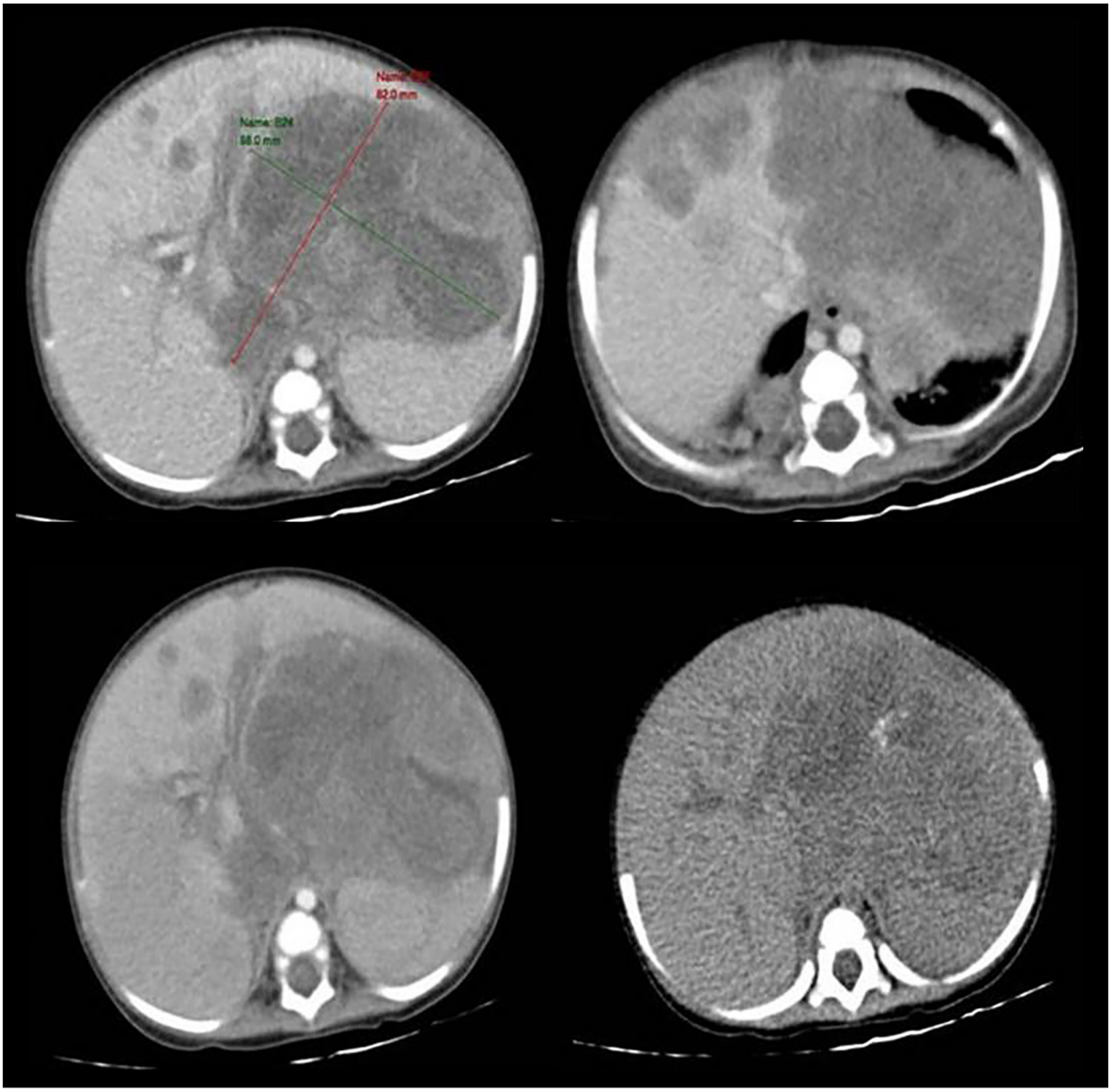

Figure 1. Abdominal computed tomography shows large heterogeneous enhancing soft tissue mass of the liver with central necrosis and lobulated outlines located in the left upper quadrant.

Discussion

In this report, we present a case of pediatric hepatic rhabdoid tumor, which resembled hepatoblastoma on imaging and required a surgical biopsy and immunohistochemical staining for a final diagnosis. MRT is a unique group of tumors that was initially identified as an aggressive variant of Wilms tumor [19]. It was so named because of its histologic resemblance to a rhabdomyoblast. However, its myogenic differentiation is still not confirmed [20]. The 3 most common locations of occurrence are the central nervous system (50%), kidneys (25%), and soft tissue (19%) [21]. MRTs have been described in other sites, including the liver, adrenals, pelvis, and jejunum [22-24]. The median age of diagnosis is 11 to 18 months [25]. Patients younger than 2 years old make up the majority of cases [26]. These tumors are highly aggressive and have a poor prognosis. Histologically, these tumors are characterized by the presence of non-cohesive sheets of cells with abundant cytoplasm, eccentric vesicular nuclei, centrally located prominent nucleoli, and eosinophilic perinuclear inclusion [27]. One of the most distinguishing features of these tumors is the negative expression of INI-1, which can be demonstrated by BAF47 immunohistochemical staining [9,14,28]. Laboratory abnormalities detected in these tumors include anemia, thrombocytosis, high

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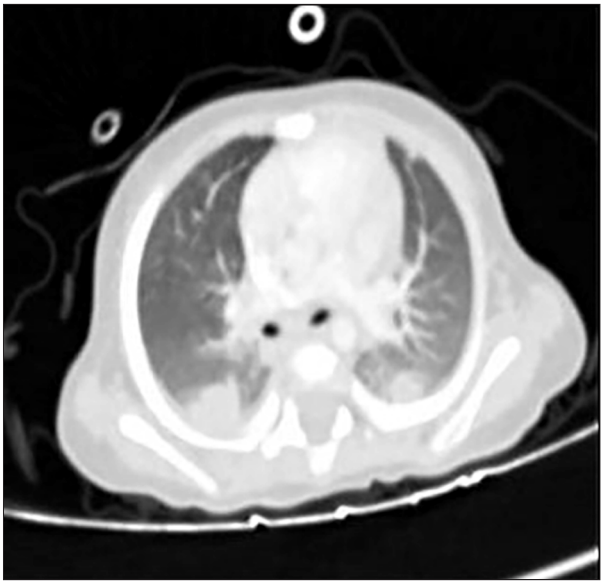

Figure 2. Lung computed tomography shows multiple metastatic lung nodules.

liver enzymes, and high lactate dehydrogenase [15]. Some studies have reported common imaging findings associated with such tumors, including solid, lobulated, heterogeneously enhancing masses on CT and magnetic resonance imaging (MRI), with occasional cystic components [29]. A shared immunohistochemical feature of these tumors is the expression of vimentin and epithelial markers and the lack of expression of S-100, myoglobin, and desmin [30].

Primary hepatic MRTs are considerably less common, with only a few cases reported in the medical literature, including 55 cases of MRT of the liver [1]. The first evidence in the literature of a liver tumor with rhabdoid features was described in 1982 by Gonzalez-Crussi et al [31]. The age and clinical presentation of our case report were consistent with the same findings in the literature that demonstrate that MRTs of the liver are most common in the infantile period, with a median age of 8 months; the vast majority of cases occur in children younger than 3 years of age and show a slight male predominance [21]. These tumors typically present with a right upper

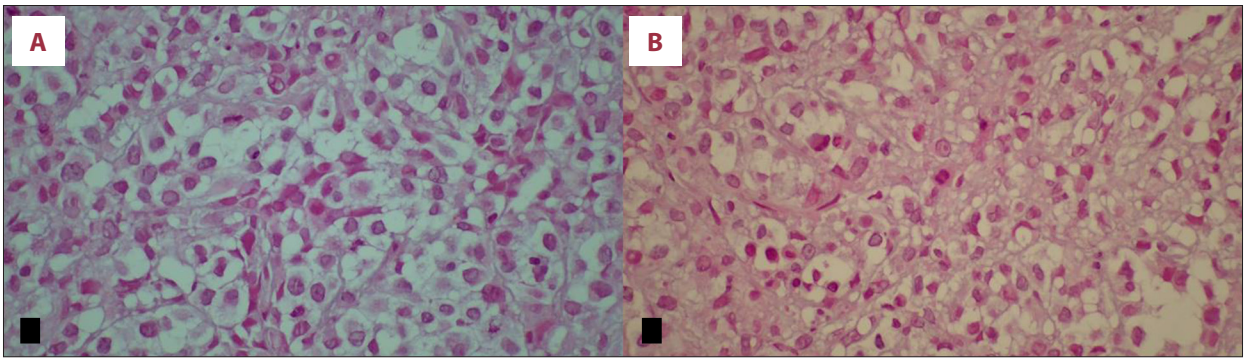

Figure 3. Hematoxylin and Eosin (×60) histopathological examination of the lesion: (**A**) nests of tumor cells embedded in myxoid stroma; and (**B**) nests of tumor cells with rounded nuclei and eosinophilc cytoplasm and rhabdoid morphology.

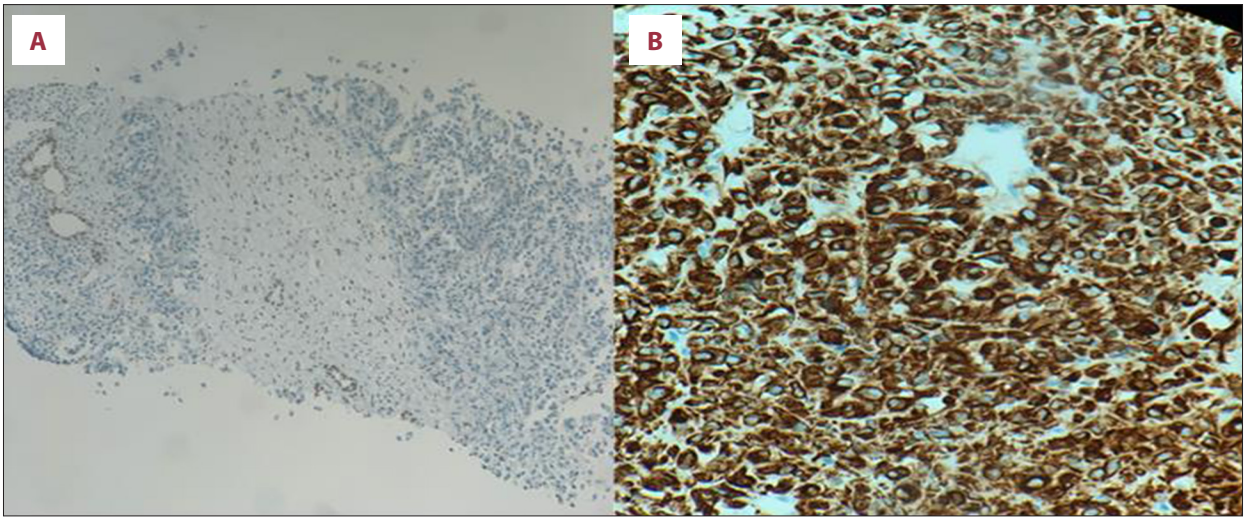

Figure 4. Immunohistochemical staining pattern of the lesion: (**A**) loss of integrase interactor 1 (1INI [BAF47]) nuclear staining; and (**B**) diffuse cytokeratin (CKAE1/AE3) immunostain positivity.

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abdominal mass (35.8%) or abdominal distention (17.0%), usually accompanied by systemic symptoms including fever (26.4%), anorexia, and loss of appetite [15,21]. The alpha-fetoprotein level is usually within normal limits. Because of their rarity and nonspecific findings on imaging, diagnoses are often given as more common hepatic tumors.

Hepatoblastoma, hepatocellular carcinoma, and mesenchymal liver tumors, like infantile hemangioma and mesenchymal hamartoma, are included in the differential diagnosis of hepatic rhabdoid tumors. Hepatoblastoma presents in children less than 2 years of age, and 90% of patients with hepatoblastoma have markedly high levels of serum alpha-fetoprotein [22]. On imaging, they are often well-circumscribed, with possible lobulation and septation. They may appear heterogeneous or homogenous. The presence of calcification in more than 50% of hepatoblastoma cases is a useful distinguishing feature [32]. CT and MRI will reveal a complicated cystic mass with septal and solid stromal enhancement if a mesenchymal hamartoma is present. Peripheral globular/nodular enhancement in the arterial phase is characteristic of cavernous hemangiomas on dynamic CT/MRI [33].

In the present case, immunohistochemistry results confirmed the diagnosis of rhabdoid tumor, as these cells showed a lack of alpha-fetoprotein, which is a marker of hepatoblastoma. It is noteworthy to mention that several genes encoding subunits of the SWI/SNF complex, including SMARCB1, show frequent mutations in a variety of cancers, like ovarian, lung, liver, pancreas, kidney, and brain cancers. The gene associated with rhabdoid tumors was named BAF47 due to its approximate molecular weight of 47 Kd [34]. Loss of function in SMARCB1/INI1 has been observed in a group of SMARCB1/INI1-deficient neoplasms. Somatic alterations, mainly deletions, in the SMARCB1 gene accompanying loss of expression were identified as a molecular marker of MRTs [35,36]. However, in our patient, the cells demonstrated a lack of muscle markers expression and a loss of nuclear INI-1 protein in these cells.

For the treatment and follow-up, our patient was transferred to another center. However, the survival rate of these patients with recommended chemotherapy is very low due to the poor outcomes (days to a few months) [1,8].

Conclusions

While MRTs are extremely rare and highly aggressive, with poor prognosis, they should be included in the differential diagnosis to assist with early diagnosis and treatment. In the liver, they can resemble hepatoblastoma and mesenchymal liver tumors, which highlights the importance of combined imaging, pathology with immunohistochemistry, and laboratory correlation. This report emphasizes the use of diagnostic imaging and histopathology analysis to diagnose an uncommon pediatric tumor, like MRT.

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Department and Institution Where Work Was Done

Department of Pathology, An-Najah National University Hospital, Nablus, Palestine.

Declaration of Figures' Authenticity

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