

A new inflammatory disease on the rise

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Although little known, eosinophilic esophagitis is an inflammatory disease whose prevalence has increased considerably in recent years. According to a recent clinical study, an antibody that blocks this inflammation significantly improves the symptoms associated with this disease.

As the name suggests, eosinophilic esophagitis is inflammation of the esophagus mediated by the presence of excess eosinophils, a class of innate immune system cells that are frequently involved in allergic reactions. This inflammation can be considered a modern disease, as it was first described in 1993 (1). The disease mainly affects children and young adults, the vast majority of whom are male, and is often accompanied with atopic disorders (eczema, asthma, allergic rhinitis).

In adults, the symptoms of the disease take the form of dysphagia (difficulty swallowing) and food impaction (food that gets stuck in the esophagus), while in children there is mainly a refusal to eat, vomiting and stomach or chest pain.

RISE IN CASES

The frequency of diagnosis of eosinophilic esophagitis has increased enormously in recent years in Western countries, now being similar to that of ulcerative colitis (50–100 cases/100,000 people), and the disease accounts, for at least currently, as the leading cause of food impaction in children and adults under 50 years of age.

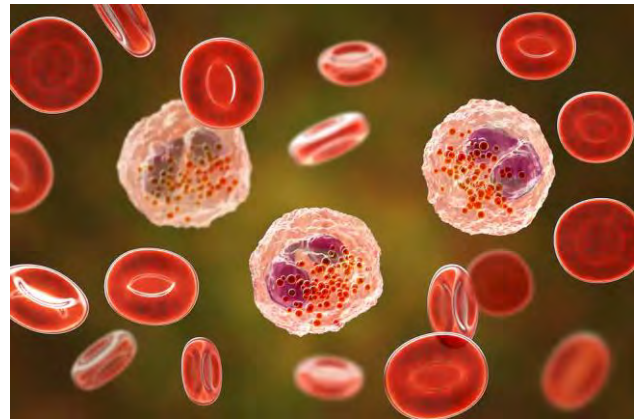
The reasons for the rapid increase in the incidence and prevalence of eosinophilic esophagitis, particularly over the past decade, remain unclear. Four main explanations have been offered:

1) The hygiene hypothesis: according to this theory, too much hygiene would reduce early exposure to infections and microbes, which would lead to disruption of the microbiome (dysbiosis) and poor education of the immune system for the antigen recognition. The increase in the prevalence of allergic, autoimmune and inflammatory diseases would be a consequence of this dysbiosis.

2) Dietary changes: modifications to the food production process (treatment of animals with hormones and antibiotics, food additives, ultra-processed foods) also disrupt the microbiome and would promote the emergence of inflammatory diseases.

3) Helicobacter pylori: The frequency of infection with the intestinal bacterium *H. pylori* has decreased dramatically over the past few decades. This eradication is positive for the prevention of stomach cancer, but this bacterium nevertheless activates certain regulatory T lymphocytes of the immune response that could protect against esophagitis and other inflammatory or allergic diseases.

4) Esophageal reflux: the frequency of esophageal reflux has risen sharply in recent years, in particular due to the significant increase in the



number of overweight people. Contact of the lining of the esophagus with stomach acid can alter the integrity of the lining and allow antigens present in food to penetrate inside the cells of the esophagus and trigger an inflammatory response.

A NEW TREATMENT

Whatever the mechanism favoring its development, eosinophilic esophagitis remains a disease that significantly reduces the quality of life and which can, over time, cause fibrosis leading to a tightening of the esophagus and make absorption of food very difficult.

Currently, treatment primarily involves testing whether elimination diets (which exclude major food allergens such as wheat, dairy, fish/seafood, peanuts/tree nuts, eggs, and soy) can decrease symptoms. If this is not the case, corticosteroids can be swallowed to locally coat the wall of the esophagus to reduce inflammation.

However, these treatments fail in a significant proportion of cases, so alternative options must be developed to improve the treatment of the disease.

A major advance in this direction comes from a phase 3 clinical study where the effect of dupilumab, an antibody that blocks an essential element (signaling of interleukins -4 and -13) of the response in several inflammatory diseases, including eosinophilic esophagitis, was tested (2).

The study shows that a weekly dose of the antibody, given by subcutaneous injection to adolescents and adults suffering from the disease, causes the disappearance of eosinophils from the esophageal tissue in 60% of patients, compared to only 5% of patients who received placebo. The antibody also reduces dysphagia symptoms and improves patients' quality of life much more than placebo, without major side effects.

This new drug could therefore prove to be a welcome addition to the current treatments for eosinophilic esophagitis, which are still too few in number.

- (1) Attwood SE et al. Esophageal eosinophilia with dysphagia. A distinct clinicopathologic syndrome. *Dig. Dis. Sci.* 1993; 38: 109–16.
- (2) Dellon E et al. Dupilumab in adults and adolescent patients with eosinophilic esophagitis. *N. Engl. J. Med.* 2022 ; 387 : 2317-30.