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Atypical Hemolytic Uremic Syndrome

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Keywords

• Atypical hemolytic uremic syndrome • Complement • Acute kidney injury
• Thrombocytopenia

Key points

- The classic triad of hemolytic uremic syndrome (HUS) is a microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury, but ischemic injury can occur in any organ.
- HUS in children is most commonly due to *Escherichia coli* infection, but may be caused by defects in the complement system (atypical HUS).
- Atypical HUS is a hereditary disorder or acquired disorder that may present at any age and has a high risk of causing permanent kidney failure.
- Treatment options for atypical HUS include plasmapheresis and liver transplantation, but the complement inhibitor eculizumab has emerged as the preferred treatment for many patients.

INTRODUCTION

Atypical hemolytic uremic syndrome (aHUS) is a rare, life-threatening disease caused by uncontrolled activation of the alternative pathway of complement. Clinically, patients usually have the classic triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury (AKI), although almost any organ in the body is susceptible to injury. An increasing number of genes encoding complement regulatory proteins have been identified where mutations make patients susceptible to the development of aHUS. Supportive

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care, including blood transfusions and dialysis when indicated, is the initial focus of treatment. A subset of patients respond to plasma infusion or plasmapheresis, which may transiently correct the underlying defect in the regulation of complement. Liver transplantation has been used to repair the underlying genetic defect in a small number of patients with aHUS. More recently, eculizumab (Soliris), a monoclonal antibody that binds to the terminal complement component C5, has been shown to be an effective short-term and long-term treatment for aHUS.

TERMINOLOGY AND DIFFERENTIAL DIAGNOSIS

aHUS is a thrombotic microangiopathy (TMA). As illustrated in Box 1, there are many different causes of TMA, which was classically divided into 2 major groups: HUS and thrombotic thrombocytopenic purpura (TTP). The most common cause of HUS in children is infection with shiga-toxin producing *Escherichia coli* [1]. In addition, there are rare cases of other shiga-toxin–producing organisms (eg, Shigella) triggering HUS. Because most cases of HUS due to shiga-toxin–producing *E coli* are preceded by bloody diarrhea,

Box 1: Thrombotic microangiopathies

- Hemolytic Uremic Syndrome (HUS)
  - Shiga and Shigalike toxin–producing bacteria
    - *Escherichia coli*
    - *Shigella dysenteriae*
  - *Streptococcus pneumoniae*
  - Defect in cobalamin metabolism
  - Atypical HUS
    - Disorders of complement regulation
    - Disorders of coagulation
- Thrombotic thrombocytopenic purpura (ADAMTS13 deficiency)
  - Acquired (autoantibody)
  - Congenital (recessive inheritance)
- Secondary
  - HIV infection
  - Pregnancy
  - Antiphospholipid antibody syndrome
  - Malignancy
  - Medications (chemotherapy, calcineurin inhibitors)
  - Radiation
  - Transplantation
  - Severe hypertension