

## KAZUISTIKA

# Infantile hepatic hemangioendothelioma

## *Jaterní infantilní hemangioendotelium*

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### SUMMARY

**Unzeitig M, Hladík M, Bajčiová V, Skotáková J, Tůma J, Ježová M, Mottl H. Infantile hepatic hemangioendothelioma**

Infantile hepatic hemangioendothelioma (IHH) is a rare, benign vascular tumor that originates from mesenchymal tissue in the liver. Although IHH is benign, it may develop life-threatening complications. We describe a 5-week-old female with a tumorous mass in the right hepatic lobe. Imaging methods pointed to an IHH diagnosis, but we could not rule out hepatoblastoma. Due to the risk of life-threatening complications, the tumor was surgically removed. Histological analysis confirmed the diagnosis of IHH.

**Key words:** hepatic hemangioendothelioma, hemangioendothelioma of the liver, infantile hemangioendothelioma, hemangioendothelioma in infants

### SOUHRN

**Unzeitig M, Hladík M, Bajčiová V, Skotáková J, Tůma J, Ježová M, Mottl H. Jaterní infantilní hemangioendotelium**

Jaterní infantilní hemangioendotelium je vzácný benigní vaskulární tumor pocházející z mezenchymální tkáně jater. Přestože jde o nádor benigní, může způsobit až život ohrožující komplikace. V této kazuistice popisujeme případ 5týdenního kojence s tumorózním ložiskem v pravém jaterním laloku. Zobrazovací metody ukazovaly na diagnózu infantilního hemangioendotelium, ale přítomnost hepatoblastomu nebylo možné zcela vyloučit. Vzhledem k riziku život ohrožujících komplikací byl nádor chirurgicky odstraněn. Histologický rozbor potvrdil diagnózu infantilního hemangioendotelium.

**Klíčová slova:** jaterní infantilní hemangioendotelium, infantilní hemangioendotelium, hemangioendotelium jater

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## INTRODUCTION

Liver tumors are quite rare in children. Infantile hepatic hemangioendothelioma (IHH) is the most common benign liver tumor in infancy and the third most common liver tumor in children; however, it is rarely encountered in clinical practice. Although IHH is benign, it is also aggressive, and it may cause life-threatening complications, fulminant hepatic failure, or malignant transformation. Moreover, IHH can be readily mistaken for hepatoblastoma. Here, we describe the detection, diagnosis, and treatment of IHH in a 5-week-old infant.

## CASE REPORT

A 5-week-old girl was admitted to the hospital for a suspected liver tumor detected on an abdominal ultrasound. The birth was a normal spontaneous delivery, after 36 + 6 weeks of gestation. The Apgar score was 8-9-10, and the birth weight was 3030 g. Prior to the physical examination, she showed no symptoms, but her parents had observed excessive weight gain. During a routine physical examination, the pediatrician discovered abdominal distension. The liver margin was palpable at 1 cm below the right costal margin. Nevus flammeus lesions were also found in the frontal and parietal areas of the head and on the right ear.

A routine blood examination showed moderate anemia (hemoglobin, 90 g/l) and the platelet count was within the normal range. Liver tests were normal, apart from slightly

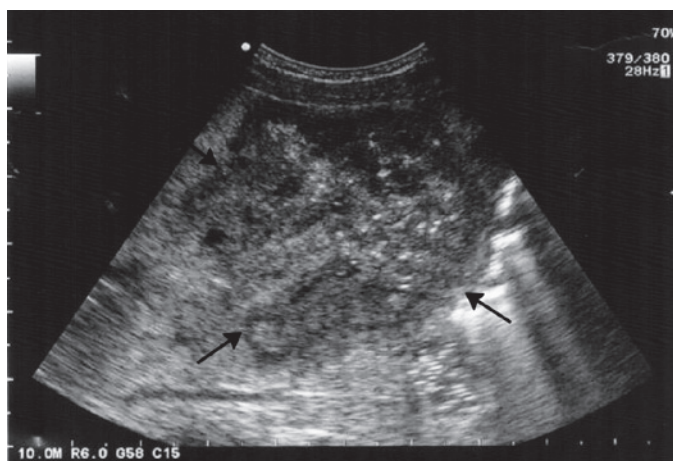


Fig. 1: Abdominal ultrasonogram shows heterogeneous hypoechoic mass (arrows) in the right lobe with numerous calcifications.

increased gamma-glutamyl transferase (1.91  $\mu$ kat/l). The thrombin time was extended to 23.2 s, and D-dimer levels were elevated to 5.88 mg/L. At 5 weeks, the alpha-fetoprotein (AFP) level was moderately elevated (8263  $\mu$ g/l).

Abdominal ultrasonography revealed extensive expansion in the right lobe of the liver. The image was dominated by a heterogeneously hypoechoic mass, and the expansion was bounded by a quite poorly defined hyperechoic rim. Numerous calcifications were also observed within the mass. Doppler imaging showed that the tumor was massively perfused with wide, regularly pulsating blood vessels (Fig. 1).

A contrast CT showed peripheral enhancement in the arterial phase and an irregular central density in the venous phase, probably due to calcifications, hemorrhage, and necrosis (Fig. 2).

An unenhanced MRI showed a bulky tumor located in the right lobe of the liver, which pressed caudally on the right kidney and medially on the inferior vena cava. After intravenous gadolinium administration, a dynamic MRI demonstrated early peripheral enhancement of irregularly-shaped nodes, with delayed centripetal filling in the central region (Fig. 3).

These images pointed to a diagnosis of IHH, but hepatoblastoma could not be ruled out. In hepatoblastoma, AFP levels are typically elevated, and this tumor showed moderate AFP elevation. A liver biopsy was considered unsafe, due to the high risk of life-threatening bleeding. Thus, we decided to perform a right-sided hemihepatectomy with cholecystectomy.

Histologically, the tumor was relatively poorly defined and infiltrative, and vascular spaces of varying sizes dominated. The vessels were lined with plump endothelial cells with no evidence of hyperchromasia. The vessels were supported by a hypocellular myxoid stroma that contained chaotically distributed bile ductules. Among the blood vessels, we observed plentiful calcifications, pockets of extramedullary hematopoiesis, signs of hemorrhage, and sporadic

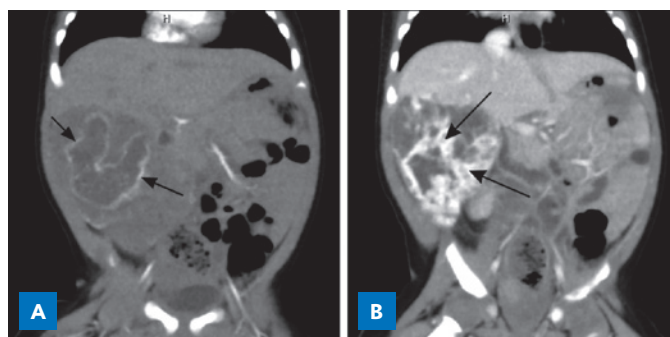


Fig. 2: CT images of infant abdomen. A – Contrast CT in the arterial phase shows hypodense liver mass with peripheral enhancement (arrows). B – In the venous phase, the central area of the mass is filled with hyperintense material (arrows), irregular due to calcifications, hemorrhage, and necrosis.

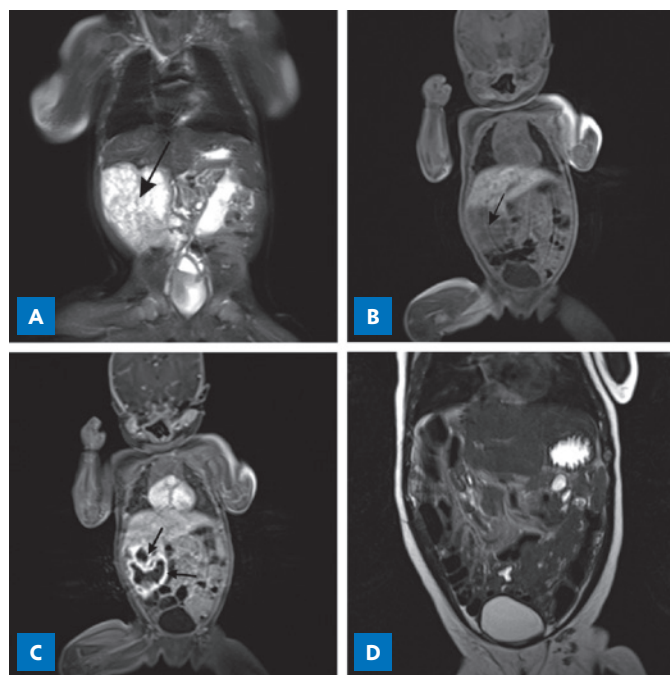
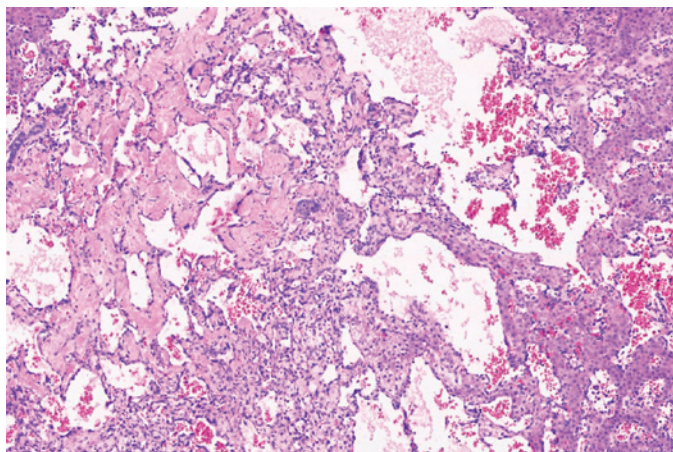


Fig. 3: MRI images of infant abdomen before and after treatment. A – T2-weighted MR image demonstrates a large hyperintense mass. B – Hypointense mass on T1-weighted images. C – MR imaging after administration of gadolinium shows peripheral enhancement with absence of gadolinium in the center of the mass. D – MR imaging month and a half after surgery shows no recurrence.

thrombosis. These vessels showed no GLUT1 (glucose transporter 1) immunoreactivity. Therefore, the histological analysis confirmed the diagnosis of IHH type 1 (GLUT1-negative; Fig. 4).

The infant recovered well post-operatively. A control MRI, performed one and a half month post-surgery, showed no recurrence.



**Fig. 4: Vascular lesion with indistinct margins. It is composed of capillary-type vessels and irregular dilated vessels within fibrotic scar-like stroma and entrapped hepatocytes and bile ducts (hematoxylin-eosin, 50×).**

## DISCUSSION

IHH is a benign tumor derived from the mesenchymal tissue of the liver, and it occurs in girls twice as often as it occurs in boys. In 85% of cases, the tumor manifests within the first six months of life.<sup>(1)</sup> The center of the tumor harbors areas of necrosis, thrombosis, and calcification.<sup>(2,3)</sup> Clinical and laboratory findings are non-specific, and a liver biopsy is often not recommended, due to the risk of life-threatening bleeding.<sup>(4)</sup>

The most common symptoms of IHH are abdominal distension, a palpable mass, and hepatomegaly. Other symptoms include skin hemangiomas, anemia, thrombocytopenia, jaundice, hypothyroidism accompanied by elevated TSH levels, failure to thrive, poor feeding, and intestinal obstruction. Life-threatening complications can also develop, such as arteriovenous shunts within the tumor that lead to congestive heart failure and Kasabach-Merritt syndrome (consumptive coagulopathy caused by trapped thrombocytes).<sup>(5)</sup> Other complications include tumor rupture with secondary shock, fulminant hepatic failure, or a malignant transformation into angiosarcoma.<sup>(6)</sup>

There are two types of IHH. Type I IHH comprises variable-sized vascular channels lined with a single layer of plump, immature endothelial cells. The supporting fibrous stroma contains chaotically distributed bile ductules.<sup>(7)</sup> Often, calcification and pockets of extramedullary hematopoiesis are present. Type II IHH has a more disorganized appearance, and the vascular spaces are lined with larger, pleomorphic cells with hyperchromatic nuclei. No bile ductules are present in type II.<sup>(8,9)</sup>

Mo et al.<sup>(10)</sup> classified IHH according to positive and negative GLUT1 immunoreactivity in endothelial cells. GLUT1-positive IHH is characterized by multiple small nodules without vascular malformation, arteriovenous shunting, or

calcification. Moreover, in many cases, the tumor responds to corticosteroid and interferon treatment. GLUT1-negative IHH is characterized by a single large mass with central necrosis, large abnormal vessels, hemorrhagic areas, and calcification. Compared to GLUT1-positive IHH, GLUT1-negative IHH more frequently evolves to cardiomegaly, anemia, congestive heart failure, and coagulopathy. Conservative treatment typically has no effect, and surgical intervention is necessary.

The main imaging modalities for diagnosing IHH include abdominal ultrasonography, CT, and MRI. An abdominal ultrasound typically reveals a solid, well defined, hypoechoic or isoechoic lesion, accompanied by hyperechoic calcifications.<sup>(11)</sup> When substantial arteriovenous shunts are present, anechoic regions may be observed with detectable flow.<sup>(7)</sup> MRIs reveal a hypointense mass on T1-weighted images and a hyperintense mass on T2-weighted images. After administering gadolinium, the periphery is enhanced during the arterial phase, and the central area is filled after variable delays during the venous phase. CT scans typically demonstrate a well-defined hypodense mass. Contrast-enhanced CTs show an enhancement pattern similar to that observed with contrast-enhanced MRI.<sup>(2,12)</sup>

The differential diagnosis includes hepatoblastoma, metastatic neuroblastoma, mesenchymal hamartoma, cavernous hemangioma, and angiosarcoma.<sup>(9,13)</sup>

Hepatoblastoma is the most common primary hepatic neoplasm that typically occurs in the first 2 years of life. This malignant, embryonic tumor typically forms a large solitary lesion in the right liver lobe, accompanied by highly elevated AFP levels.<sup>(14)</sup> The imaging features and clinical findings of a hepatoblastoma and IHH may be similar, which makes differentiation difficult.<sup>(6)</sup> For this tumor, surgical resection is the most important part of the treatment.

IHH treatment is based on imaging findings. Conservative therapy commonly includes steroids and  $\alpha$ -interferon to accelerate the natural involution of the tumor. Surgical resection is typically indicated when life-threatening symptoms are present, or when the mass cannot be radiologically distinguished from malignancy. Xin Long et al.<sup>(4)</sup> recommended a hepatectomy in patients with high AFP, even in the absence of symptoms. An unresectable IHH may become resectable after medical therapy. Hepatic artery embolization is considered for patients that fail to respond to medical treatment and are not candidates for surgery. A liver transplant is possible as a last resort.<sup>(4,14,15)</sup>

In conclusion, solitary liver tumors in infants under 1 year old are not always associated with a hepatoblastoma. Symptoms and laboratory findings of IHH are typically non-specific, and life-threatening complications may appear. Imaging methods provide the basis for a differential diagnosis of this tumor. Lack of experience with this tumor leads to different treatment approaches. Conducting a GLUT1 immunoreactivity screening in endothelial cells could provide the needed insight in determining further treatment. |

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