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Understanding HHT and THE LIVER
Guide for Patients and General Practitioners
April 19th 2023

Preface

Hereditary Haemorrhagic Telangiectasia (HHT) is a rare hereditary genetic disease that affects 1 in 5000 people worldwide and is characterised by vascular malformations (direct connections between arteries and veins) in the skin, mucous membranes, and internal organs.

This guide on HHT and the Liver is written to assist patients to understand the implications of hepatic vascular malformations. This information can also be shared with your general practitioner. It is highly recommended that symptoms related to HHT in the liver be managed in consultation with a HHT Centre, as therapeutic choices are very specific to each affected individual. This guide does not substitute for such specialist care.

HHT in the LIVER

The liver is one of the organs most commonly affected by HHT vascular malformations (present in the liver of 41 to 74% of HHT patients carrying any associated genetic mutation). The presence of vascular malformations does not imply liver insufficiency, and most HHT patients with liver vascular malformations (85 to 92% of patients) have no resulting symptoms or signs. However, in a small percentage of cases, these malformations can cause clinical manifestations that need to be addressed.
Clinical effects of HHT in the liver, if they occur, do not always manifest in the liver itself, and therefore, identifying the cause of symptoms and signs due to liver HHT requires specialist knowledge. That is why understanding liver implications of HHT is very important for patients and clinicians.

Screening the Liver

Because HHT liver vascular malformations are mostly asymptomatic (and there is no preventive therapy), screening for liver involvement by HHT is not part of the standard screening protocol.

Such screening (using Doppler Ultrasound, CT and/or MRI) is performed in some centres internationally, as awareness of asymptomatic VMs can help in predicting possible future issues, help management and make prognosis easier. Echocardiography of the heart, which

is part of the standard screening protocol (for pulmonary vascular malformations) may reveal evidence of complications from liver malformations.

Understanding causes, symptoms and treatments of rare HHT liver complications

Although liver AVMs remain asymptomatic in the majority of patients, when symptoms occur, they are caused by intrahepatic shunting that occurs when an artery connects directly to a vein in the liver. Please keep in mind that these complications are rare in HHT patients.

The liver presents three important types of normal vein/artery connections. Vascular malformations in each of these connections can (in a small minority of patients) result in a specific clinical pattern, as the vascular malformation alters the flow of blood within the liver. Typical specific clinical patterns include:

1. High output cardiac failure (HOCF): This is the predominant complication in symptomatic liver HHT when there is shunting between the hepatic artery and an hepatic vein. The size of the shunt results in increased pressure on the heart to pump additional blood. If severe/chronic anaemia is also present, the situation can become more complicated, as anaemia also increases pressure on the heart. **Symptoms can include** shortness of breath, leg swelling, abnormal accumulation of fluid in the abdomen or lungs. **Treatment:** Manage general anaemia, reducing salt in diet, diuretics, other antihypertensive and antiarrhythmic drugs. When all baseline treatment fails HHT specialists will evaluate the use of anti-angiogenic drugs or liver transplant (in rare cases). Patients with HOCF need to be followed by an cardiologist and liver specialist with knowledge of HHT.

2. Portal hypertension: Complicated portal hypertension can occur in patients with shunting between the hepatic artery and the portal vein (which ordinarily drains blood from the gut to the liver). This causes high pressure in the portal vein. Signs of portal hypertension can be mistaken for cirrhosis due to liver disease from other causes. **Symptoms & signs:** abnormal accumulation of fluid in the abdomen, varices (enlarged veins in specific locations), enlargement of the spleen (which may be associated with low white blood cell and platelet counts), possibility of worsening of bleeding in the intestines. **Treatment:** Same as for any other cause of portal hypertension, including management of varices. Rarely, when this approach fails, specialists will evaluate the possibility of a liver transplant. **Additionally:** Portal hypertension can lead to increased pressure in the pulmonary circulation, increasing breathlessness and fatigue, resulting in hepato-pulmonary syndrome or a form of

porto-pulmonary hypertension, the latter of which must be recognised and diagnosed as it can be improved by taking specific vasodilator drugs.

3. Hepatic Encephalopathy: This rare event is caused by a shunt between the portal vein and an hepatic vein, allowing blood that enters the liver from the gut to bypass the normal processing of nutrients and toxins that occurs in the liver. Toxins can then make their way through the liver to other parts of the body, including the brain, causing hepatic encephalopathy. **First typical symptoms:** confusion, lack of concentration, change in sleeping pattern. **Treatment:** Same as for any other cause of hepatic encephalopathy, with medication and, if ineffective and symptoms worsen, possible consideration for liver transplant.

4. Cholangitis due to biliary ischemia (reduced blood supply), causing damage to the bile ducts in the liver - **Treatment:** antibiotics for acute episodes.

Important

The international HHT Guidelines underline the importance of the following:

- Imaging (Ultrasound, CT or MRI) appearances on the liver in HHT may be unusual, raising suspicion of other disease. Shunting in the liver results in a higher-than-usual incidence of focal nodular hyperplasia, a benign liver change that can look very like other masses. These appearances can lead to consideration of liver biopsy. This should be avoided, if at all possible (and may not be necessary, when the imaging is reviewed by a specialist radiologist familiar with HHT). When vascular malformations are present in the liver a biopsy carries a high risk of bleeding.
- Avoid hepatic artery embolization - this procedure carries a high risk of complication and possible mortality and does not solve the underlying problem permanently even when successful. At most, it offers only temporary benefit.

Takeaway message for General Practitioners

HHT is a multisystemic rare disease that requires specialist knowledge to assess the possible cause of symptoms and signs. This is especially the case for clinical consequences of liver vascular malformations, which, although rare, need to be properly assessed and understood for effective management.

Takeaway message for HHT Patients

Understanding the causes and symptoms of HHT allows you to collaborate with your general practitioner and other specialists. Use this guide and a specific description of any unusual symptom you may present to allow your GP or specialist to evaluate the possibility of clinical consequences of liver complications in a timely manner.

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Special Thanks
HHT Italia would also like to thank all the patients who contributed to the design of this guide and shared their perspective, to develop patient friendly information for the entire HHT community.

Translated into English by HHT Ireland
English version endorsed and adapted by Prof. Adrian Brady, National HHT Centre, Mercy University Hospital, Cork.

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VASCERN HHT DOs and DON'Ts
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