

Mesenchymal Hamartoma of the Liver in an Infant With Beckwith-Wiedemann Syndrome: A Rare Condition Mimicking Hepatoblastoma

Lucas F. Abrahao-Machado, MD^{1,2}, Fabiane C. de Macedo, MD^{2,3}, Carlos Dalence, MD⁴, Glenn Stambo, MD⁵, Eduarda F. Abrahao-Machado, MD⁶, Elaine C.F. Abrahao-Machado, MD⁷, Armita Bahrami, MD², and Antonio G. Nascimento, MD²

¹Department of Pathology, Barretos Cancer Hospital, Barretos, São Paulo, Brazil

²Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN

³Department of Pathology, Hospital Federal de Ipanema, Rio de Janeiro, Brazil

⁴Department of Pathology, St. Joseph's Hospital, Tampa, FL

⁵Department of Radiology, St. Joseph's Hospital, Tampa, FL

⁶Jundiaí Medical College, Jundiaí, São Paulo, Brazil

⁷Catholic University of Campinas, Campinas, São Paulo, Brazil

Abstract

Patients with Beckwith-Wiedemann syndrome (BWS) are known to be at an increased risk for childhood malignancies, particularly Wilms tumor and hepatoblastoma. We report a case of genetically confirmed BWS in a 5-month-old girl who presented with a 9.5-cm abdominal mass associated with elevated α -fetoprotein levels. The clinical impression was strongly suggestive of hepatoblastoma. Histologic examination of the surgically excised mass revealed mesenchymal hamartoma of the liver (MHL), a benign hepatic neoplasm.

Introduction

Beckwith-Wiedemann syndrome (BWS) is a heterogeneous condition classified as an overgrowth syndrome and is characterized by macrosomia, macroglossia, abdominal wall defects, hemihypertrophy, and ear anomalies.¹⁻⁵ Children with BWS have an increased risk for embryonic tumors, mainly Wilms tumor and hepatoblastoma.^{1,6,7}

Case Report

A 5-month-old female infant with known Beckwith-Wiedemann syndrome (BWS) was admitted following episodes of diarrhea and the discovery of an abdominal mass. The patient was born through an uneventful spontaneous vaginal delivery at 34 weeks of gestation, with a birth weight of 3,275 g (>97th percentile). Early in the postnatal period, the patient manifested hemihypertrophy, omphalocele, a “dimple” on the right ear lobe, capillary hemangioma, and persistent hypoglycemia; methylation analysis confirmed BWS.^{4,5} Serum α -fetoprotein (AFP) level was elevated at 814.3 ng/mL. Abdominal ultrasound (US) confirmed a large heterogeneous mass in the upper abdomen, displacing regional structures. Computed tomography (CT) and magnetic resonance imaging (MRI) suggested that the mass originated from the liver, measuring 8.8 x 8.4 x 7.7 cm (Figure 1). These clinical and laboratory findings suggested the mass was a hepatoblastoma.

Exploratory laparotomy and excision of the abdominal mass found a 268-g, 9.5 x 7.0 x 5.0-cm well-circumscribed cystic mass with a smooth, pink-tan and glistening external surface (Figure 2). On sectioning, the mass

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Correspondence: Lucas F. Abrahao-Machado, Rua Antenor Duarte Villela, 1331, Barretos, 14784-400, São Paulo, Brazil (lucasfariamachado@yahoo.com).



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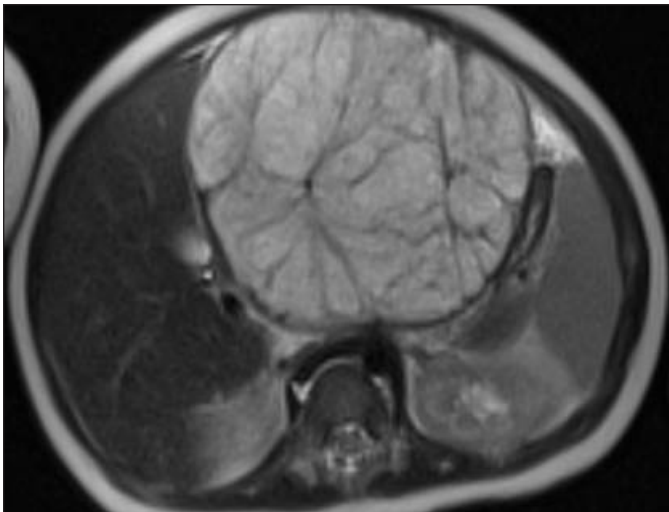


Figure 1. Abdominal magnetic resonance imaging (T2) demonstrates a large mass in the anterior upper abdomen.

was predominantly cystic with a variegated red to white-tan gelatinous cut surface containing multiloculated cystic and lobulated solid areas (Figure 2). The tumor was predominantly composed of a mesenchymal component with a vaguely lobulated and myxoid appearance, containing stellate fibroblasts and thin-walled blood vessels. Within the loose mesenchymal tissue, particularly at the periphery of the lesion, there were entrapped cords of hepatocytes (Figure 3). Atypical epithelial elements were not present, and no heterologous differentiation was seen in the mesenchymal component. Small foci of extramedullary hematopoiesis were present within the tumor (Figure 4).

Discussion

Children with BWS are at a 7.5–10% risk of developing several types of tumors, mainly embryonic malignancies that vary based on the genetic alterations involved.^{1,6,7} The most

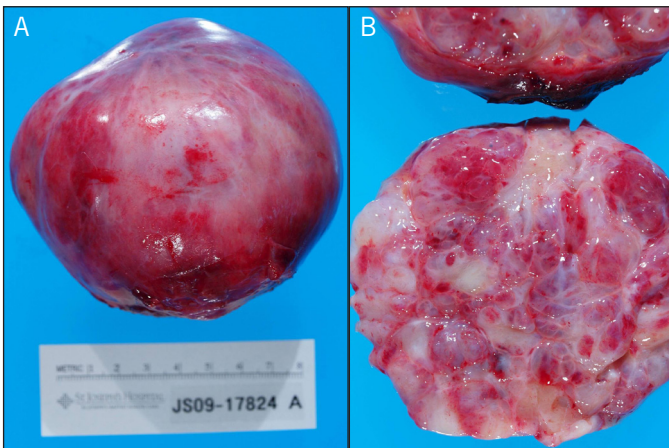


Figure 2. The mass shows (A) a smooth and glistening external surface, and (B) a multiloculated cystic and solid appearance on cut section.

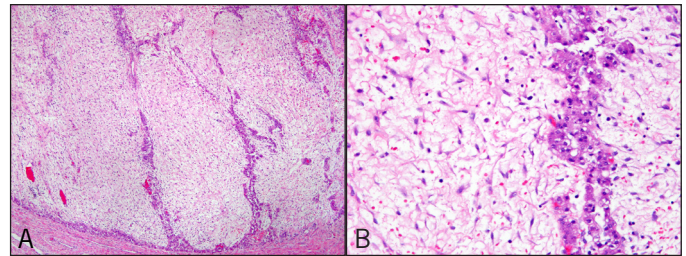


Figure 3. (A) Entrapped cords of immature hepatocytes in a myxoid stroma (100x). (B) A group of small hepatocytes in detail within the loose myxomatous stroma.

common tumors seen in these patients are Wilms tumor and hepatoblastoma, and less frequently, rhabdomyosarcoma, adrenal cortical carcinoma, and neuroblastoma.⁶⁻⁸ The majority of the tumors occurs before age 4 years and only rarely develop after the first decade of life.¹ With positive findings, focused investigation for an underlying tumor should be undertaken in consultation with a pediatric oncologist.¹ AFP can be measured periodically to age 4 years for early detection of hepatoblastoma.^{7,9}

The association between BWS and benign hamartomatous tumors is rare,^{3,10} and there are only 2 other cases of MHL in patients with BWS previously described in the literature, neither of which had a confirmed diagnosis of BWS by molecular analysis.^{11,12} Of note, one of the reported cases did not meet all the clinical diagnostic criteria for the syndrome.

MHL is an uncommon tumor, accounting for just 6% of pediatric liver tumors.¹³ It presents with an upper abdominal mass or abdominal swelling that varies in size from a few centimeters to up to 30 cm.¹⁴ There is no specific laboratory marker for MHL. Serum AFP levels can be elevated, but other liver function tests usually remain normal.^{13,15,16} Although the serum AFP in patients with BWS may be higher than in normal children, the serum level in our patient was beyond the expected baseline range in these patients, causing concern for hepatoblastoma.^{1,3} On imaging studies, MHL often appears as a nonspecific heterogeneous solid-cystic tumor that may be mistaken for hepatoblastoma, particularly when cysts are absent.¹⁶⁻¹⁸ The characteristic histopathologi-

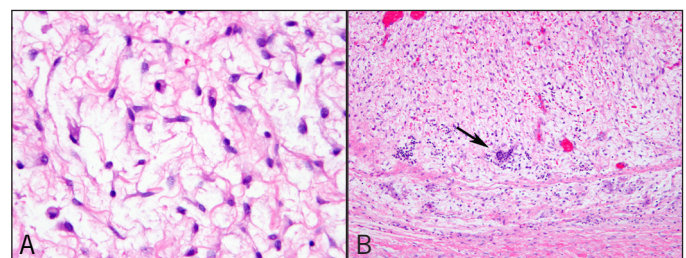


Figure 4. (A) The mesenchymal component composed of bland spindled to stellate cells at high magnification. (B) Foci of extramedullary hematopoiesis.

cal features consist of mesenchymal and epithelial (hepatocytes) components without atypia.¹⁴ However, if the groups of hepatocytes are abundant and large in size, MHL may resemble other tumors (such as hepatoblastoma), particularly in small biopsies.¹⁸ Hence, a generous sample of the tumoral tissue is essential for the correct diagnosis. MHL is a benign tumor with excellent outcome following surgery, and malignant transformation in MHL is rare.^{13,19}

It is not clear whether patients with BWS are more likely to develop MHL compared to healthy children. The molecular characteristics of BWS, mainly alterations involving 11p15 chromosomal region, do not seem to be related to cytogenetic abnormalities of MHL.^{20,21} Although the presence of a liver mass in children with BWS with a high serum AFP should be concerning for hepatoblastoma, other tumors of the liver including MHL should be considered in the differential diagnosis in such patients. Tissue diagnosis, therefore, is mandatory for proper management plan, even in the presence of high clinical suspicion for a malignant process.

Disclosures

Author contributions: LF Abraham-Machado participated in the histopathological analysis, developed and led the overall manuscript, and is the article guarantor. FC de Macedo assisted with the histopathological analysis and manuscript preparation. C. Dalence assisted with clinical diagnosis and pathological analysis and provided clinical data. G. Stambo provided the radiological images. EF Abraham-Machado, ECF Abraham-Machado, and A. Bahrami revised the manuscript. A. Nascimento is the senior author and participated in the histopathological diagnosis.

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