Title: Immune-Mediated Enteropathy: A Unique Gastrointestinal Disease Entity

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Background: Diarrhea, vomiting, failure to thrive, and abdominal cramping, in conjunction with intestinal villus blunting, is not an uncommon encounter for a pediatric gastroenterologist. A subset of this particular pediatric population lack food allergies, exhibit unresponsiveness to avoidance diets, and have no serological or histological findings of Crohn’s, ulcerative colitis, or celiac disease. This subset also lacks anti-enterocyte antibodies and FOXP3 mutations that are present in classical autoimmune enteropathy.

Objective: To assay for T-helper cell activation markers in children with immune-mediated enteropathy (IME) that lack anti-enterocyte antibodies and have normal FOXP3 expression.

Design/Methods: We assayed serum and stained small bowel biopsies from three patients with chronic diarrhea for lymphocyte activation markers (LAM). We compared our results to normal controls.

Results:

![Lymphocyte Activation Markers in Immune-mediated Enteropathy](image)

In all three patients (symbols), peripheral blood T-cells showed significantly elevated markers (range 30 to 70%) of CD25, CD69, CD40L, CD71, and HLA-DR. A similar pattern of LAM was observed in small bowel biopsies. (Figure 1)

Conclusions: In patients with food allergies, T-cell activation levels that are antigen specific are low in peripheral blood, approximately 0.01%, making this the unlikely etiology for our patients’ disease process. We do see global T-cell activation in ulcerative colitis and Crohn’s disease, but our patients’ histology is not consistent with these etiologies. Based on serologic and biopsy findings, our patients also do not appear to have celiac disease even though the T-cell activation response is not known in this condition.

We propose that there is a distinct cohort of patients with "immune-mediated enteropathy" that have chronic diarrhea, blunting of villi, and non-specific global activation of LAM, in the absence of anti-enterocyte antibodies, but with normal FOXP3 expression. This appears to be a strictly T-cell mediated gut injury.