The Celiac Warriors: Intraepithelial Lymphocytes

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Over the last few years, the concepts of the management of celiac disease have undergone several more in depth changes due, mainly to better knowledge of the disease and increased awareness of its presence. This has resulted in the description of different forms of the disease and the need to revise the diagnostic criteria.

We currently face a broad spectrum of possibilities with very varied clinical symptoms and ages that previously did not form part of the suspected diagnosis. The door has been opened to a very large perimeter of patients with many complex accompanying variables in which the only certain and unmovable factor is the role of the immune system as the trigger of the disease.

At a time when greater sensitivity and specificity is demanded in the diagnostic tests we still depend on a gold-standard test that although it orientates and helps with diagnosis is far from being pathognomic or even specific for the disease, given that it is restricted/limited to analysing the changes presented in the epithelium with the very variable idiosyncrasy of one individual to another at the time of facing the lesions, the great variability in diet, the possible influences of age and microbiota and of course the different types of immunological response. Consequently several years ago our laboratory established a diagnostic method based on the analysis of the immunological populations that are activated and are the cause of the immunological attack in celiac disease. We coined this method: phenotype of intra-epithelial lymphocytes (IELs): Lymphogram.

The first step observed in this histological battle is the increase in the population of intestinal epithelium lymphocytes, defined as Marsh 1 or 'the army preparing for battle'. From this moment the next anatomopathological grades take charge of describing the 'fight' and its effects as good war reporters, taking diagnostic decisions about the lesion advances shown in this epithelium, obviously highly influenced by the homeostasis mechanisms and the capacity of this tissue to face its lesion (the courage of the resistance).

The IELs phenotype ignores these variables as it directly analyses the populations involved in the battles the warriors. There are many publications supporting the alterations in the immunological populations observed in celiac disease. This characteristic phenotype: CD45^{+} increases, iNK reduction and rise of LT TCR $\gamma\delta$ permits the army direct assessment, questioning the immune system whether or not celiac disease is the cause or whether it is another process, infections, allergy, food intolerance, tumors, autoimmune diseases, inflammatory disease etc. which ultimately give rise similar mechanisms of epithelial lesions graded by Marsh and the elevations of auto-antibodies against the self-same molecules of the intestine such as transglutaminase -2.

Our experience has enabled us to diagnose patients years before presentation of intestinal lesions classified as Marsh 3, obtaining benefit in quality of life and recovery in the patient, ruling out or diagnosing the disease in doubtful or atypical cases, orientating the diagnosis and naturally avoiding pigeonholing the wrong patients in a chronic disease which conditions their diet and lifestyle.

In such an interesting period of a disease which despite being so long lasting is still thriving and powerful, with so many challenges for the future, in which many aspects are questioned anew and for which new and better diagnostic arms are demanded, what better evaluation than an authentic 'crystal ball' which allows us to ask the immune system: What are you doing?