Oncostatin M as a Predictor for Non-Response to Anti-TNFα Therapy

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Introduction: Anti-TNFα therapy is currently the first line treatment for pediatric Crohn's disease (CD). However, long-term response to these drugs is low – after 1 year of treatment less than half of CD patients had mucosal healing on endoscopy and few attained deep remission. As new biologic therapies become available, there is a need for an anti-TNFα companion diagnostic that can predict which patients will respond to this treatment. Oncostatin M (OSM) is an inflammatory marker that has been shown to be strongly associated with anti-TNF non-response.

Hypothesis: Elevated OSM, both in the plasma and the intestinal tissue, will be predictive of biochemical non-response to infliximab in the pediatric CD cohort.

Methods: Peripheral blood was obtained from 40 CD patients prior to starting infliximab and we measured plasma OSM using an ELISA assay. The primary outcome was biochemical response (fecal calprotectin <400 mcg/g). Clinical remission at Year1 (wPCDAI<12.5) was also evaluated. Intestinal biopsy specimens were obtained from 23 CD patients and we measured tissue mRNA expression of OSM using qPCR. The primary outcome was correlation to plasma OSM values, and the secondary outcome was any response (decrease in fecal calprotectin) at Month3.

Results: The plasma OSM values were significantly higher for biochemical non-responders compared to responders (p=0.03). The Year1 biochemical remission rates for OSM^{low} (OSM<143.5 pg/ml) was 72.7%, compared to 35.3% in the OSM^{high} group (p=0.026). There was no correlation between plasma OSM and tissue OSM mRNA expression for both ileal and rectal biopsy specimens. OSM mRNA expression in rectal biopsy specimens was significantly higher for patients with no response at month 3 compared to responders (p=0.034).

Conclusions: In a prospective pediatric CD cohort starting infliximab, we found an elevated pre-treatment plasma OSM and an elevated rectal OSM mRNA expression were associated with poor biochemical and clinical outcomes. The lack of a clear correlation between plasma OSM and tissue OSM may be attributed to the small sample size, and further work will include enrolling more patients to elucidate this relationship.

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