ATYPICAL HEMOLYTIC UREMIC SYNDROME (aHUS)

aHUS OVERVIEW

Atypical hemolytic uremic syndrome (aHUS) is a genetic, chronic, ultra-rare disease that progressively damages the vital organs.1,2 aHUS is caused by chronic, uncontrolled activation of complement, a part of the body’s natural immune system, resulting in complement-mediated thrombotic microangiopathy (TMA)—the formation of blood clots in small blood vessels throughout the body.1-4 TMA can lead to stroke, heart attack, kidney failure and premature death. aHUS affects both adults and children. In a large group of aHUS patients, about 60% were diagnosed under the age of 18.5

CAUSES

aHUS is caused by a genetic mutation in one or more complement regulatory genes, which results in uncontrolled and excessive activation of complement.4,5 In healthy individuals, complement is used to attack foreign particles, and the system is highly regulated to prevent it from causing damage to tissues and organs. However, in patients with aHUS, when complement is activated, it cannot be controlled due to underlying genetic mutations.4

CONSEQUENCES

Patients with aHUS are at immediate and ongoing risk of the life-threatening and destructive consequences of complement-mediated TMA.1,2,3 These complications can occur throughout the body, including the kidneys, brain, heart and other vital organs.6,7 Among patients with aHUS:

- More than 50% experience impaired kidney function that leads to end-stage renal disease (ESRD)6,8
- 48% experience neurological symptoms, including stroke and seizure5,10
- 46% experience pulmonary symptoms, including dyspnea (trouble breathing) and pulmonary edema11,12
- 43% experience cardiovascular symptoms, such as heart attack and high blood pressure9,12,13
- 37% experience gastrointestinal complications such as diarrhea, colitis, nausea and vomiting10,14,15,16
- 34% experience thrombosis outside of the kidneys11
- 100% of patients in one study (N=30) experienced effects of aHUS in more than one organ system11

Historically, 79% of all patients with aHUS have died, required kidney dialysis or had permanent kidney damage within three years after diagnosis despite plasma exchange/plasma infusion (PE/PI).5 Moreover, 33% to 40% of patients die or progress to end-stage renal disease with the first clinical manifestation of aHUS despite PE/PI.5,6

DIAGNOSIS

aHUS can be difficult to diagnose; because the disease is so rare, many doctors have never encountered a case of it. Additionally, symptoms can vary from patient to patient, and some patients may not have symptoms for extended periods of time while others may feel sick frequently.2,18
Initial signs and symptoms of aHUS include confusion, stomach pain, vomiting and diarrhea. One of the most common signs of aHUS is kidney failure. If aHUS is suspected, laboratory tests should be conducted to measure red blood cell and platelet counts, as well as creatinine levels. If red blood cell and platelet counts are low and creatinine levels are elevated, it may be a sign of aHUS. Although 50% to 70% of patients with a confirmed diagnosis of aHUS have identifiable genetic mutations, genetic testing is not required for diagnosis.

aHUS shares symptoms with two diseases, thrombotic thrombocytopenic purpura (TTP) and Shiga toxin E. coli-related hemolytic uremic syndrome (STEC-HUS). Laboratory tests can help differentiate aHUS from these two diseases. Unlike aHUS, TTP is an autoimmune disorder caused by low levels of a protein called ADAMTS13 in the blood. If a patient has less than 5% of normal ADAMTS13 levels, he or she is likely to have TTP, not aHUS. STEC-HUS results from an isolated episode of infection. Patients who have gastrointestinal symptoms such as diarrhea can be tested for STEC-HUS using a stool sample. However, it’s possible to have both aHUS and STEC-HUS, so a patient who tests positive for STEC-HUS may be monitored for signs of aHUS.

DISEASE MANAGEMENT

Disease management approaches such as plasma therapy, dialysis or kidney transplant do not specifically target uncontrolled complement activation, the underlying cause of TMA in patients with aHUS, and have been proven to be clinically ineffective.

In recent years, increased understanding of the role of complement in the pathophysiology of aHUS has led to major advances in diagnosing and caring for patients with the disease. An early and accurate diagnosis and ongoing care are critical because patients with aHUS are at ongoing risk of sudden, catastrophic, and life-threatening symptoms and complications.

To learn more about aHUS, visit aHUSsource.com.


