Understanding HHT and THE LIVER
Guide for Patients and General Practitioners
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Preface

This guide on HHT and the Liver is written for patients to fully understand the implications of hepatic vascular malformations. This information can also be shared with your general practitioner. It is highly recommended to address symptoms related to HHT in the liver in an HHT Center as therapeutic choices are on a person to person basis. This guide does not substitute your HHT Center in handling your care.

Understanding HHT

Although those reading this guide are most likely already familiar with HHT, remember that HHT stands for Hereditary Hemorrhagic Teleangiectasia, a rare hereditary genetic disease that affects 1 in 5000 people worldwide and is characterized by vascular malformations of the skin, mucous membranes, and internal organs and vascular malformations occur when an artery connects directly to a vein.

HHT in the LIVER

The Liver is one of the organs most commonly interested by HHT vascular malformations that are present in 41 to 74% of HHT patients of all gene types. The presence of malformations does not imply liver insufficiency. While liver vascular malformations are typically asymptomatic (85 to 92% of patients), it is important to keep in mind that, in a small percentage of cases, they can cause clinical manifestations that need to be addressed.
Manifestations of HHT in the liver can be tricky to detect as patients focus on the good news that liver AVMs rarely cause complications and when symptoms occur, they do not always manifest in the liver itself. That is why, understanding liver implications of HHT is very important for patients and clinicians.

Screening the Liver

While HHT liver VMs are mostly asymptomatic and with no preventive therapy, liver screening remains important in HHT because awarness of asymptomatic VMs can be an important predictor, help management and make prognosis easier. Furthermore, screening the liver is efficient way to diagnose HHT. Screening is conducted through Doppler ultrasound, CT scan with contrast, and/or contrast MRI (contrast is not advised in patients with severe renal failure). An additional test is echocardiography of the heart because complications of liver malformations are not always restricted to the liver itself. Follow-up check ups of the liver are individually determined by your HHT Center based on predictors such as age, gender, anemia, comorbidities and clinical manifestations so there is not one standard rule for all HHT patients.

Understanding causes, symptoms and treatments of rare HHT liver complications

Although liver AVMs remain asymptomatic in the majority of cases, when symptoms occur, they are caused by intra-hepatic 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, and present prevalently in HHT 2 and in women over 45 years of age.

The liver presents three important vein/artery junctions and, in the rare event one of these present a symptomatic vascular malformation, each can present a specific complication as the vascular malformation forces an additional flow of blood to the liver.

1. High output cardiac failure (HOCF): This is the predominante complication in symptomatic HHT liver when there is shunting between the hepatic artery and a hepatic vein. The size of the

malformation and the dimension of the organ, forces the heart to pump additional blood to the liver. If severe/chronic anemia is also present,the situation can become more complicated as other organs are also requesting the heart to pump additional blood. Symptoms can include: shortness of breath, pulmonary hypertension, leg edema, abnormal build up of fluids in the abdomen or lungs. Treatment: Manage general anemia, reducing salt in diet, diuretics, antihypertension and antiarrhythmic drugs. When all baseline treatment fails HHT specialists will evaluate the use of anti-angiogenic drugs or liver transplant. Patients with HOCF need to be followed by an HHT cardiologist.

2. Portal hypertension: complicated portal hypertension occurs at a rate comparable to that of HOCF in patients with shunting between the hepatic artery and portal vein that is draining blood from the gut to the liver. This causes high pressure in that portal vein (which can also be mistaken for cirrhosis that has the same manifestation but a different cause). Symptoms: abnormal build up of fluids in the abdomen, varices, enlarged spleen that can be detected with low white blood cell and platelet counts, likeliness of worsening of gastrointestinal bleeding. Treatment: management of varices or, when this approach fails, specialists will evaluate the possibility of liver transplant. Additionally: Portal hypertension can lead to increased pressure in pulmonary circulation, increasing breathlessness and fatigue, resulting in a 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 a portal vein and a hepatic vein in the region where blood flows to the heart away from the liver. Blood that enters the liver from the gut loaded with nutrients but also with toxins. If there is shunting it could also occur that the toxins are not cleaned by the liver. Toxins, like ammonia, could 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: treatment of encephalopathy with medication and, if ineffective and symptoms worsen, liver transplant can be evaluated.

4. Cholangitis due to biliary ischemia which is damage to the bile ducts in the liver - Treatment: antibiotics

Important

The international HHT Guidelines underline the importance of the following:

- Avoid biopsy of the liver if possible - liver vascular malformations can present focal nodular hyperplasia, a benign condition often mistaken for masses or tumor. When vascular malformations are present in the liver a biopsy can create a very high risk of bleeding.
- Avoid hepatic artery embolization - this procedure is high risk in complication and mortality and does not solve the problem entirely even when successful.

Takeaway message for General Practicioners

HHT is a multisystemic rare disease that requires in depth considerations of symptom onset to idenitfy the possible origin of the complication that may not reside in the organ with clinican manifestations. More so for consequences of liver AVMs that, although rare, need to be promptly identified for effective management. Underestimating patient reported symptoms can lead to a late identification of problems with severe consequences.

Takeaway message for HHT Patients

Understanding the causes and symptoms of HHT allows you to collaborate with your general practitioner and non HHT specialists. HHT patients learn to live with fatigue and malaise that may delay the detection of certain liver related manifestations. 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 liver complications in a timely manner.

This patient friendly information was created by
HHT Italia APS
www.hhtitalia.org
info@hhtonlus.org

In collaboration with
HHT Center Bari - Prof. Carlo Sabbà, Dr. Patrizia Suppressa
HHT Center Gemelli Roma - Prof. Eleonora Gaetani
HHT Center Pavia – Prof. Fabio Pagella, Dr. Elina Matti, Dr. Laura Scelsi

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Translated into (Put your language) by Insert your organization
(insert your language) version endorsed by Insert HHT center and clinicians.

Sources

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