Uploaded to the VFC Website

2017

This Document has been provided to you courtesy of Veterans-For-Change!

Feel free to pass to any veteran who might be able to use this information!

For thousands more files like this and hundreds of links to useful information, and hundreds of "Frequently Asked Questions, please go to:

Veterans-For-Change

If Veterans don't help Veterans, who will?

Note: VFC is not liable for source information in this document, it is merely provided as a courtesy to our members & subscribers.

Hemolytic Uremic Syndrome: Management and Complications

Dr Liji Thomas, MD

Acute renal failure in young children is most commonly linked to hemolytic uremic syndrome (HUS). In this situation, it often comes as a shock, occurring as it does in a child who was previously healthy but is now in mortal danger. This illness is caused by the toxin produced by certain bacterial strains, most commonly found in beef.

At present, no specific treatment has been developed to intervene in the course of the proinflammatory and prothrombotic changes triggered by the toxin after it enters the bloodstream and binds to Gb3 receptors on the endothelial cells of the kidney, brain and other organs.

In most cases, HUS is self-limited, and 95% of children recover with effective supportive treatment. The mortality has dropped from above 30% to as low as 1% in some studies. This is linked to close monitoring and effective support throughout the phases of the illness.

The best practice in such cases includes:

1. Addressing the impaired renal function and correction of metabolic abnormalities by dialysis: this is required in half to three-quarters of patients in the acute phase. Peritoneal dialysis is used in most cases of HUS and has been uniformly effective. Hemodialysis may be preferred in atypical HUS because of the capability it offers to perform plasma exchange through the same catheter. While early dialysis is not encouraged, it should be instituted in time to prevent fluid overload, which may push a critically ill patient over the edge. The following indications should be followed:
    - Oliguria
    - Anuria
    - Significant increase in blood urea, nitrogen and creatinine
    - Metabolic acidosis
    - Difficulty with nutritional support because of the need for severe fluid restriction
2. Nutritional support
3. Maintenance of the red cell count by red cell transfusions as appropriate has been found necessary in 80% of patients and is essential in preventing cardiorespiratory complications.
4. Despite the steep fall in the platelet count, platelet transfusions are dangerous and may exacerbate the formation of microthrombi in vulnerable vascular beds and are therefore avoided, unless in situations such as an active hemorrhagic episode or an invasive procedure (such as insertion of a central venous catheter or dialysis catheter) in presence of a low platelet count.
5. Fluid-electrolyte balance: firstly the fluid volume should include the amount and type of fluid that is essential to maintain adequate nutrition. In addition, urine output needs to be maintained. Balancing the fluid needs with the equally important objective of avoiding fluid overload may be facilitated by loop diuretics, which have the additional benefit of helping to control hypertension along with appropriate antihypertensives.
6. The symptoms of prodromal gastroenteritis may be agonizing, yet this is usually self-limited. Thus it is wise to look for STEC by means of stool culture or, for a more rapid diagnosis, for STEC toxin (STX) testing in stool. If this can be confirmed, antidiarrheals and antibiotics should be avoided as they are associated with a worse outcome in these patients. This may be because of the increased exposure time to the bacterial toxins caused by lowered intestinal motility.
7. Toxin binders and blockers specific for Shiga-like toxins (STX) were designed to block the absorption of STX into the blood, but were not effective in improving the outcome of D+HUS. Similarly, inactivating monoclonal anti-STX antibodies have been designed to prevent the negative consequences of the toxin, but the problem of timing remains perplexing. The antibodies need to be given before the onset of complement system activation, with thrombotic and inflammatory events following in a cascade. This precise moment at which this occurs remains unpredictable, hindering the administration of these antibodies and the selection of potential recipients.
8. In atypical HUS, sometimes caused by genetic mutations in 5% of children, the illness is the result of abnormal complement system activation. Plasma exchange is the best mode of treatment in this subset of patients and should be started as soon as indicated.

9. The thrombotic microangiopathy in complement-mediated atypical HUS is responsive to the complement inhibitor eculizumab. It is a recombinant molecule which consists of humanized monoclonal anti-C5 antibody. It prevents the cleavage of this factor, and thereby inhibits formation of the membrane attack complex, hindering cellular destruction. This therapy has been shown to perform better than plasma exchange in both preventing and treating atypical HUS in some trials. In children below the age of 2 years, as well, it may be considered the first line of treatment since plasma exchange is not technically feasible in all centers for them.

Complications

Factors which predict the onset of complications and death include:

- Oliguria persisting beyond 10 days
- Anuria for more than 5 days
- Dehydration in the acute phase
- High total count above 20 000 per mm3
- Hematocrit over 23%

D+HUS is a systemic disease and its effects are seen on many organs. They include:

Central Nervous System Involvement

This is found in 20-50% of children with HUS. It is also the most severe, and a fifth may die of these complications while half of the patients recover completely. Many patients may have permanent neurologic damage.

Features of CNS involvement include:

- Seizures
- Stupor and coma
- Strokes
- Hemiparesis
- Facial palsy
- Pyramidal or extrapyramidal symptoms
- Dysphasia
- Diplopia
- Cortical blindness
- Complications due to hypertension, including posterior leukoencephalopathy syndrome and cerebral hemorrhage

Death

5% of patients may die, most commonly during the acute renal injury phase.

Acute Renal Failure

Oliguria or anuria usually occurs, with marked shifts in the fluid-electrolyte balance, leading to a requirement for renal replacement in 50-70% of patients.

End-stage Renal Disease (ESRD)

Atypical HUS may run in families, and has a worse prognosis than the typical form, resulting in end-stage renal disease in most patients. In this group, transplanted kidneys tend to develop the condition, ending in graft loss.

Digestive Tract

This system may experience severe complications as well, such as:

- Severe hemorrhagic colitis
- Necrosis of the intestines
- Bowel perforation
- Rectal prolapse
- Peritonitis

- Intussusception

Long-term Sequelae

In up to a quarter of patients, complications persist for life, such as hypertension and chronic renal failure, occurring even 20 years after an apparently complete recovery. Kidney damage persists in a third of cases. Long-term monitoring of HUS patients is required to check for the later development of high blood pressure or protein loss in urine. This is explained by the fact of the immense reserve of nephrons, which leads to compensation for the missing nephrons by those that remain. The most accurate predictor of long-term prognosis is a renal biopsy which shows:

- more than half the glomeruli are destroyed by microangiopathic damage
- arterial microangiopathy
- cortical necrosis

Other Complications

- Chronic pancreatitis may occur, leading to diabetes mellitus, though the latter is usually transient
- Cardiomyopathy
- Cardiac ischemia

Reviewed by Afsaneh Khetrapal, BSc (Hons)

References

- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4062558/
- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4204535/
- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4278190/
- http://www.aafp.org/afp/2006/0915/p991.html
- http://www.hindawi.com/journals/ijn/2011/908407/
- https://ijponline.biomedcentral.com/articles/10.1186/s13052-014-0101-7

Further Reading

- Hemolytic Uremic Syndrome (HUS) - Renal Disease
- Hemolytic Uremic Syndrome: Investigation and Diagnosis
- Hemolytic Uremic Syndrome Prevention
- Hemolytic Uremic Syndrome Epidemiology
- Hemolytic Uremic Syndrome in Children
- What Causes Hemolytic Uremic Syndrome in Children?

Last Updated: Aug 16, 2016