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## Case Report

# Symptomatic congenital hemangiomatosis in a neonate: Imaging of a life-threatening presentation with multifocal liver involvement<sup>☆</sup>

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## ABSTRACT

Hemangiomas are the most common benign vascular neoplasms of infancy. Congenital hemangiomas proliferate in utero, and are fully formed at birth. They are usually solitary. Generalized forms are exceptional. The liver is the second most common site of hemangiomas after the skin. When >5 cutaneous hemangiomas are present, screening abdominal ultrasound is recommended. Based on the degree of liver parenchyma involvement, 3 hepatic hemangiomas' subtypes are defined: focal, multifocal, and diffuse. Hepatic hemangiomas' clinical presentation varies from asymptomatic to life-threatening. High output cardiac failure, consumptive coagulopathy, abdominal compartment syndrome, and liver dysfunction are possible complications. We report an unusual case of symptomatic congenital hemangiomatosis in a male infant born with innumerable generalized cutaneous hemangiomas whose screening abdominal ultrasound revealed multifocal hepatic hemangiomas with extensive mixed shunts. We aim to highlight this unique entity with severe associated complications and stress the role of imaging at initial presentation, for follow-up, and to guide therapeutic choices.

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## Background

Congenital hemangiomas are benign endothelial neoplasms with unknown precise incidence. They proliferate in utero and are fully formed at birth. Their natural evolution follows one of three patterns: RICH (rapidly involuting by 2 years of age), PICH

(partially involuting), and NICH (noninvoluting: grow in proportion to the patient). Congenital hemangiomas stain negative for Glut-1 [1,2]. Usually solitary, congenital hemangiomas exceptionally present a generalized distribution [2]. Hemangiomas' diagnosis is based on the patient's history, physical examination, and imaging. Pathological confirmation is rarely needed [1].

Abbreviations: RICH, Rapidly involuting congenital hemangioma; PICH, Partially involuting congenital hemangioma; NICH, Noninvoluting congenital hemangioma.

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**Fig. 1 – Clinical appearance of the patient: Multifocal cutaneous papules (Black arrows) and nodules (Black circles).**

Since the liver is the most commonly involved site following the skin, once >5 cutaneous hemangiomas are present screening abdominal ultrasound is recommended [3]. The degree of liver parenchyma involvement differentiates three hepatic hemangiomas' subtypes: focal, multifocal, and diffuse. Associated shunting and high flow features' reporting is crucial [1].

Most congenital hepatic hemangiomas are unifocal [3]. Hepatic hemangiomas' clinical presentation varies from innocuous to life-threatening. The overall mortality of asymptomatic hepatic hemangiomas is high. Focal asymptomatic forms are managed conservatively with sonographic surveillance whereas symptomatic lesions with significant shunting receive  $\beta$  blockers and/or corticosteroids. When pharmacological therapy fails, embolization/surgery is indicated [2,3]. We report an unusual case of symptomatic congenital hemangiomatosis in a male infant born with innumerable generalized cutaneous hemangiomas whose screening abdominal ultrasound revealed multifocal hepatic hemangiomas with extensive mixed shunts. Our aim is to highlight this entity with possible severe complications and stress the role of imaging at initial presentation, for follow-up and to guide therapeutic choices.

### Case presentation

A 23-day-old boy born at 35 weeks of gestation with innumerable cutaneous hemangiomas (Fig. 1) was referred to our radiology department for screening hepatic and transfontanellar ultrasound. Pregnancy screening US exams were not performed.

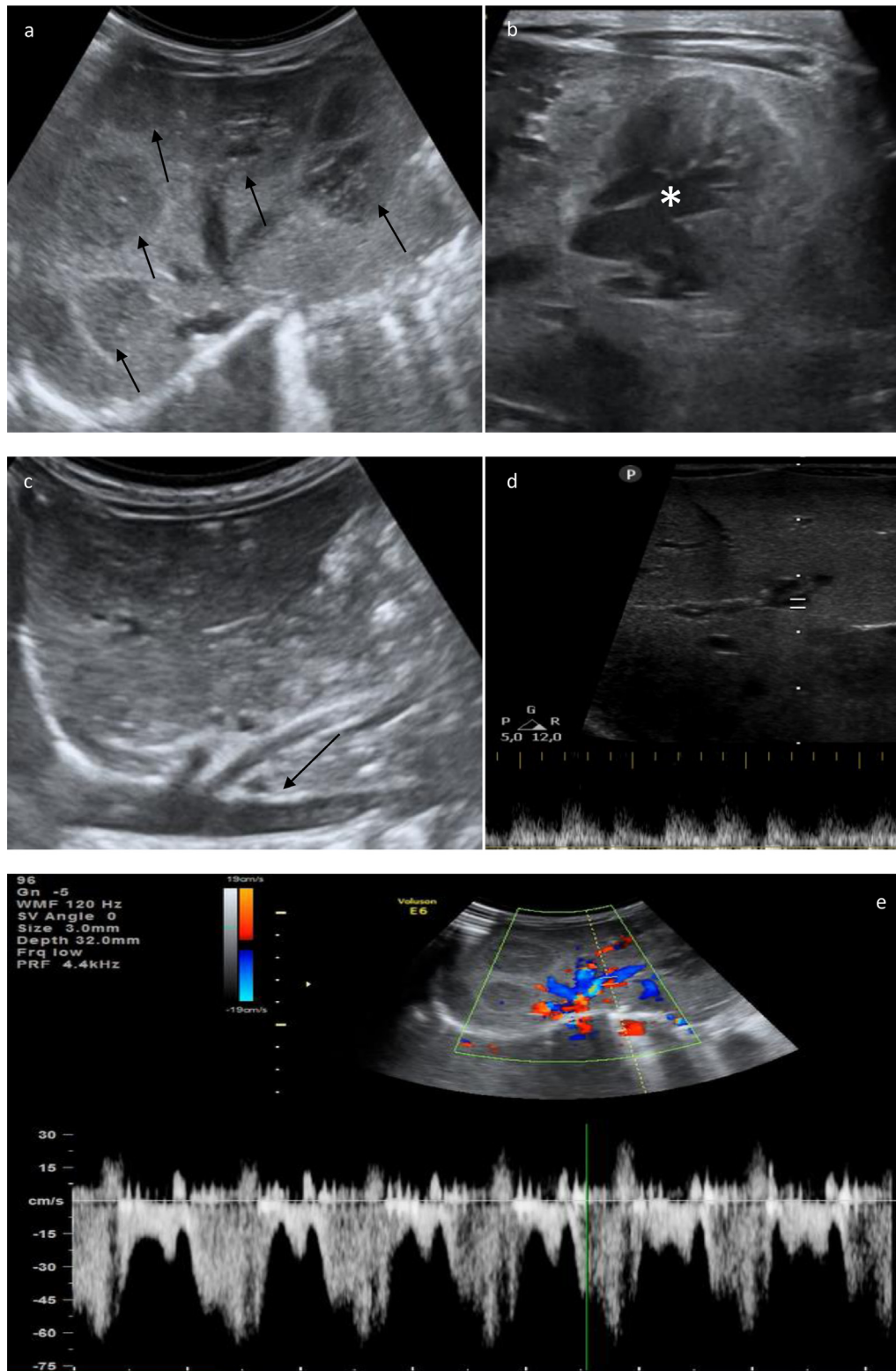
On initial physical examination respiratory and heart rates were normal, and the liver margin was palpable approximately 3 cm below the right costal margin.

Ultrasound scanning of the abdomen revealed an enlarged liver measuring 7.5 cm in the sagittal plane with a heterogeneous echostructure. Multiple well-defined spherical hypoechoic nodules to tumors with central varices, and direct shunts between dilated peripheral portal and hepatic veins were identified (Fig. 2 a,b). Sagittal images of the upper abdomen showed tapering of the aorta distal to the celiac axis (Fig. 2c). Doppler interrogation of portal branches showed an arterial waveform (Fig. 2d). Velocities in the hepatic veins were increased (Fig. 2e).

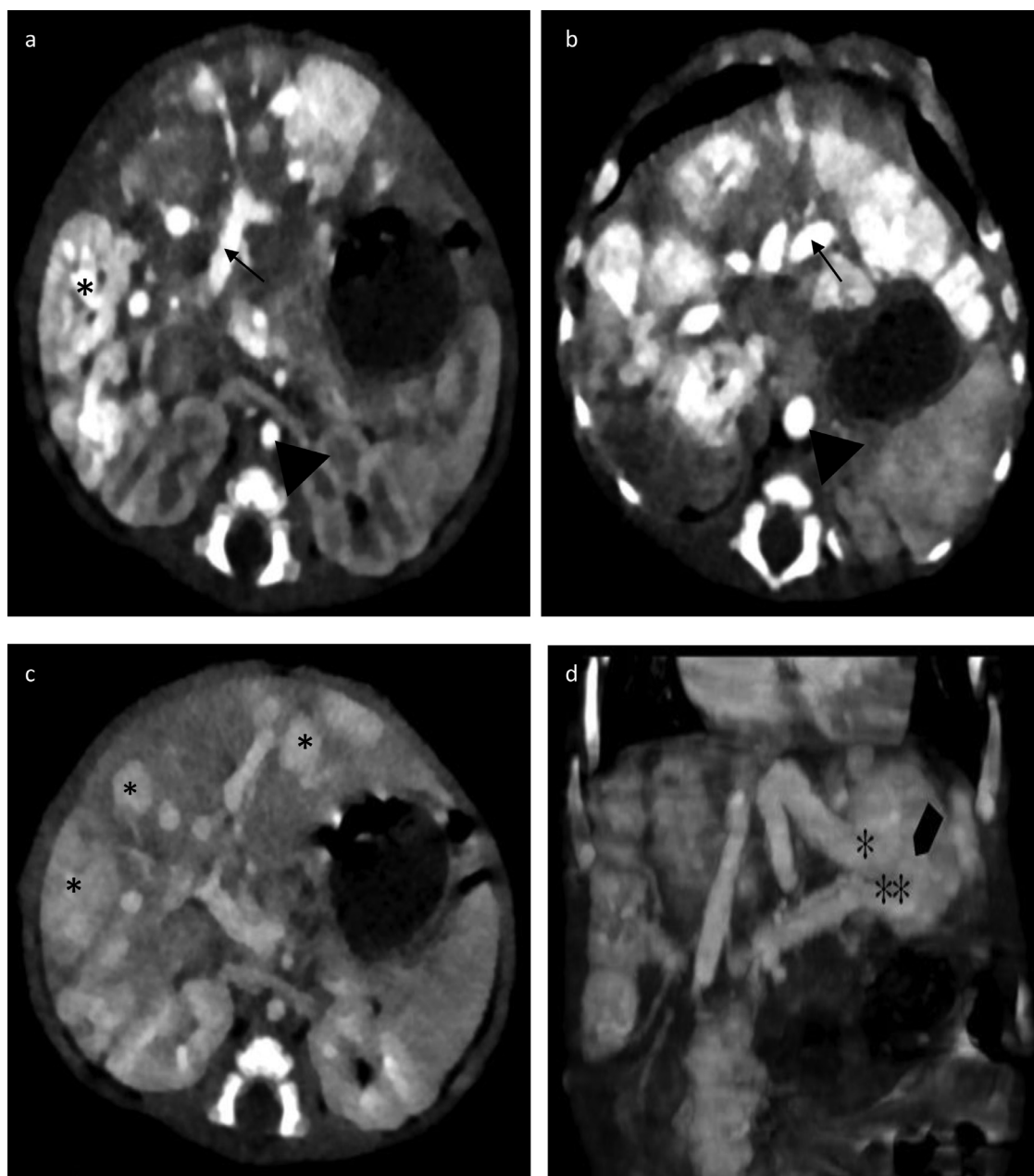
The transfontanellar ultrasound showed no abnormalities. Echocardiography revealed a type IIa 4 mm perimembranous ventricular septal defect with left to right shunting, left atrial and left ventricular enlargement, and normal cardiac function.

Abdominal contrast-enhanced CT was performed. Nodules and tumors were hypodense compared with the liver before contrast medium administration. In the arterial phase, the nodules and tumors presented avid peripheral enhancement and large enhancing central varices (Fig. 3a). On the portal phase, the entire lesions showed uniform enhancement (Fig. 3c). CT showed evidence of high flow with dilatation of the proximal abdominal aorta, hepatic arteries and veins, and a reduced size of the infra-hepatic aorta. Early filling of the portal and hepatic venous branches was suggestive of associated arteriportal and arteriovenous shunting (Fig. 3a, b). Intrahepatic portosystemic venous shunts were also identified (Fig. 3d).

The patient was started on propranolol, diuretics, and potassium supplementation.



**Fig. 2 – (a)** Transverse liver ultrasound image shows multiple well-defined rounded hypoechoic nodules to tumors with an echogenic rim (Black arrows). **(b)** Transverse liver ultrasound image shows a hemangioma with a central varix (White asterix). **(c)** Sagittal ultrasound image of the upper abdomen shows tapering of the abdominal aorta below the superior mesenteric artery (Black arrow). **(d)** Doppler interrogation of a segmental portal vein shows an arterialized waveform. **(e)** Spectral waveform of the left hepatic vein showing increased velocities.



**Fig. 3 – (a) An axial contrast-enhanced CT image of the upper abdomen in the arterial phase showing multiple spherical liver hemangiomas with strong peripheral enhancement and large enhancing central varices (Black asterisk). Early enhancement of the portal vein branches is noted (Black arrow). (b) An axial contrast-enhanced CT image showing early filling of the hepatic veins in the arterial phase (Black arrow). (c). An axial contrast-enhanced CT image of the upper abdomen in the portal phase showing multiple uniformly enhancing liver hemangiomas (Black asterisks). (d). A coronal contrast-enhanced CT image showing a hemangioma with a large enhancing central varix and direct shunt (black arrow) between the dilated left hepatic (\*) and portal veins (\*\*).**

Clinical deterioration was rapidly noted. The patient developed jaundice, dyspnea, and perioral cyanosis when crying.

Laboratory tests results were as follows: PTA 65% (70-100%), HGB 108 g/L (103-141 g/L), MCH 30.9 pg (28-37 pg), Platelets 485.000/ $\mu$ l (150.000-420.000/ $\mu$ l), total bilirubin (BilT) 217 mg/L (2-12 mg/L), BilD 132 mg/L (0-5 mg/L), AST 564 U/L (5-34 U/L), and ALT 175 U/L (0-55 U/L).

An abdominal ultrasound was performed and showed a slight volumetric reduction of the hepatic hemangiomas. Signs of high blood flow persisted.

Corticosteroids were initiated. The patient received low flow oxygen, diuretic therapy, fluid restriction, and ferrous supplementation.

No improvement was noted, and the patient regrettably died.

## Discussion

We report an unusual case of symptomatic congenital hemangiomas with multifocal cutaneous and hepatic involvement. Congenital hemangiomas' generalized forms are exceptional [2]. Screening abdominal ultrasound is recommended once > 5 cutaneous hemangiomas, a cutaneous hemangioma measuring >5 cm or a segmental hemangioma are present [3]. Other organs' hemangiomas involvement has been documented: trachea, lungs, adrenals, dura, and others more [4]. Glut-1 is infantile hemangiomas' specific histologic marker. Infantile hemangiomas proliferate after birth then involute gradually until three to nine years of age [1]. In the liver, lesions' distribution determines three subtypes: focal, multifocal and diffuse. Focal hepatic hemangiomas are assimilated to cutaneous rapidly involuting congenital hemangiomas (RICH). Multifocal and diffuse hepatic hemangiomas are related to true infantile hemangiomas [5]. In multifocal forms, multiple spherical masses are separated by normal liver, while in diffuse forms, confluent hemangiomas massively replace the liver parenchyma [3].

Liver Doppler ultrasound is the recommended imaging tool at initial presentation [1]. Hepatic hemangiomas radiologic features are specific and generally allow a confident diagnosis [1]. Classically they appear as single or multiple well-defined hypo- or hyperechoic masses. Small lesions are usually homogenous. Large lesions may present an inhomogeneous echostructure with calcifications, cystic areas, and fibrosis spaces. Spectral Doppler interrogation detects shunting and high flow features [1]. In *arterio-venous shunts*: hepatic veins and arteries are dilated, arterial resistive indices diminished, venous pulsatility and velocities augmented [3,6]. Hepatic veins present arterialized waveforms in advanced stages. *Arterio-portal shunts* demonstrate one or many direct hepatic arteries and portal vein branches fistulae with hepatic artery dilatation and low resistive indices, affected portal vein branches enlargement and arterialized flow, tapered abdominal aorta below the celiac trunk. *Porto-systemic shunts* are an abnormal tortuous portal to hepatic veins communications with flow turbulence on color doppler analysis and pulsatile bi- or triphasic porto-mesenteric veins waveforms. Contrast-enhanced sonography shows rapid peripheral nodular lesions' enhancement with later concentric progression [3].

On unenhanced CT, hepatic hemangiomas usually appear well-defined and hypodense. Dynamic contrast-enhanced computed tomography demonstrates early peripheral enhancement with progressive centripetal filling. Small lesions show avid uniform enhancement. Focal hepatic hemangiomas usually appear heterogenous and present variable enhancement patterns. They may contain calcifications and show central necrosis, thrombosis or bleeding [4,7]. Radiation exposure is CT's major disadvantage in infants.

On MRI, hemangiomas are hypointense in regards to the normal liver on T1-weighted sequences and hyper-intense on T2-weighted images. T1 hyperintensities in hemangiomas generally correspond to bleeding. Post-contrast dynamic acquisition images show early nodular peripheral enhancement which progresses centripetally on delayed phases. T1 and T2 weighted images' central foci of dark signal represent fibro-

sis, a potential cause of inhomogeneous appearance due to incomplete filling. On delayed imaging with hepato-biliary contrast, hemangiomas tend to appear hypointense [3].

Dynamic contrast-enhanced CT and MRI high flow and concomitant shunts features include tapering of the aorta, hepatic arteries/veins dilatation, early arterial phase portal branches and hepatic veins enhancement characteristic of arterio-portal and arteriovenous shunts, abnormal communications between the portal and hepatic veins related to intra-hepatic portosystemic fistulae [6,7]. When present, these features indicate an echocardiogram [3].

Hepatic hemangiomas' focal forms' main differential diagnoses include hepatoblastoma, mesenchymal hamartoma, and sarcoma while multifocal forms are to be discriminated from metastatic neuroblastoma [3,4]. Discrimination is based on the following elements: enhancement pattern, unremarkable adrenal glands, ZuckerKandel organs, and para-spinal chains, lack of invasion and lymphadenopathy, absence of alpha-fetoprotein rising and urinary catecholamines [8].

Our patient's imaging findings corresponded to multifocal hepatic hemangiomas with concomitant mixed shunts (arterio-portal, arterio-venous, and portosystemic). MRI was not performed because of unavailability. Echocardiography revealed an associated ventricular septal defect. Coexistent congenital malformations (heart defects, biliary anomalies, renal agenesis, hemihypertrophy ...) have been scarcely reported [4]. Hepatic hemangiomas' diagnosis can be made prenatally for the congenital form, incidentally, or in the presence of complications. Multifocal and diffuse hepatic hemangiomas yield the highest risk of complications with a high mortality rate (up to 53.8%) [4]. Congenital hemangiomas' possible complications include high output cardiac failure, intratumoral bleeding, and consumptive coagulopathy. Infantile hemangiomas can cause: cardiac and liver failure, hypothyroidism, abdominal compartment syndrome, and growth retardation [3].

Management is based on hepatic hemangiomas' subtype (focal, multifocal, or diffuse), size, flow/shunting assessment, and severity of concomitant complications [3,4]. Asymptomatic hepatic hemangiomas with no significant hemodynamic shunting are monitored with serial ultrasounds according to a recommended initial 2-week period [3,4]. Following every stable examination, two weeks are added to the surveillance interval. Observation is continued until stable size and vascularity are noted twice in succession for congenital hemangiomas. For infantile hemangiomas, monitoring continues until complete involution [3]. Symptomatic patients initially receive pharmacologic treatment, propranolol being the current gold-standard. Combining propranolol and corticosteroids may be useful. When pharmacologic therapy fails, radiological (hepatic artery embolization) or surgical intervention (hepatic artery ligation, resection, partial or complete liver transplantation) is indicated [4].

Despite early pharmacological treatment initiation and optimization, unresponsiveness and rapid clinical deterioration were noted with cardiac and liver dysfunctions onset due most likely to the extensive high flow mixed shunting and associated ventricular septal defect in our patient's case.

In conclusion, congenital cutaneous hemangiomas with associated multifocal hepatic disease is a rare scenario with potentially life-threatening complications.

Hepatic hemangiomas' evolution pattern imitates its cutaneous homonym. Doppler ultrasound screening for liver involvement once >5 skin hemangiomas are present is recommended and allows earlier detection and intervention. Imaging studies play a pivotal role at initial presentation and for follow-up. A biopsy is only required when there is diagnostic uncertainty. Reporting the following elements: focal/multifocal/diffuse, intratumoral bleeding/calcifications/necrosis, enhancement pattern, and high flow/shunting features guarantees diagnostic accuracy, predicts the clinical course, and guides therapeutic interventions.

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### Patient Consent Statement

Written, informed consent was obtained from the patient's guardian.

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### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.radcr.2022.05.071](https://doi.org/10.1016/j.radcr.2022.05.071).

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