



Elimination of Cow's Milk Protein and Gluten from the Diet Induces Gut Healing in "Refractory" Pediatric Celiac Patients

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Letter to Editor

In the August 2020 issue of Annals of Pediatrics Capone, et al reported on 4 female pediatric patients who were diagnosed with Celiac Disease (CeD) based on abnormal celiac autoantibodies and duodenal histology [1]. While all patients improved symptomatically on a Gluten Free Diet (GFD), they all had persistently elevated autoantibodies and ongoing villous atrophy on repeat duodenal biopsies despite strict adherence to the

GFD. After additional elimination of Cow's Milk Protein (CMP) from the diet (CMP-GFD), all 4 patients had prompt normalization of their celiac serologies for the first time since diagnosis, suggestive of an additional Cow's Milk Protein Intolerance (CMP-I). Patients 1 and 3 underwent repeat endoscopies on the CMP-GFD, which displayed complete normalization of the duodenal mucosa for the first time since diagnosis. Patient 3 tested negative for a cow's milk immunoglobulin E antibody.



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The mechanism of action leading to the persistent elevation of CeD-specific autoantibodies and villous atrophy in patients with coinciding CMPI and CeD remains unclear. Our speculation remains that CeD associated enteropathy leads to an increased mucosal permeability and subsequent, inappropriate immune responses to other dietary antigens, including CMP. The homologous amino acid sequence between β -casein found in cow's milk and gliadin may result in an antigenic mimicry allowing for this response to occur. This hypothesis of antigenic mimicry is supported by other studies which have linked CMP and gluten [2,3].

We write to report on the long term follow up for patient 3 from this previous case series.

Following her repeat endoscopy on the CMP-GFD free diet displaying a normal gross duodenal appearance, as well as complete histologic recovery, she remained on a CMP-GFD with complete resolution of her GI symptoms and return to her pre-diagnosis height and weight percentiles within 6 months on the combined elimination diet. She reintroduced cow's milk 18 months after its elimination with no recurrence of symptoms or alterations to her height or weight velocities. Repeat serologies remained normal 2 months after CMP reintroduction. The patient was scheduled for a repeat endoscopy at that time, but secondary to the impact of COVID it was ultimately completed 20 months following CMP reintroduction. The upper endoscopy displayed no active CeD grossly or histologically.

Not only has our data shown that it is possible for a simultaneous CMPI to create the appearance of "refractory" CeD in children, but we have now additionally displayed that unlike the life-long sustained inflammatory response to gluten seen in CeD, the inflammatory response to CMP is transient and tolerance can be achieved following prolonged, but temporary, elimination from the diet.

We conclude that given this novel information, pediatric, and possibly adult, CeD patients with suspected "refractory" CeD and no detectable gluten exposures, should be trialed on a combined CMP-GFD with close monitoring for disease activity resolution prior to consideration of more restrictive diets, such as the Gluten Contamination Elimination Diet (GCED) [4], or initiation of immunosuppressive therapies for refractory CeD [5].

References

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