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Letter to Editor

Hemophagocytic lymphohistiocytosis: An overview

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Hemophagocytic lymphohistiocytosis (HLH) is a dangerous condition characterized by excessive inflammation that can affect people of all ages, including new borns and adults. This disorder involves an abnormal immune response causing severe inflammation and failure of multiple organs. The review discusses how HLH is diagnosed and treated, emphasizing the importance of a team of healthcare professionals in managing this condition.[1]

HLH results from the inappropriate activation of certain immune cells such as natural killer cells, CD8+ cytotoxic T-cells, and macrophages. It is categorized into primary (caused by inherited genetic mutations) or secondary (caused by an abnormal response to infection, cancer, or autoimmune diseases). Primary HLH typically appears in childhood due to genetic mutations, while secondary HLH usually occurs in adults and is triggered by acute illnesses like infections or cancers. Treatment involves suppressing the immune system and using chemotherapy, which is crucial for improving survival rates.[2]

Factors causing HLH

1. Primary HLH emerges early in childhood due to genetic mutations affecting immune cell interactions, leading to excessive inflammation. It can be further classified based on specific genetic mutations or associated clinical syndromes.
2. Secondary HLH occurs in adults as a response to acute illnesses rather than genetic causes. Common triggers include infections, cancers, and autoimmune disorders. Sometimes, adult HLH is termed macrophage activation syndrome (MAS), although it's mostly considered a part of HLH. Interestingly, a portion of adult patients may have genetic abnormalities linked to primary HLH genes, possibly contributing to their predisposition to the condition when triggered by certain factors.[3]

Histopathology: Doctors usually conduct biopsies of lymph nodes, bone marrow, or the spleen to confirm suspected HLH. The hallmark histopathological finding is hemophagocytosis, where macrophages engulf bone marrow cells. However, this finding isn't necessary for diagnosis and might not be present in all cases that otherwise meet diagnostic criteria.

Clinical and laboratory evaluation

The HLH 2004 criteria outline that at least 5 out of 8 specific criteria need to be met for diagnosis.[4] These are:

1. Fever.
2. Cytopenias (at a minimal two lineages)
3. Splenomegaly.
4. Hypertriglyceridemia +/- hypofibrinogenemia.
5. Biopsy-proven hemophagocytosis.

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6. Ferritin greater than 500 ng/ml.
7. Low or absent NK-cell activity.
8. Elevated sIL2Ra levels greater than or equal to 2400 U/ml.

Interestingly, biopsy-proven hemophagocytosis is no longer a mandatory requirement for diagnosis according to these criteria.

Differential diagnosis

HLH symptoms are often nonspecific or can be attributed to known conditions like sepsis or cancer. In children, symptoms may resemble Kawasaki disease or toxic shock syndrome. In adults, HLH can be challenging to diagnose as it might overlap with other multi-organ system disorders like malignancies, sepsis, or autoimmune diseases. A high level of suspicion is crucial when a patient exhibits multiorgan failure and does not respond to standard treatments.[5]

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None.

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