Celiac disease and Hashimoto's thyroiditis: a shared plot?

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Dear Editor:

Celiac disease (CD) is a chronic autoimmune disease characterized by permanent intolerance of dietary gluten in genetically susceptible individuals. It is an enteropathy of the proximal small intestine defined by inflammation, crypt hyperplasia, and villous atrophy that regress on withdrawal of gluten from the diet. A bulk of evidence suggests a strong association between CD and a number of immune-mediated disorders such as Hashimoto's thyroiditis (HT). Common genetic predisposition has been proposed as a candidate explanation for the positive association between CD and HT. However, ongoing chronic inflammation has been supposed to contribute to the onset of both diseases. Autoimmune and endocrine disorders are related to predominance of T helper cell type 1 (Th1) pattern response with the involvement of Th1 cell-associated cytokines such as interleukin-18 (IL-18) and interferon- γ (IFN- γ). Interestingly, CD has been connected with an altered Th1 cytokine production profile. Among the pro-inflammatory cytokines detected in Th1 response after gluten exposure, IL-18 and IFN- γ have been reported to be considerably involved in the onset of CD. It has been shown that IL-18 and IFN- γ levels are higher in samples from CD patients in comparison to healthy controls. IL-18 within epithelium has been correlated with enterocyte damage. IFN- γ is considered as a key factor in gut permeability as well as in inflammation in CD. IFN- γ has been demonstrated to be the primary effector of increased gluten peptide translocation during active dis-

ease. IL-18 is considered as an important inducer of IFN- γ . Concordantly, the early response following gluten intake characterized by high levels of IFN- γ seems to be driven by IL-18. It has been advised that IFN- γ gene polymorphisms may play an important role in susceptibility to CD. In addition, it has been supposed that haplotypes of the promoter region of IL-18 may have an impact on CD development. HT is an autoimmune condition in which imbalance of Th1-mediated responses results in the destruction of thyroid follicular cells. Similarly to CD, an abnormal expression of both IL-18 and IFN- γ has also been observed in HT. Intrathyroidal interactions between IL-18 and IFN- γ have been described to play a critical role in inducing and maintaining the local immune response leading to the destruction of thyrocytes in HT. Interestingly, the existence of a nexus between IL-18 genotypes and the risk for developing HT has been shown. Furthermore, genetic variants in the IFN- γ gene have been related to the severity of HT. With respect to the above, we hypothesize a causal link between CD and HT. We think that the common immunological Th1 pattern may concur in the pathophysiological basis of the association between CD and HT by polymorphisms in gene expression of both IL-18 and IFN- γ . Research studies are required in order to define whether polymorphisms in the IFN- γ and IL-18 genes may affect the onset and progression of both diseases. Single nucleotide polymorphisms (SNPs) in both IL-18 and IFN- γ genes might be used as biomarker for early diagnosis of autoimmune diseases including CD and HT. In patients with CD, the possible existence of HT should be taken into account and an accurate screening is recommended at diagnosis and follow-up. Administration of neutralizing antibodies against IFN- γ and/or IL-18 may represent a fruitful avenue for future therapeutic options.

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