Primary Hemophagocytic Lymphohistiocytosis (HLH)

About Primary HLH

Hemophagocytic lymphohistiocytosis (HLH) *is an ultra-rare, rapidly-progressive, fatal syndrome of hyper-inflammation caused by an overactive, abnormal response of the immune system.*[1]

There are two forms of HLH

Primary: A genetic disorder often caused by an inherited problem in the immune system

Secondary: A form of HLH that occurs for a variety of reasons, such as an infection or autoimmune disorder, but is not necessarily caused by a genetically inherited abnormal immune system function

Primary HLH, also known as familial HLH, is caused by mutations in cells in the immune system. When triggered by an event, such as infection, defective cells—including T-cells and natural killer (NK cells)—cause the immune system to attack the body's tissues and organs, including the bone marrow, liver and brain.[2-4]

It is estimated that fewer than 100 cases of primary HLH are diagnosed each year in the U.S.[5] The syndrome most often affects infants from birth to 18 months but can affect individuals of any age.[6]

Symptoms of Primary HLH

Signs and symptoms of HLH may appear at any age. The onset, severity and symptoms can vary greatly between individuals.[1] Symptoms may include the following:

- Fevers
- Rash
- Swelling of the liver and spleen
- Severe low red and white blood cell counts
- Bleeding disorders
- Infections
- Neurological symptoms
- Organ dysfunction
- Organ failure

Diagnosis of Primary HLH

The diagnosis of HLH is often challenging due to the rarity of the syndrome, prevalence of various clinical and biochemical criteria that differ between age groups and the absence of signs and symptoms specific to this disease.[1] Diagnosis may be established through a positive blood test for genetic markers associated with the disease or presentation of five of eight identified criteria.[7]

- Fever
- Enlarged spleen
- Low blood cell count
- High levels of fatty molecules in the blood
- Certain cells or bacteria in the bone marrow, spleen, lymph nodes or liver
- Low or absent NK cell activity
- High iron count
- Elevated CD25 (a protein found in humans)

At least four different genes have been identified that result in predisposition to primary HLH.[6]

HLH can be fatal without treatment, with median survival of less than two months.[1]

Primary HLH Management

The immediate goal of treatment is to quickly bring the hyper-inflammatory emergency under control to prepare for hematopoietic stem cell transplant, which is the only cure.[1,8] Conventional treatment prior to transplant includes steroids and chemotherapy, which are not specifically approved to treat primary HLH. There have been no significant treatment advances in the space for 24 years.[9]

References

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