

# Hereditary hemorrhagic telangiectasia of liver: Pathophysiology with role of radiology in diagnosis and treatment

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## Abstract

Hereditary hemorrhagic telangiectasia (HHT) or Osler–Weber–Rendu syndrome is a rare condition which can result in significant *systemic and hepatobiliary* abnormalities. Liver involvement in HHT consists primarily of the consequence of various intrahepatic shunts. Even though these vascular shunts are present in the majority of patients with HHT, symptoms occur only in *minority* with clear predilection to *female gender*. The symptoms and imaging findings of liver vascular malformations can be easily overlooked or misdiagnosed which can result in delay in treatment or potentially harmful vascular interventions. In this case report, we discuss the pathophysiology of HHT in liver involvement, role of imaging in diagnosis, and the possible role of interventional radiologist in the treatment.

**Key words:** Embolization for shunt reduction; hereditary hemorrhagic telangiectasia; intrahepatic shunts; liver vascular malformation

## Introduction

Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant disorder seen approximately in one in 5000–8000 individuals.<sup>[1]</sup> It presents with vascular malformations (VM) in the nose, skin, liver, gastrointestinal tract, brain, and lung. Telangiectasia is the VM seen in HHT where there is direct communication between the arterioles and venules without the intervening capillaries. This abnormal communication can result in shunts between various vascular beds in the solid organs and hollow viscera. Definitive clinical diagnosis of HHT can be made based on the presence of at least three of four Curacao criteria,<sup>[2]</sup> published in 2000. They are 1. Epistaxis, 2. Cutaneous or mucosal VM, 3. Presence of visceral telangiectasia,

and 4. Positive family history. Liver involvement is seen in approximately 75% of people with HHT.<sup>[2]</sup> Although only a small 8%–10% of these patients develops symptomatic liver pathology, the rest remains asymptomatic.

## Case Report

We are presenting a patient who presented with upper gastrointestinal (GI) bleed and epistaxis with anemia. On further evaluation, she was found to have telangiectasia in the nose and multiple angioectasias in the stomach and in the duodenum in upper GI endoscopy. This

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**Cite this article as:** Viyannan M, Balalakshmoji D, Leelakrishnan V. Hereditary hemorrhagic telangiectasia of liver: Pathophysiology with role of radiology in diagnosis and treatment. Indian J Radiol Imaging 2020;30:98-101.

**Received:** 03-Sep-2019

**Revised:** 24-Nov-2019

**Accepted:** 11-Feb-2020

**Published:** 30-Mar-2020

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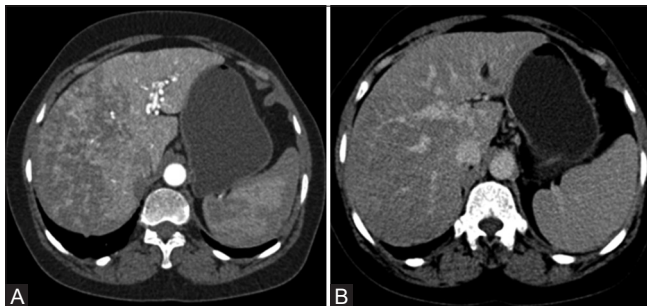
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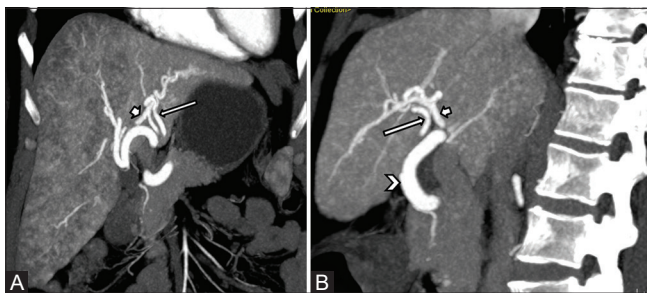
triad of findings, 1. Spontaneous recurrent epistaxis, 2. Telangiectasia of nose, and 3. Visceral telangiectasia, fulfill 3 Curacao criteria to qualify for definitive diagnosis of HHT. Further evaluation with contrast-enhanced computed tomography (CECT) was done to rule out chronic liver parenchymal disease. The CECT revealed heterogenous enhancement of the periphery of the liver in the arterial phase [Figure 1A] which becomes homogenous in the venous phase [Figure 1B]. In addition, there was moderately enlarged proper hepatic artery measuring 10 mm in diameter (normal <7 mm) and abnormally dilated intrahepatic branches of the hepatic artery and early filling of the portal venous branches [Figures 2A, B and 3]. There were abnormal tortuous vascular channels along the ligamentum teres with early filling of the branches of portal vein [Figures 3 and 4]. There were faintly enhancing tortuous vascular channels along the intrahepatic branches of the hepatic artery. There was slight reduction in the volume of the left lobe of liver. The surface of the liver was smooth. All these imaging features were suggestive of intrahepatic arterio-portal shunts with possible secondary chronic liver parenchyma disease. She was treated symptomatically with cauterization of the nasal telangiectasia, nasal packing, and blood transfusion for anemia. Few small telangiectasia lesions in the stomach showed active bleed during endoscopy and these lesions were treated with argon plasma coagulation.

## Discussion

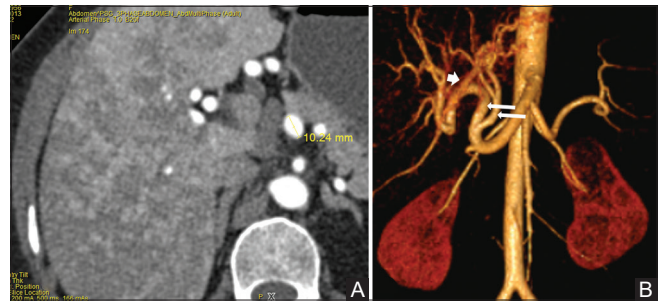
In HHT, clinical symptoms occur in approximately 8% of the people.<sup>[3]</sup> There is a distinct female preponderance in symptomatic patients, with majority of the patients presenting in their fourth decade.<sup>[3]</sup> Presenting features are secondary to high-output cardiac failure (most common),<sup>[3]</sup> portal hypertension, GI bleed either from varices due to portal hypertension or angioectasia of the mucosa of the GI tract, and biliary disease. Other less common forms of clinical presentation in the liver and GIT are portosystemic encephalopathy and abdominal angina. The basic pathophysiology in liver involvement is development of intrahepatic VMs. Liver vascularity is unique by the way of presence of dual arterial supply and presence of dormant, potential portosystemic shunts, like paraumbilical vein, which can open up in any form of disturbance in the equilibrium of liver circulation.



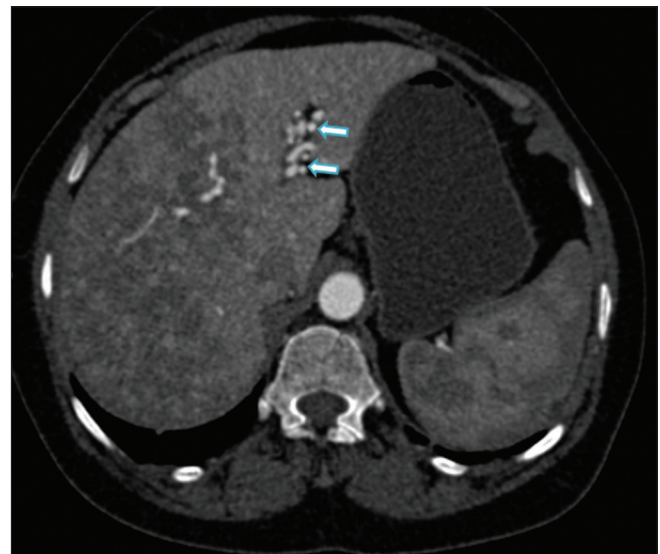
**Figure 1 (A and B):** Contrast-enhanced CT axial section shows heterogenous enhancement of the liver parenchyma in the arterial phase (A) which becomes homogenous in the venous phase (B)



**Figure 3 (A and B):** Coronal (A) and sagittal (B) maximum intensity projection (MIP) images showing enlarged hepatic artery branches—long thin arrows (in A and B)—and early filling of the portal venous branches—short thick arrow (in A and B). The enlarged main hepatic artery is marked with arrow head in B



**Figure 2 (A and B):** Axial CT image in the arterial phase acquisition (A) and 3D volume rendered image (B) showing enlarged hepatic artery proper, measuring more than 10 mm. There is enlarged proper hepatic artery and its branches (long thin arrows in B) and early filling of the portal venous branch (short thick arrow in B) seen with fuzzy margins



**Figure 4:** Axial CT image showing multiple tortuous early filling portal venous branches along the ligamentum teres (arrows) seen along with the left hepatic artery branches

The VMs in the liver can lead to three different types of vascular shunts.<sup>[3,4]</sup> These are 1. Arterio-venous (AV) shunt (between the hepatic artery and hepatic vein), 2. Arterio-portal (AP) shunt (between the hepatic artery and portal vein), and 3. Portal venous (PV) shunt (between portal vein and hepatic vein).<sup>[1]</sup> Shunts are usually extensive. The shunts can be visualized by imaging studies if they are macroscopic. Frequently they can be microscopic and not seen in imaging. Each predominant type of shunt gives rise to distinct clinical manifestation.

#### AV shunt

This is the most common symptomatic VM. It usually affects women. The presenting clinical feature is related to high-output cardiac failure.<sup>[1]</sup> AP shunt can also involve liver leading to biliary ischemia and ischemic necrosis of the bile duct<sup>[5]</sup> due to steal phenomenon. The loss of integrity of the bile duct due to ischemia can lead to biliomas and intrahepatic biliary cysts mimicking Caroli's disease. In chronic cases, *secondary sclerosing cholangitis* develops with stricture and abnormal dilatation of intrahepatic bile ducts. Biliary ischemia-related complications are seen *exclusively* in women.<sup>[3]</sup>

#### AP shunt

This is the second most common shunt after AV shunting. Shunting of blood from the hepatic artery to the portal vein causes *portal hypertension*. Secondary to portal hypertension, there can be ascites, varices formation, and GI bleed. In addition, there can be formation of focal nodular hyperplasia and *nodular regenerative hyperplasia in the liver*. It equally affects men and women. The diagnosis is made based on hepatic venous pressure gradient which should be more than or equal to 10 mmHg.

#### PV shunt

This is the least common type of shunt and usually causes high-output cardiac failure. Rarely, this can cause focal nodular hyperplasia and nodular regenerative hyperplasia in the liver which can lead to portal hypertension and cirrhosis.

Diagnosis of HHT is made based on the Curacao criteria.<sup>[2]</sup> Imaging is indicated to confirm the diagnosis if three of the four clinical criteria are not met. In addition, imaging has to be done to look for associated complications like liver cirrhosis. In a known case of HHT, the presence of ascites, GI bleed, and abdominal pain should raise the suspicion of liver involvement and imaging should be performed. Doppler study can show abnormal tortuous vessels in the liver. CECT and MRI can reveal multiple liver VMs. There can be enlarged hepatic artery, normal  $\leq 7$  mm,<sup>[1]</sup> heterogenous enhancement of the liver in the arterial phase of contrast study which becomes homogenous in the venous phase.

CT is the recommended *imaging modality* of choice. In CECT, the type of shunt can be determined in two-third of patients. The majority of patients with liver disease will show AV shunt. Biliary disease is generally seen in the late phase of the disease. The gold standard to establish the type of shunt is angiography.<sup>[3]</sup> Angiography can clearly demonstrate the early, subtle VMs and mesenteric steal syndrome. However, in the majority of the patients, the diagnosis can be established with less invasive imaging methods like CECT.

#### Treatment

No treatment needed in asymptomatic patients with liver involvement. Primarily, the management is medical with treatment of anemia and correcting coagulation abnormalities.<sup>[6]</sup> High-output cardiac failure and complications of portal hypertension are treated in the standard way like treating cardiac failure and portal hypertension due to other etiologies. It should be noted that trans-jugular intrahepatic porta systemic shunt (TIPS) creation may not be effective in the treatment of GI bleed secondary to telangiectasia of the GI tract. Shunt reduction procedures like embolization may be considered in patients with cardiac failure and mesenteric ischemia.<sup>[7]</sup> However, these procedures are associated with high morbidity and mortality and have only transient therapeutic effect. In carefully selected patients, few sessions of endovascular embolization may be effective in reducing portosystemic shunt and alleviating mesenteric ischemia. Ultimately patients might require liver transplantation, which can be curative.

#### Conclusion

HHT is a rare cause of vascular dysplasia involving many organs and systems. Although the majority of the patients remain asymptomatic, high index of suspicion should be kept not to miss liver involvement by the disease. Radiologists should be aware of the imaging findings and possible treatment options like shunt reduction embolization offered by us. Life-threatening complications like high-output cardiac failure not responding to maximum medical therapy and severe biliary ischemia should be recognized and these patients should be referred for an early liver transplant.

#### Financial support and sponsorship

Nil.

#### Conflicts of interest

There are no conflicts of interest.

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