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# Hepatic Vascular Variants in Hereditary Haemorrhagic Telangiectasia

## *Imaging findings*

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**Abstract**

Hereditary Haemorrhagic Telangiectasia (HHT) is an autosomal dominant disorder characterized by vascular dysplasia. Hepatic Vascular Malformations (VMs) range from small telangiectases to significant vascular shunting. Here we report two cases of HHT. Case 1 had diffuse ectasia of the hepatic artery along its intrahepatic and extrahepatic course with a hepatic arterial aneurysm. Case 2 presented with ileal and hepatic telangiectases. Knowledge of these vascular variants is indispensable for clinicians and radiologists in aiding diagnosis and surgical and interventional management.

***Keywords:*** Vascular Malformations, HHT, Arteriovenous Malformation, Ileal Telangiectasis.

## Introduction

Hereditary Haemorrhagic Telangiectasia (HHT), also known as Osler Weber Rendu syndrome, is a multi-system autosomal dominant vascular disorder, with an incidence of one in 5000 to 8000 individuals.[1] It was initially recognized as a mucocutaneous vascular disorder presenting with epistaxis, gastrointestinal haemorrhage, and iron deficiency anaemia. However, with the

increasing use of imaging modalities, many patients come to attention with incidentally detected visceral Vascular Malformations (VMs)**.** Recent studies have demonstrated the frequent occurrence of pulmonary, hepatic and cerebral vascular malformations, with an estimate that at least 30% of HHT has hepatic involvement.[2,3] With such high prevalence, it is fundamental for all radiologists, physicians and hepatologists to be acquainted with hepatic vascular involvement in HHT. Gastric and small bowel telangiectases are rare manifestations of HHT, most commonly involving the stomach, duodenum and jejunum. The ileum is less commonly affected.[4] This case report presents two cases of HHT with hepatic vascular variants and one with ileal telangiectases.

**Case reports**

**Case One**

A 35-year-old gentleman presented with a complaint of recurrent epistaxis for many years. He had a vague upper abdominal discomfort for 2 years for which he underwent a screening ultrasound abdomen which revealed the presence of hepatic arterio-portal shunting. On detailed physical examination, there were multiple small reddish-purple lesions over both ear lobes, fingertips and multiple oral telangiectases (Figure 1a, 1b). In presence of epistaxis with multiple mucocutaneous telangiectases, the possibility of Hereditary Hemorrhagic Telangiectasia (HHT) was considered. However, there was no family member affected by HHT.

After a preliminary examination, he was referred to the Radiodiagnosis department for dedicated Ultrasonography (USG) and Contrast-Enhanced Computer Tomography (CECT) abdomen scan.

On USG, multiple dilated and tortuous vessels were seen in the liver, which showed arterial waveform with peak systolic velocity in the range of 140 to 155cm/s. The portal vein, hepatic vein, and inferior vena cava were usual with typical waveform. The liver showed normal echotexture with smooth margins. (Figure 1c, 1d)

Triple phase CECT scan was acquired with arterial, portal, and venous phases after bolus injection of contrast. On CECT arterial phase (Figure 2), variant hepatic arterial anatomy was seen, with the left hepatic artery arising directly from the coeliac axis and common hepatic artery

arising from the coeliac axis giving rise to the middle hepatic artery and gastroduodenal artery (GDA). The right hepatic artery was seen arising from the superior mesenteric artery (SMA). All three hepatic arteries were tortuous and dilated (~12 mm) throughout their intrahepatic and extrahepatic course. GDA, left gastric artery and splenic artery were normal in course and calibre. The coeliac artery and SMA were dilated. An intrahepatic saccular aneurysm was seen from a branch of the left hepatic artery. The portal vein and all three hepatic veins showed normal contrast uptake. There was opacification of the peripheral portal branches in the arterial phase, consistent with the presence of arterioportal shunting. Cranial magnetic resonance imaging and Computed Tomography (CT) of the chest were normal.

These dilated and tortuous patterns of hepatic arteries with high peak systolic velocities led to radiological suspicion of HHT. Based on Curaçao criteria [Table 1],[2] a diagnosis of HHT was established.

**Case Two**

A 56-year-old gentleman with HHT who had been followed up for 3 years got admitted owing to multiple episodes of blood in his stools, primarily dark red. There was no history of fever, loose stools, abdominal pain, or distension. His vitals were stable on admission (Pulse rate – 70 bpm, Blood Pressure – 120/70 mmHg, Temperature – 99F, SpO2 – 98% in room air). Per Rectal examination was unremarkable. Haemoglobin profile showed moderate anaemia (9 g/dL), with normocytic normochromic anaemia. On CECT enterography (Figure 3), multiple arterial-enhancing ileal lesions were seen. Incidental multiple arterial enhancing lesions were also found in the liver. On enteroscopy, the stomach and proximal small bowel appeared unremarkable. Multiple blood clots were evident within the bowel loops with coffee brown-coloured fluid. Multiple punctate lesions with pulsatile bleeding were seen in the terminal ileum (type 2A – Yano Yamamoto classification),[5] confirming the radiological diagnosis (Figure 3c).

Written consent was obtained from both patients for publication purposes.

## Discussion

HHT is an autosomal dominant disorder characterized by vascular malformations. Nearly 80% of HHT patients have identifiable mutations, most commonly ENG (endoglin, HHT1 genotype), ACVRL1 (Activin A, HHT2 genotype) and MADH4 mutations.[6] These causative genes are involved in the TGF-β/BMP cell signalling pathway, which has a role in vascular remodelling.[7] Mutations in these genes lead to altered TGF-β/BMP signalling pathways disrupting the endothelial response, smooth muscle differentiation, and vascular integrity resulting in small, fragile vessels.[8]

Diagnosis of HHT is based on four criteria - recurrent epistaxis, mucocutaneous telangiectases, visceral vascular lesions and an affected first-degree relative (The Curaçao criteria) [Table 1].[2] According to these criteria, diagnosis of HHT is "definite" when three criteria are satisfied and "possible" when two criteria are present. Vascular manifestations in HHT include telangiectasis, aneurysms, and shunting. Common visceral vascular lesions include vascular malformations in gastrointestinal, pulmonary, hepatic and central nervous system circulation.

Most hepatic vascular malformations in HHT are asymptomatic, with less than 10% of patients having symptoms related to these lesions. Clinical manifestations are related to either high-output heart failure or portal hypertension due to arterioportal shunting. Arteriovenous shunting causes high-output cardiac failure due to reduced systemic vascular resistance which in turn leads to activation of the renin-angiotensin-aldosterone system, causing water and salt retention. Portal hypertension occurs when the portal flow or vascular resistance is increased. Arterioportal shunt is an uncommon cause of presinusoidal portal hypertension and is believed to be the result of increased blood flow in the portal system. Hepatomegaly, ascites, bleeding episodes, and splenomegaly can all be symptoms of portal hypertension. These clinical manifestations result from deviations from Starling's law, where the force maintaining fluid in the vascular space is less powerful than the force removing fluid from the vascular space.[9]

Follow-up of liver vascular malformations has shown up to 5% mortality and 25% morbidity over a median follow-up period of 44 months.[10] With the advent of cross-sectional imaging modalities, visceral vascular manifestations are frequently detected. A recent study using

multidetector Computed Tomography (CT) has demonstrated hepatic involvement of around 74 – 79%.[11,12]

Hepatic involvement in HHT ranges from tiny telangiectasis to large confluent vascular masses. Telangiectases are the most common vascular lesions seen in the liver in HHT.[13] One of our cases saw an incidental finding of telangiectasia in the liver (Case 2). Maximum Intensity Projection (MIP) imaging helps appreciate these inconspicuous lesions from the hepatic parenchyma as in our case. These telangiectasias can progress to form more complex vascular malformations. Hence the patient has to be monitored for long-term follow-up.

Hepatic arteries are dilated and tortuous in HHT. Doppler study helps differentiate between the dilated biliary radicles and tortuous hepatic arteries in HHT. In our case (Case 1), the hepatic arterial velocity was similar to that of the mean velocity 153+/-65.2cm/s illustrated by Nagamuna et al. in their study.[14]

Viyannan et al., in their case report, demonstrated that their patient had hepatic arterio-portal shunting which was also seen in our case (Case 2).[15] Proper phased protocol (arterial, portal, and venous phase) helps in identifying inconspicuous shunting.[13]

In addition to dilated and tortuous hepatic arteries, a saccular aneurysm of the left hepatic artery was found in our first case. However, very few cases of hepatic artery aneurysms have been reported in the literature.[16,17] There is still a paucity of qualitative research on the role of intervention in the management of aneurysms in HHT.

Complications of Vascular Malformations (VMs) include recurrent endothelial damage and micro-vascular thrombosis may eventually cause improper hepatocyte proliferation and fibrosis. Cirrhosis development may ultimately result from chronic micro-vascular ischemia.[18]
Hepatic arterial insufficiency results in numerous types of ischemic biliary damage (ischemic cholangiopathies). Several clinicopathological categories, including bile duct necrosis, bile leak and biloma, biliary strictures, and biliary casts, make up ischemic cholangiopathies.[19]

Management of symptomatic hepatic VMs is mostly conservative. Patients manifesting with high output cardiac failure are treated with salt restriction, diuretics, beta-blockers, ACE inhibitors, digoxin, antiarrhythmic agents, cardioversion and radiofrequency ablation. Patients presenting with complications of portal hypertension are treated with vasopressors, variceal ligation (for variceal bleeding), diuretics (for ascites), lactulose and rifaximin (for encephalopathy). This is accompanied by iron administration for anaemia along with definitive treatment for bleeding sources. With this therapy, around 63% of patients show complete and another 21% show partial response.[10]

In patients not responding to initial medical management, invasive options can be considered including peripheral, staged trans arterial embolization of liver VMs.[20]

Liver transplantation is the only definitive curative option, indicated for intractable high-output heart failure, complicated portal hypertension and ischemic biliary necrosis.[21,22] Bevacizumab was shown to reduce cardiac index in patients with severe liver VMs with high output cardiac failure.[23] Asymptomatic liver VMs at high risk of poor outcomes (grade 4) can be targeted for prophylactic therapy.[1] Sufficient data on the natural history and management of liver VMs are lacking and there are no clear recommendations to prefer one treatment option over another.

Gastrointestinal telangiectases are rare manifestations of HHT. It generally affects the caecum or colon and rarely the small intestine.[24] An extensive literature search in Pubmed, Embase and Cochrane, CT angiographic manifestations of gastrointestinal telangiectases is less reported. Only one case of jejunal telangiectasis is reported.[24] This article thus describes the CT angiographic manifestations of ileal telangiectasis.

**Conclusion**

A cluster of findings led to high-end radiological suspicion, which unveiled the diagnosis of HHT in one of our cases. Screening for hepatic VMs is recommended in asymptomatic individuals suspected to have HHT as this leads to confirmation of diagnosis and better management of these patients with Doppler ultrasound being proposed as a first-line

investigation. Ileal telangiectases should be considered in patients of HHT with gastrointestinal bleeding.

**Authors' Contribution**

AA and JHP drafted the manuscript. BS and MKP supervised the work. TT critically reviewed and edited the manuscript. All authors approved the final version of the manuscript.

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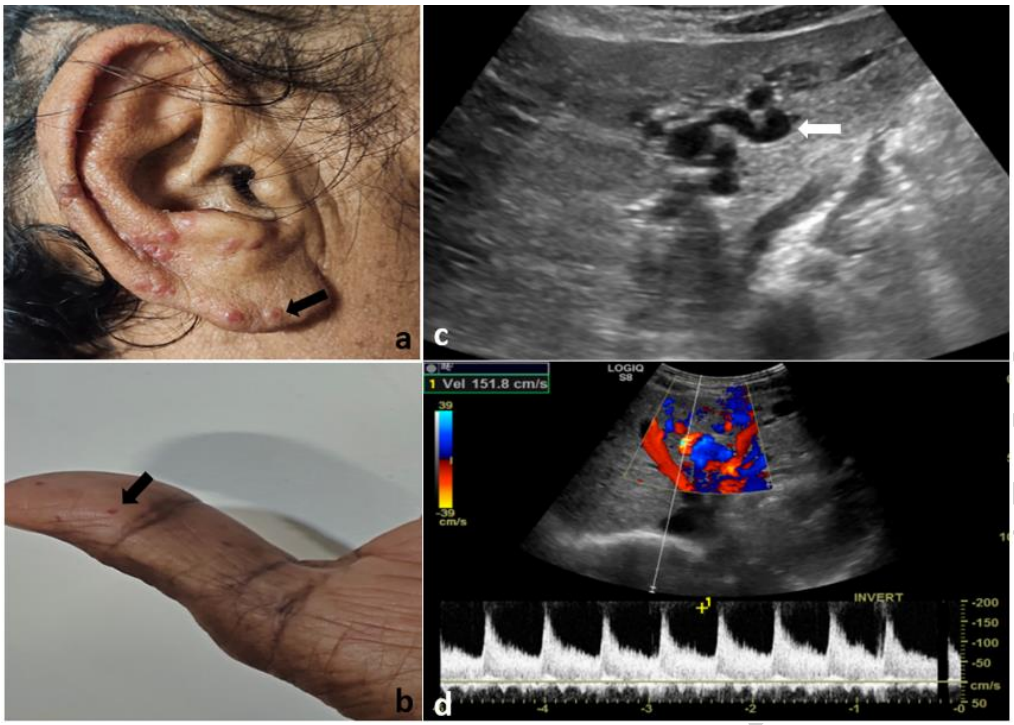


**Figure 1:** Case 1 - (a and b) showing telangiectatic foci in pinna and hand (black arrows) (c) Gray scale ultrasound image of the left lobe of the liver showing tortuous and dilated left hepatic artery (white arrow) with corkscrew appearance; (d) Duplex Doppler image of left hepatic artery shows normal waveform with markedly elevated peak systolic velocity (152 cm/s); (c and d)

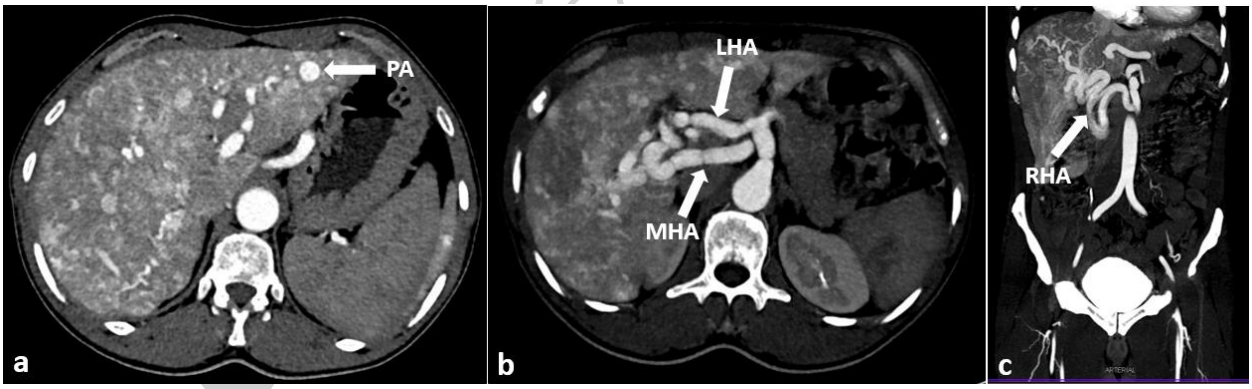


**Figure 2:** Case 1 - CECT Arterial phase axial images (a, b) showing dilated and tortuous left (LHA) and middle (MHA) hepatic arteries with evidence of arterio-portal shunting. LHA was directly arising from the celiac trunk. MHA was seen as a direct continuation of the common hepatic artery arising from the celiac trunk. A pseudoaneurysm (PA) is noted in the left lobe of the liver arising from a branch of LHA. Liver contour is normal. Arterial phase coronal image (c) showing dilated and tortuous right hepatic artery (RHA) arising from the superior mesenteric artery (replaced RHA).

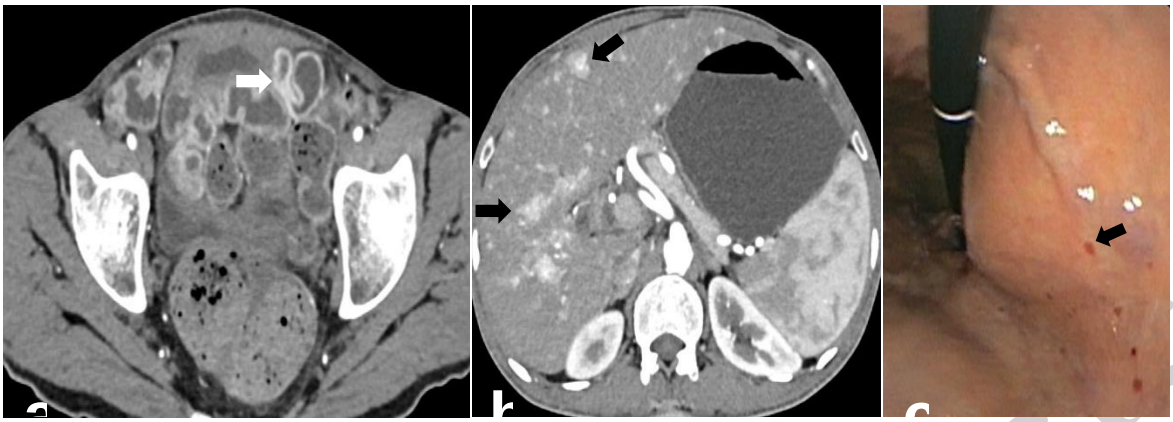

**Figure 3:** Case 2 - CECT Arterial phase axial image (a) showing mural enhancement in the ileum (white arrow). Arterial phase axial images (b) showing multiple arterially enhancing telangiectatic foci (black arrows) in both lobes of the liver. The hepatic artery is seen of normal calibre with no arterio-portal shunting (c) enteroscopic image showing multiple punctate telangiectases in ileum (black arrows).