PH and HHT: What's the Connection?

As isolating and scary as it can be to have a rare disease like pulmonary hypertension (PH), imagine having a second rare disease with its own set of challenges. That's exactly what some individuals with pulmonary hypertension and hereditary hemorrhagic telangiectasia (HHT) face.

What is HHT?

HHT is a blood vessel disorder in which blood vessel abnormalities develop throughout the body that increase with age. When the large blood vessels are affected, patients develop arterio-venous malformations (AVMs), which typically develop in the lung, liver or brain and can cause bleeding and strokes and induce heart failure. Meanwhile, affected small vessels, or telangiectasias, are commonly found on the skin, nose or gastrointestinal tract and can be quite annoying as well as cause chronic bleeding, leading to iron deficiency anemia.

What causes HHT and how are genes involved?

HHT is a genetic disorder, meaning it is caused by abnormalities in genes or chromosomes. Mutations in at least three genes are known to cause HHT: Endoglin 1, ALK-1 and SMAD-4. It is suspected that two other genes on chromosomes 5 and 7 may cause HHT, but this has not been scientifically proven.

Genetic testing plays a large role in diagnosing HHT, and because many HHT patients are not yet experiencing symptoms (90 percent of affected individuals in the U.S. are oblivious to their condition), genetic testing is often used to screen asymptomatic family members. HHT can also be diagnosed on clinical grounds, if any three of four criteria are met: 1) family history consistent with HHT, 2) spontaneous and recurrent nosebleeds, 3) telangiectasias of the skin or oral cavity and 4) internal AVMs.

When do PH and HHT occur together and how are individuals affected?

PH in HHT is not the same in everyone, and the disease presents in two forms. In either case, patients may present with shortness of breath and fatigue, but for different reasons. Most commonly, PH in HHT results from excessive blood flow through the lung. This occurs when the pulmonary pressures are modestly elevated (systolic pressure 40–60), cardiac output (amount of blood pumped through the circulatory system each minute) is high and the net relationship between pressure and flow, known as pulmonary vascular resistance or PVR, is normal or low. Over time this can cause the heart to "overheat" and lead to a form of heart failure known as high-output failure, which in turn worsens pulmonary hypertension.

Less commonly, PAH occurs in HHT and is similar to idiopathic pulmonary hypertension (IPAH) or heritable PAH, in which the small arteries of the lung progressively narrow or close off. This causes severely elevated pressure in the lung, decreased cardiac output over time and a high PVR. The incidence of HHT-associated PAH, a WHO Group I diagnosis, is unknown, but non-invasive echocardiography suggests that about 20 percent of HHT patients develop PH during their lifetime. HHT-associated PAH appears to be rare and primarily involving families with ALK-1 mutations.

How is PH-associated HHT treated?

Before treatment begins, it is essential to determine what type of PH exists. This requires a right heart catheterization, which calculates the pulmonary vascular resistance. It is also important to look for excessive blood return to the heart via the liver, which is the usual mechanism for the high-output variety of pulmonary hypertension.

If PH and a high-flow state are confirmed and the PVR is low, then PAH is not the primary issue and does not need specific treatment. PAH medications in this situation may actually make things worse by further increasing the high flow state. Instead, factors contributing to the high-flow state need to be addressed as well as possible (i.e., correcting anemia or possibly liver transplantation). Alternatively, if PH occurs in combination with a low or normal measure of blood-flow and an elevated PVR, patients should be considered for PAH-specific treatments. For these patients, many of the approved PAH-specific treatments have been used sporadically. While these therapies have been successful in individual cases, significant unique adverse effects can occur in HHT patients. Therefore, it is essential that only appropriate HHT patients receive therapies by a specialist.

STORY CONTINUED ON NEXT PAGE

STORY CONTINUED FROM PREVIOUS PAGE

If I have PH and HHT, where can I go for help?

Currently, there are 12 specialized 'HHT Centers of Excellence' throughout North America. (For a complete list of centers, see **http://hht.org**) These centers are led by a director and a network of specialists qualified to address the many complex aspects of HHT. At three of these 12 locations, Dr. James Gossage (Medical College of Georgia), Dr. Murali Chakinala (Washington University in St. Louis) and Dr. Karen Swanson (Mayo Clinic in Rochester, Minn.) direct their HHT centers and are also actively involved in the fight against pulmonary hypertension, which provides them with unique insights about these two conditions. If you or someone you know has or may have PH possibly in the setting of HHT, you should seek treatment by a specialist. ◆

Answers provided by Murali Chakinala, MD, Washington University in St. Louis; James Gossage, MD, Medical College of Georgia; and Karen Swanson, DO, Mayo Clinic Rochester

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For more information on PHA resources for patients managing multiple illnesses or to join the "PH Plus" email group, refer to the article on p.3 or contact Emma Bonanomi, PHA Patient Outreach and Services Manager, at Emma@PHAssociation.org or 301-565-3004 x777.

Living with PH and HHT, a Patient's Experience

My name is Christine, and I have pulmonary arterial hypertension (PAH) and hereditary hemorrhagic telangiectasia (HHT). My PAH was diagnosed in November 2006. I knew months before that there was something wrong; I could not physically keep up with co-workers, family or friends. I just assumed that my age (49) and weight (well beyond pleasingly plump) had finally caught up with me. I currently take sildenafil (Revatio™), bosentan (Tracleer™), and as of October 21, 2009, I began taking treprostinil (Tyvaso™) which replaced my iloprost (Ventavis™) and seems to be really working well for me.

HHT is something that has always been a part of my life. Ever since I can remember, my father has had nosebleeds; it was just a part of my family members' lives. I have had AVMs (arterio-venous malformations) coiled in my lungs and have had to have nasal cauterization to help manage my nosebleeds. My father and one of my sisters have been diagnosed with HHT; three of my four other siblings have been screened and do not have HHT. We also suspect that my four-year-old niece has it since she has an unusual amount of nosebleeds for such a young child, and we plan to have her screened when she is a little older.

Living with these two diseases is a challenge. I am still employed full time. I enjoy my job very much though it has evolved in the past three years to accommodate my PAH and HHT. At times my fatigue, which I believe is a combination of anemia from the HHT and just a part of PAH, can set me back. I'm still learning to accept my 'bad days' and to enjoy my 'good days.' 'Bad days' are the days when I can't seem to muster the energy to get out of bed to go to work or when just getting ready to go to work is so tiring that I consider my 45-minute commute a chance to rest! 'Bad days' are also the days when I have the opportunity to babysit my nieces and nephews and have to decline because I just do not have the energy. 'Good days' are those days when I feel like my 'old' self. I can do normal, simple things like grocery shopping, house cleaning and putting in a good day of work without exhausting myself. With the love of my family, all my days are truly blessed. ◆

By Christine Fini
PH and HHT Patient