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Short communication

STAT 3 mutations, Giardia infection and the IL-17 pathway

Abstract:

Parasitic infections may be common globally in endemic areas. Giardia spp. infections are widespread globally and not endemic to one region. The presence of parasitic infections and high serum IgE levels, can be found in isolation or as a clinical manifestation of certain immune defects.

The Hyper-IgE syndromes as a group of distinct primary immune disorders should be considered in the differential and treatment of parasitic disease.

Key Words:- HIES, Giardia, Job's syndrome

Introduction:

Hyper IgE syndromes are characterized by immune defects leading to recurrent infections and abscesses, based on diminished immune and inflammatory responses. Patients with the Autosomal Dominant form of HIES have heterogeneous mutations in the Signal Transducer and Activator of Transcription factor 3 gene. The defects result in Th-17 related impairment of host defenses against Giardia and other infections including Staphylococcus (1).

Other mutational defects associated with Hyper-IgE include those in DOCK8 (Dedicator of cytokinesis8) and PGM3 (Phosphogucomutase 3). Hyper-IgE responses are important in host defense against parasitic infections, but these infections may be related to underlying immune defects (2).

Specifically, the presence of STAT3 mutations which lead to dysregulation of IgE production, and are associated with clinical features such as atopic dermatitis and recurrent lung infections, should be considered in the presence of parasitic Giardia infection of the gastrointestinal tract.

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Clinical Considerations:

In the evaluation of patients with parasitic disease, the anticipated elevation of serum IgE in the presence of certain features may lead to the diagnosis of an underlying primary immune defect. The pattern of infections caused by a variety of fungi, Staphylococcus bacteria, leading to skin and lung abscesses can be important in establishing the diagnosis. The gastrointestinal disease is variable among these patients, but may be associated with eosinophilia. Thus, physical examination and pattern of microbiologic signatures are useful in identifying those patients with parasitic disease who may have an underlying primary immune defect.

Giardia Infection and Host Defense:

Giardia spp. is a protozoan parasite found globally that causes the disease giardiasis. Clinical symptoms of abdominal pain and watery diarrhea are common. Immune responses involve CD4 T cells that generate anti-Giardia antibodies. B cell independent CD4 regulated responses include the IL-17 pathway (3).

AD-HIES is a primary defect with Gastrointestinal and multi-system disease manifestations. Among these include the presence of a prominent forehead, retention of primary teeth and scoliosis. The Gastrointestinal disorders associated with AD-HIES include GI lymphoma, dysmotility, and eosinophilic esophagitis. The patients afflicted with this disease, are more prone to Salmonella and Giardia infections (2).

In the evaluation of a patient with Giardia, an immune defect in the production of IL-17 can be considered in the context of the patient's history, physical examination findings and patterns of prior infections.

Laboratory findings and immune profiling:

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One of the hallmark laboratory results for patients with AD-HIES is an extremely elevated serum IgE level. The differential of this finding includes parasitic disease and allergic pulmonary bronchoaspergillosis (ABPA). The serum IgE in childhood is typically greater than 2000 IU/ml. The levels of IgA, M and G are normal and specific antibody responses may be lower or normal. Cellular profiles may include neutropenia (2).

Lymphocyte profiling reveals low memory B and T cells. Further analysis reflects a defect in the IL-17 responses with very low numbers of IL-17 producing Th-17 cells. STAT 3 is a key transducer protein for many cytokines, including IL-17. STAT 3 is required for the differentiation of naïve T cells into Th-17 cells. Th-17 responses have been found to be aberrant even among HIES patients without STAT 3 mutations (3, 4).

Conclusions:

The Hyper-IgE syndromes comprise a group of primary immune defects with distinct genetic mutational defects. Patients may be prone to parasitic disease based on defects affecting the IL-17 pathway. Upon presentation of patients with parasitic disease, particularly in non-endemic areas, evaluation for HIES may be indicated. Further studies can be conducted to elucidate the immune mechanism of gastrointestinal parasitic disease among these patients.

References:

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