Transcript Details
This is a transcript of an educational program accessible on the ReachMD network. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/medical-industry-feature/acute-hepatic-porphyria-ahp-looking-beyond-the-obvious/12782/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Acute Hepatic Porphyria (AHP): Looking Beyond the Obvious

Announcer:
Welcome to ReachMD.

This medical industry feature, titled “Acute Hepatic Porphyria: Looking Beyond the Obvious” is sponsored by Alnylam Pharmaceuticals. This program is intended for healthcare professionals.

Here’s your host, Dr. Charles Turck.

Dr. Turck:
Acute hepatic porphyria, or AHP, refers to a family of rare and genetic diseases characterized by debilitating and potentially life-threatening attacks. Some patients report chronic symptoms and can wait up to 15 years for an accurate diagnosis. What do we need to know about this rare condition? And how can we better detect it?

This is ReachMD, and I'm Dr. Charles Turck. Joining me to discuss this rare disease that could be responsible for a patient's unexplained abdominal pain is porphyria expert Dr. Manish Thapar, who is a gastroenterologist and Associate Professor of Medicine in Philadelphia.

Dr. Thapar, thanks for being here today.

Dr. Thapar:
Thank you. Thank you for having me on. It's an honor and a privilege to be here.

Dr Turck:
Now before we begin, let's hear directly from a few people living with AHP to better understand life with the condition.

Patient Soundbites:
“Pain is the biggest thing – the biggest symptom. And, it’s abdominal pain. It was crippling. By crippling I mean it’s like someone is holding, squeezing, stabbing – you’re not able to function. You can’t do anything. You just – you just want to die. It is that bad.”

“I was doubled over on the floor vomiting and just crippled with the most intense pain from head to toe. Having excruciating pain in my stomach. It was like somebody was just taking the sharpest thing you could possibly imagine and just ripping through me.”

“When I think about the pain, it’s very excruciating. I don’t know what it feels like to have a baby, but I know what it feels like to scream and cry in the emergency room. And, to be a grown man in the emergency room screaming and crying, it is – it is just something that I wouldn’t want anyone to go through.”

Dr. Turck:
Those experiences really paint a vivid picture of the excruciating manifestations of AHP.

So, Dr. Thapar, as an expert in AHP, can you give us some background on this disease?

Dr. Thapar:
Absolutely. Porphyria refers to a family of metabolic disorders and is classified as either acute hepatic porphyria, which is commonly referred to as AHP, or erythropoietic porphyria, depending on the primary site of overproduction of heme precursors. AHP may present with acute neurovisceral attacks, characterized by severe abdominal pain and other debilitating symptoms. Erythropoietic porphyrias

primarily present with photocutaneous symptoms, such as blistering of the skin, pain, and/or redness, and swelling in sun exposed areas.

There are four types of AHP, which stem from different enzyme deficiencies in the heme biosynthesis pathway. Acute intermittent porphyria, or AIP, variegate porphyria, or VP, hereditary coproporphyria, or HCP, and ALA deficiency porphyria, or ADP.

In the liver, the heme pathway is controlled by an enzyme called aminolevulinic acid synthase 1, or ALAS-1. When ALAS-1 activity is increased due to triggers, porphyrin precursors, aminolevulinic acid, or ALA, and porphobilinogen, or PBG, build up in the liver and are released throughout the body. ALA and PBG are harmful to nerve cells and can lead to the symptoms and attacks of AHP.

Some known factors that cause upregulation of ALAS-1 and trigger acute attacks include medications, hormones, alcohol, smoking, stress, and extreme dieting.

Dr. Turck:
And with that background in mind, can you tell us what types of symptoms are associated with AHP?

Dr. Thapar:
AHP features a combination of symptoms reflecting neurotoxic effects across the autonomic, peripheral, and central nervous systems, and individual patients can differ in their clinical experiences with AHP. The disease can be characterized by potentially life-threatening acute attacks, and some patients may even experience chronic debilitating symptoms.

Now when a patient presents with an acute attack, they usually report severe diffuse abdominal pain, which is often accompanied by nausea, vomiting, hypertensive crisis, tachycardia, constipation, hyponatremia, and neuropathy. These attacks usually last anywhere between three to seven days and can be life threatening if severe and not treated urgently.

Patients may also experience chronic symptoms between AHP attacks, such as nausea, vomiting, anxiety, and depression, and may report pain in the limbs, back, or chest.

Dr. Turck:
Now, based on what you're describing, these symptoms sound similar to those of many other well-known diseases, particularly gastrointestinal diseases, but even some non GI conditions. Which conditions does AHP most often resemble?

Dr. Thapar:
That is very true. The nonspecific nature of AHP signs and symptoms often leads to a misdiagnosis of gastrointestinal conditions, like irritable bowel syndrome, and other conditions such as endometriosis, fibromyalgia, and appendicitis to name a few.

In some patients with AHP, the correct diagnosis may be delayed up to 15 years. And as a result of this delay, patients may undergo unnecessary treatments, surgeries, or procedures.

An early diagnosis is important, as AHP is associated with progressive elements, and serious long-term complications, including primary liver cancer, chronic kidney disease, and hypertension. These patients may suffer from anxiety, depression, and suicidal ideations.

Dr. Turck:
For those just tuning in, you're listening to ReachMD. I'm Dr. Charles Turck. And today I'm speaking with Dr. Manish Thapar about acute hepatic porphyria, or AHP, a family of rare genetic diseases.

Now that we've reviewed how AHP can manifest in patients, let's dive into how a doctor can spot this rare disease.

Dr. Thapar, knowing that many specialties may encounter a patient with AHP, how can doctors better recognize symptoms to help diagnose it sooner?

Dr. Thapar:
Great question. And you're correct. Many specialties including gastroenterologists, gynecologists, primary care physicians, psychiatrists, hem/oncs, and neurologists could encounter someone with AHP since its symptoms are so wide ranging.

One should suspect AHP when patients present with unexplained severe and diffuse abdominal pain paired with one or more symptoms related to the autonomic, central, or peripheral nervous systems. Some classic symptoms of AHP to look out for include dark reddish urine, neuropathy, seizures, and hyponatremia. Patients with HCP and VP may also present with cutaneous symptoms.

Also, while AHP affects people of all races, ethnicities, ages, and gender, most cases, about 80%, are seen in women of reproductive age between the ages of 15 and 45.

Dr. Turck:
What should doctors do if they suspect AHP in patients?

Dr. Thapar:
Now, if a doctor suspects AHP, there are a couple of tests that can help confirm the diagnosis.

One of the most definitive tests a doctor can use to help determine if a person has AHP is a random spot urine test to check for substantially elevated ALA, PBG and porphyrin levels. It's important to remember that ordering lab tests for urine porphyrins does not automatically include assessment of ALA and PBG levels. So be sure to order these labs as well. Urine porphyrins alone are not sufficient to diagnose AHP, as they can be elevated for several reasons.

The optimal time to perform these tests is during or shortly after an attack when ALA and PBG levels have spiked, because levels may fall when symptoms resolve. It is typically recommended that urine samples be light protected, frozen or refrigerated, and are normalized to creatinine.

Genetic testing can be used to determine the specific type of AHP and for family members of patients with AHP who want to know if they carry the genetic mutation and may be addressed to develop AHP symptoms. It's important to note that not everyone who has a mutation for AHP will develop symptoms.

Dr. Turck:
Now, Dr. Thapar, what is life like for patients with AHP? And how is it managed once a diagnosis is reached?

Dr. Thapar:
As we heard earlier, firsthand, AHP can be a devastating disease.

In a prospective natural history study of 112 patients with AHP, patients with recurrent attacks average more than three hospitalizations in a one-year span, spending an average of 30 days in the hospital during the timeframe.

Life with AHP often results in the loss of career prospects, missed social opportunities, and less time spent with loved ones. And many patients with AHP report negative impacts on their daily lives.

Although AHP is a chronic disease, there are management strategies to reduce the chance of AHP attacks. Some of these management approaches include avoiding triggers that may exacerbate AHP symptoms, working with a healthcare team, and relying on the support of a care team. That could be family, friends, or neighbors.

Dr. Turck:
This is all really helpful information and important for doctors to be aware of. But before we wrap up, Dr. Thapar, any last words for our listeners?

Dr. Thapar:
Some points to keep in mind are that missing AHP can have devastating consequences. But knowing what to look for, and ways to test can help. And also, every AHP attack matters. The sooner it is diagnosed and managed, the better for patients.

You can learn more about AHP from online resources and websites such as porphyriadiagnosis.com. I would urge your listeners to visit sites that provide reliable, accurate, and scientific information.

Dr. Turck:
Well, with those considerations in mind, I want to thank my guest, Dr. Manish Thapar, for helping us better understand acute hepatic porphyria and the importance of recognizing and diagnosing this rare disease.

Dr. Thapar, it was great speaking with you today.

Dr. Thapar:
Thank you for having me.

Announcer:
This program was sponsored by Alnylam Pharmaceuticals. If you missed any part of this discussion, visit reachmd.com/industryfeature. This is ReachMD. Be Part of the Knowledge.