Growth Hormone Deficiency and Celiac Disease: The Long and Short of It

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In this issue of Indian Journal of Pediatrics, Walia et al. have evaluated the growth hormone axis in 10 children with celiac disease (CD) who failed to have catch-up growth on a gluten-free diet (GFD), and found that 70% had concomitant growth hormone deficiency (GHD) [1].

The coexistence of CD-GHD was first reported by Bozzola et al. in 3 children with short stature [2]. Subsequently, a multicentric study evaluating 7066 children with short stature found 16 (0.23%) to have CD-GHD [3].

Does this mean that one should suspect GHD in all children with CD on GFD with persistent growth failure? Probably Not. This is because there are some pertinent issues with the published literature on CD-GHD that need to be addressed. Firstly, in all studies “serological remission” is taken as a surrogate marker for compliance to GFD. However, in a meta-analysis of patients with CD undergoing follow-up biopsy on GFD, it has been found that serum tissue transglutaminase (tTG) immunoglobulin A (IgA) has a low sensitivity (50%) in detecting persistent villous atrophy. This means that many patients with normal tTG on GFD have villous atrophy [4]. So, it would be prudent to perform biopsy and demonstrate normalization of the villous architecture before embarking on a search for other causes of persistent symptoms in CD patients on GFD; otherwise, there is a chance that children with active CD will be inadvertently

evaluated for GHD. False negative GH responses to pharmacological stimuli have been observed in active CD, which normalizes once there is compliance to GFD. In a study from the 1970s before serology became available and CD activity was based solely on histopathology, it was found that 69% children with active CD had a GH peak 2 standard deviations (SD) below the mean [5].

Secondly, in these studies, a GH cutoff of 10 mcg/L has been used to demonstrate GHD, which has limited literature support. Many societies now recommend lower cutoffs of around 7 mcg/L to reduce false-positive detection rates [6].

Thirdly, in most studies in which the GHD-CD patients were treated with GH therapy, a short duration of follow-up and the lack of a control “only GFD” group makes it difficult to draw meaningful inferences.

Finally a definite pathological cause for the GHD-CD coexistence is not well defined and though autoimmune causes have been postulated, these are uncommon causes of GHD in childhood and need further elucidation. Walia et al. did not find a significant difference in antipituitary antibody (APA) levels between the cases and controls. Furthermore, Aguado et al. reported the presence of APA in 30% patients with non-CD enteropathies, putting a question mark on their significance [7].

The current study gives some food for thought for approaching children with nonresponsive CD. However, with the limitations discussed above, it is difficult to make any recommendations regarding GH testing or treatment in CD based on the available literature. In the future, studies with a larger sample size of CD in biopsy-proven remission, using appropriate GH cutoffs and a control non-GH treated group with a long follow-up and final height data would be required to give definite answers regarding the CD-GHD association.

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Declarations

Conflict of Interest None.

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