Atypical Hemolytic Uremic Syndrome

Atypical Hemolytic Uremic Syndrome (aHUS) presents as non-immune hemolytic anemia, thrombocytopenia and organ disfunction (e.g. renal impairment). These symptoms are often caused by uncontrolled activation of the alternate pathway of the complement system. The incidence of aHUS in the USA is estimated to be 2 per million per year, for an estimated 600 cases per year. aHUS is has an equal frequency among males and females in childhood but shows a slight increase in female cases in adults. Approximately 60% of aHUS cases are diagnosed in children vs. 40% in adults. In children, 70% of cases have the first acute episode before 2 years of age.

Onset of symptoms is generally sudden and severe. More than half of pediatric and adult cases require dialysis at admission. Without immediate and aggressive treatment, death will result in the majority of cases.

Focused on success with your patient

At BloodCenter Diagnostic Laboratories, we never lose sight of why our work with you is important. Like you, our team is dedicated to delivering the very best care for your patient. That's why, from start to finish, we are your partner every step of the way.

Citations:

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3. Iain Moore, Lisa Strain, Isabel Pappworth, David Kavanagh, Paul N. Barlow, Andrew P. Herbert, Christoph Q. Schmidt, Scott J. Staniforth, Lucy V. Holmes, Roy Ward, Lynn Morgan, Timothy H. J. Goodship, and Kevin J. Marchbank. Association of factor H autoantibodies with deletions of CFHR1, CFHR3, CFHR4, and with mutations in CFH, CFI, CD46, and C3 in patients with atypical hemolytic uremic syndrome. Blood. 2010; 115:379-387

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Atypical Hemolytic Uremic Syndrome

TESTING, DIAGNOSIS AND CONSULTATION

Finding answers is where we start.

Diagnostic Laboratories
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Faster turn-around time, improved patient care

BloodCenter offers the fastest turn-around time for aHUS diagnosis in the country. With detailed diagnostic information about the disease, you can provide your patients with the best treatment possible for their disease and condition.

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BloodCenter's aHUS Testing Algorithm
An integrated, innovative suite of tests

BloodCenter offers an evidence based approach and diagnostic tools to confirm or rule out aHUS and its potential causes. Our unique combination of protein and genetic tests maximize patient benefit by providing a complete, patient-specific work-up that yields a highly accurate and actionable diagnosis within 28 days.

This unique approach to aHUS management, combined with our experienced, expert team, can only be found at BloodCenter.

Kenneth Friedman, M.D., Medical Director of Hemostasis Laboratory, is readily available to consult with you on our test algorithms, discuss your patient's results and confer with you on possible treatments. Dr. Friedman leads an experienced, skilled team of laboratory scientists committed to providing you and your patients the highest quality of service.

Daniel B. Bellissimo, PhD, FACMG Director, Molecular Diagnostics Laboratory, consults on a wide range of molecular diagnostics of inherited bleeding and clotting disorders and hemolytic disease of the fetus and newborn.

aHUS Complement Protein Testing

aHUS is caused by uncontrolled activation of the alternate pathway in the complement system. Half of cases have been shown to be associated with defects in complement factors or related control proteins. Plasma protein studies of the complement system components may be informative in patients with aHUS.

C3: Complement activation is associated with consumption of C3 and a reduction in serum concentration. Reduced C3 levels may be seen in aHUS.

C4: C4 is also useful in distinguishing systemic activation of the classical versus alternative complement pathways.

Factor H (CFH): Decreased CFH plasma levels and/or mutations in CFH have been associated with a number of complement-mediated diseases, including aHUS.

Factor H Autoantibodies: Factor H autoantibodies clear Factor H protein from circulation, reducing control of the complement system leading to continual activation.

Factor I (CFI): CFI is regulates complement activation by cleaving cell-bound or fluid phase C3b and C4b. Levels less than 60% of normal are indicative of a quantitative deficiency.

Factor B (CFB): Factor B circulates in the blood as a single chain polypeptide. Reduced CFB levels are indicative of alternative pathway activation.

CD46: Membrane cofactor protein (MCP, CD46) is involved in the cell-surface control of complement. MCP expression is measured by flow cytometric analysis of white blood cells. Very low expression of MCP is detected in patients with homozygous MCP deficiency. Patients with a heterozygous MCP deficiency will have MCP expression around 50% of the normal range.

aHUS Genetic Evaluation

This test sequences all coding regions and many untranslated regions, intronic regions, splice sites, and promoter sites known to be associated with aHUS within the following genes: CFH, CFI, MCP (CD46), THBD, C4BPA, C4BPB, CFB, C3, LMNA, DGKε, ADAMTS13, CFHR1, CFHR3 and CFHR5. Multiplex PCR-based amplification is used to enrich genomic DNA and is followed by next-generation sequencing (NGS) with > 50 fold coverage at every target base. Sanger sequencing is used to provide data for bases with insufficient coverage. All pathogenic and likely pathogenic sequence variants identified by NGS are confirmed by Sanger sequencing. Deletions and duplications involving CFH, CFHR1, 3, and 5 are detected by Multiplex Ligation Probe Amplification (MLPA).