Hemolytic-Uremic Syndrome

Alternative Names
HUS

WHO International Classification of Diseases
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism

OMIM Number
235400

Mode of Inheritance
Autosomal recessive; autosomal dominant

Gene Map Locus
1q32

Description
Hemolytic-uremic syndrome is a predominantly pediatric condition that consists of the simultaneous triad of acute renal failure, thrombocytopenia, and microangiopathic hemolytic anemia associated with distorted erythrocytes. It is classified as either D+ when it is associated with a preceding diarrheal illness, which in most people is caused by infection with verotoxin-producing E. coli, is self-limiting and nonrecurring, with complete recovery in about 90% of cases, or less commonly non-diarrheal associated D-, often recurrent, and generally with a poor outcome. The syndrome may be sporadic or familial. The familial form of hemolytic-uremic syndrome is generally considered to be an autosomal recessive disorder, but dominant pedigrees have also been reported. Mortality rates are greater than 90% in patients with autosomal dominant disease and 70% in patients with the autosomal recessive form.

Molecular Genetics
Mutations have been reported in the complement regulatory protein factor H in both sporadic and familial hemolytic-uremic syndrome with mutations identified in about 30% of cases studied. The majority of mutations are missense changes in the exon encoding complement control module 20 of factor H, an area important for both binding to anionic molecules and C3b. Such mutations result in impaired protection of host surfaces against complement activation. Some patients with hemolytic-uremic syndrome have a mutation in membrane cofactor protein MCP. In some cases, the basis of hemolytic-uremic syndrome may be related to deficiency of von Willebrand factor-cleaving protease ADAMTS13.

Epidemiology in the Arab World

Jordan
Hamed (2002) reviewed the different types of renal disorders leading to chronic renal failure (CRF) in Jordanian children. He investigated CRF in 202 Jordanian children (113 males and 89 females) who presented to the Jordan University Hospital, Amman, in the period from July 1988 to April 2001. The mean age at onset of CRF was 7.5 ± 3.9 years. Patients were followed for 0.6-12.6 years (mean 6.3 years). Hemolytic uremic syndrome (HUS) accounted for CRF in nine patients (4.5%), eight of whom had the classic (diarrhea-associated) HUS; the other patient had idiopathic HUS.

Kuwait
Al-Eisa and Al-Hajeri (2001) reported 25 children (less than 18 years of age) with hemolytic uremic syndrome who were diagnosed between January 1985 and January 2000 in the Pediatric Nephrology Unit at Mubarak Al-Kabeer Hospital. Fourteen patients (56%) had typical (D+) HUS whereas 11 (44%) had atypical (D-) HUS. No bacterial or viral pathogens could be isolated in the majority of cases. The atypical HUS group had more severe anemia (P=0.03), which was significantly more prolonged than in the typical HUS group (P=0.0028). Mortality was significantly higher...
in the D- HUS patients (P<0.0001). Recurrence of HUS was documented in 63.3% of the D-HUS group compared to 14.2% of the D+ HUS group (P=0.0053). Family history of HUS was reported in 72.7% of the atypical HUS group and 14.2% of the typical HUS group. Al-Eisa and Al-Hajeri (2001) concluded that the pathogenesis of HUS in Kuwaiti children appears to be influenced by genetic factors rather than certain environmental pathogens and that atypical HUS has a higher mortality rate, a definite familial tendency and a high relapse rate. Al-Eisa and Al-Hajeri (2001) indicated that HUS remains an uncommon problem among children in the area and that the incidence of HUS in Kuwait is estimated at 0.4 per 100,000 children/year.

Palestine
Ohali et al. (1998) described the clinical course, complement components, and pathological findings of 10 infants with autosomal recessive hemolytic-uremic syndrome (HUS). All patients were the offspring of four Bedouin couples from an extended and highly inbred Bedouin family. None of the parents or siblings had any disease symptoms. The median age of presentation was 2 weeks (range 1-20 weeks). Eight patients died, 2 patients are alive, on dialysis. Renal biopsies revealed thrombotic microangiopathy with a predominant early arteriolar involvement and subsequent development of ischemic glomerular changes. Immunofluorescence was positive for C3 in glomeruli. All patients had low complement components levels during and between relapses, and in some this was evident soon after birth and prior to the onset of symptoms. This deficiency could not be normalized by repeated plasma transfusions. Biosynthetic labeling of patients' fibroblasts demonstrated normal rates of C3 protein synthesis. Serum factor H levels were greatly decreased or absent in 4 patients tested and moderately decreased in 15 of 23 healthy unaffected siblings and patients. Ohali et al. (1998) concluded that this defect may cause complement activation and consumption, possibly at the endothelial cell level. In year 1999, Ying et al. conducted further analyses on the family of Ohali et al. (1998). Ying et al. (1999) performed linkage analysis to investigate a possible linkage between the disorder and the markers near the complement factor H (CFH) gene. Mutation analysis of the CFH coding region revealed a single missense mutation. Functional analyses demonstrate that the mutant CFH is properly expressed and synthesized but that it is not transported normally from the cell. The study of Ying et al. (1999) was the first to report that a recessive, atypical, early-onset and relapsing HUS is associated with the CFH protein and that a CFH mutation affects intracellular trafficking and secretion.

Saudi Arabia
In year 1989, Mattoo et al. reported a sibling from Saudi Arabia with autosomal recessive familial recurrent hemolytic-uremic syndrome. In year 1992, Al-Herbish and Al-Rasheed described a 1.5-year-old Saudi girl with hemolytic-uremic syndrome. The patient developed hyperglycemia in the acute stage which required insulin therapy. After a short remission, she developed permanent insulin-dependent diabetes mellitus. In year 1996, Mattoo et al. reported membranoproliferative glomerulonephritis (MPGN) and hemolytic-uremic syndrome in a patient with congenital chloride diarrhea.

United Arab Emirates
Abou-Chaaban et al. (1997) studied the pattern of pediatric renal diseases among children in the Dubai Emirate during the period from 1991 to 1996. In this period, a total of 712 pediatric patients, including 230 nationals of the United Arab Emirates, were seen with various renal problems. Abou-Chaaban et al. (1997) observed four patients with acute renal failure who are nationals of the United Arab Emirates. Some of these cases were caused by hemolytic uremic syndrome following shigella or salmonella enteritis.

References


Contributors
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