Celiac disease - the monitoring challenge

Source: Leonard MM, Weir DC, DeGroote M, Mitchell PD, Singh P, Silvester JA, Leichtner AM, Fasano A. *Value of IgA tTG in Predicting Mucosal Recovery in Children With Celiac Disease on a Gluten-Free Diet.* J Pediatr Gastroenterol Nutr. 2017 Feb;64(2):286-291.

Celiac disease (CD) is an autoimmune inflammatory disease of the small bowel precipitated by the consumption of gluten. It was believed to be a childhood illness, but we now know that it can occur at any stage in life. Clinical manifestations vary greatly, from silent disease to systemic manifestations. It is also strongly associated with autoimmune conditions and genetic syndromes. Diagnostic criteria rely on serologic antibody tests while consuming gluten containing food, especially IgA anti- tissue transglutaminase (tTG) and autoantibodies against endomysium (EMA). The total IgA level should be measured before the test, because more than 2% of patients with celiac disease have a selective IgA deficiency.

The histologic evaluation according to the Marsh classification (which considers inflammatory infiltrate, crypt hyperplasia, and villous atrophy) is the gold standard for the diagnosis. Treatment consists of a strict gluten-free diet (GFD) for life[1]. The clinical response and the serological are both methods for monitoring adherence to the GFD. It is expected that a child who follows a GFD will have a serologic normalization within 12 months[2].

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This was a retrospective study conducted at two quaternary care centers, involving 103 patients under 21 years, with histological-proven CD according to Marsh criteria (Marsh 3 lesions). Those patients have undergone a second endoscopy with duodenal biopsy at least 12 months on a GFD (median of 2.4 years, ranging from 1 to 12 years). In 70% of them, the biopsy was repeated because of persistent or new gastrointestinal symptoms. 34% of the patients had persistently elevated serology when the biopsy was repeated. Only seven asymptomatic patients underwent biopsy to confirm mucosal healing. Eleven asymptomatic patients with persistently elevated tTG had a repeat biopsy. Four asymptomatic, seronegative children underwent a repeat biopsy to assess for mucosal recovery and confirm the CD diagnosis. The adherence to a GFD was based on a physicians' or dieticians' subjective assessment at the time of the clinic visit[3].

The authors found that 19% of CD children exhibited persistent villous atrophy (VA) consistent with a Marsh 3 lesion at the time of the repeat endoscopy[3].

They also found that at the time of the repeat biopsy, tTG was elevated in 43% of children with persistent VA and 32% of children with mucosal recovery. They suggest that IgA tTG was not an accurate measure of mucosal healing in

this pediatric population. It is important to note that the authors themselves mentioned that the IgA tTG assay was run in multiple laboratories, performed within 4 months of the repeat biopsy. One important finding is that only 55% of patients with persistent VA at the time of the repeat biopsy were symptomatic[3].

The authors emphasize that neither the absence of symptoms nor a negative tTG could be surrogate markers of mucosal recovery in patients with CD on a GFD[3].

In CD adults the studies demonstrate that over 50% have persistent enteropathy on repeat biopsies despite being on a GFD for 2 or more years[4].

Among adults, the VA persistency is correlated to iron-deficiency anemia, low blood ferritin level and additional risk factors for lymphoproliferative disease[5].

Commenting on the study, Doctor Ivor D. Hill highlights the urgent need for more studies to prospectively consider a repeat endoscopy to confirm remission. He argues that now very few CD children on a GFD undergo repeat biopsies, so it is possible that the amount of children with persistent enteropathy is much higher than is currently believed[6].

On the other hand, Koletzko et al commenting on the study stated that the tTGA should be performed within 2 to 4 weeks to the repeat biopsy, because mucosal lesions may be induced by incidental or voluntary ingestion of gluten. This DC group advises against re-biopsies for all CD chidren, reserving this test for selected cases - seronegative or symptom persistent children on a GFD[7].

Considering the findings in adult studies, the fact that anti-tTG do not correlate well with histological findings or symptoms in CD patients on a GFD as well as those findings, it is important to consider a repeat biopsy for monitoring those patients. This study raises the possibility to consider biopsies not only a key component for diagnosis, but also for monitoring disease in some cases.

We also agree that the management criteria of CD in childhood should be revisited as new studies and additional information are available.

References

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