Hemolytic Uremic Syndrome (HUS)

Background

1. Definition
    - Triad of
        - Hemolytic anemia (microangiopathic)
        - Thrombocytopenia
        - Renal insufficiency

Pathophysiology

1. Pathology
    - Proinflammatory process, caused by bacterial toxins or intrinsic factor invasion (commonly intestinal mucosa)
    - Infection spreads from intestine to beef in slaughterhouses
    - Toxin causes end organ damage (mesangial cells, renal tubular epithelium, etc)
    - Prothrombotic factors cause microangiopathic hemolytic anemia (Coomb's negative)
    - Microthrombi, platelet aggregates leading to occlusion of renal arterioles and capillaries
    - Possible predisposition familial, genetic or HLA-type
    - 2 forms of disease
        - Diarrhea associated (D+)
            - Most common type
            - Most cases secondary to Shiga toxin-producing E. coli (STEC) which may be part of normal flora in cattle, but not in humans
        - Non-diarrhea associated (D-)
2. Incidence/prevalence
    - 8% of infected children will develop HUS
    - Incidence higher in rural areas
    - Outbreaks occur in developing and developed countries
3. Risk factors
    - Undercooked beef
    - Young age (1-10 yo)
    - Antibiotic use for bloody diarrhea
    - Anti-motility/anti-diarrheal drugs
    - HIV
    - Autoimmune dz
    - Pregnancy
    - Caring for infected cattle
4. Morbidity/mortality
    - Diarrhea-induced HUS
        - Mortality 9%
            - CNS involvement correlated highly with death
        - ESRD 3%
        - Renal impairment, including hypertension 25%

Diagnostics

1. History and physical exam
    - Prodrome
        - Bloody diarrhea
            - Mainly in children, especially when STEC as pathogen
            - Can be asymptomatic, esp in adults
    - Fever
    - Abdominal cramps
    - Classic triad (after 3-14 d)
        - Anemia
        - Thrombocytopenia
        - Acute renal failure (oliguria, anuria, hypertension)
    - Neuro Sx in 32%
        - Irritability, seizures, altered mental status
2. Diagnostic testing
    - Stool culture for STEC
    - CBC
    - Haptoglobins (decreased)
    - Peripheral blood smear (fragmented RBCs, burr cells, helmet cells)
    - Reticulocytes (elevated)
    - LDH (increased)
    - Coomb's test (negative)
    - Coagulation components - PT, PTT (usually normal), fibrin degradation products (normal)
    - Leukocytosis
    - Thrombocytopenia (<150,000)
    - Renal function tests (azotemia)
    - C-reactive protein (elevated)
    - Urinalysis (hematuria, proteinuria or normal)
3. Diagnostic "criteria"
    - Clinical triad
        - Microangiopathic anemia
        - Thrombocytopenia
        - Renal failure
4. Recommendation
    - Stool culture for STEC while having the diarrhea stage (SOR:C)[3,4]

Differential Diagnosis

1. Other types of dysentery
2. Henoch-Schonlein purpura
    - Renal disease
    - Purpura but no thrombocytopenia
    - Arthritis
    - Abdominal pain
3. DIC
    - Low fibrinogen
    - Thrombin time prolonged
    - Low fibrin degradation products (FDP)

4. TTP
    - Hemolytic anemia, thrombocytopenia and CNS involvement
        - Occasionally renal failure, making clinical distinction difficult
    - Neurological changes
        - In 90% of TTP and 15% of HUS
    - Acute renal failure and anuria
        - In 2% of TTP and 98% of HUS
    - Protease activity
        - Decreased more in TTP (89% vs 13% in HUS)
    - Protease inhibitor
        - Exists in 51% of TTP and not in HUS
    - Important to distinguish TTP from HUS
        - TTP needs prompt plasma exchange otherwise mortality rate very high

Therapeutics

1. Acute treatment
    - Do not treat with antibiotics or antidiarrheals (SOR:C)[5,6]
    - Fluid and electrolytes
        - Some evidence suggests early rehydration after diarrhea and sodium replacement may prevent severe complications
        - Caution to avoid overload of fluids when HUS develops
        - Monitor fluids in/out, weight and vital signs, electrolytes
    - Anemia
        - Replace blood if H&H <6/18
    - Platelets
        - Rarely needed, only if bleeding and <10K
    - Acute renal failure
        - Adjust medication dose
        - Avoid nephrotoxic medications
        - Restrict fluid to insensible loss plus urine output
        - Correct electrolytes
        - Consider dialysis if uremia symptoms present, severe fluid overload, electrolyte abnormalities, early dialysis related to better outcome
    - Hypertension
        - Calcium channel blockers
            - 1st-line
            - Nifedipine
        - ACE inhibitors
            - 2nd-line, controversial data
            - Enalapril
        - Other antihypertensives medication may be considered as well
    - In rare cases when there is CNS involvement, some evidence suggests use of plasmapheresis, similar to adult patients with TTP (where CNS involvement is a major manifestation)
    - HUS is a reportable disease

2. Further management
    - ACE inhibitors
        - Recommended for long-term, but have to be watched for possible worsening renal function
    - Monitor platelets
3. Prevention
    - Avoid ingestion of infected food
        - Once infection occurs, no management proven to prevent development of HUS

Follow-Up

1. Blood pressure monitoring / treatment (ACEi)
2. Renal function tests

Prognosis

1. Complications
    - Gastrointestinal
        - Intestinal strictures/perforations
        - Intussusception
        - Pancreatitis
        - Severe colitis
    - Neurologic (rare and may confuse with TTP)
        - Altered mental status
        - Focal neurologic signs
        - Seizures
    - Renal
        - Chronic renal failure
        - Hematuria
        - Hypertension
        - Proteinuria
    - Cardiac
        - Fluid overload
        - Pericarditis due to uremia

Prevention

1. Avoid eating contaminated / undercooked meat (beef)
2. Avoid swimming in contaminated/dirty water
3. Wash hands

Patient Education

1. http://familydoctor.org/online/famdocen/home/common/kidney/905.printerview.html

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