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Non-celiac gluten sensitivity: An underdiagnosed condition in dermatology?

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Non-Celiac Gluten Sensitivity (NCGS) is a syndrome characterized by intestinal (bloating, diarrhea, ...) and/or extra-intestinal symptoms (headache, fatigue and others) alleviated by gluten free diet (GFD) in subject who do not meet the criteria for Celiac Disease (CD) or wheat allergy ¹. Gluten being the main protein complex contained in several cereals identified as the potential trigger to this syndrome. The prevalence of this syndromes is far from being defined, with only few available data, which are largely variable ².

We report the case of a 34-year-old male with a stable multiple sclerosis who had important pruritis since May 2020. A symmetrical papulo-vesicular rash was described on the hands, elbows, knees, and buttocks, associated with chronic constipation and bloating. Our first hypothesis was dermatitis herpetiformis (DH), dermocorticoids were prescribed as a first line treatment, pending further investigations. Pruritus was still important despite the well conducted treatment. The anti-endomysium and anti-transglutaminase antibodies were negative without IgA deficiency. The histological analysis showed an inflammatory infiltrate in the superficial dermis. Direct immunofluorescence technique (DIT) demonstrated granular C3 deposits on the basal membrane.

With these clinical and pathological findings, we suspected a NCGS and began a GFD as a trial treatment. After 2 weeks of GFD, the patient did not feel any itchiness, his skin condition improved drastically with no new lesions. After a meal with gluten (cereal dish consumed at home), the condition temporarily relapsed. The digestive endoscopy ruled out a CD with multiple biopsies ³ and the IgE specific antibodies for wheat, gluten and gliadine were all negative.

Bonciolini et al ⁴ proposed 3 criteria for diagnosis of NCGS related cutaneous symptoms: itching, presence of granular C3 at the dermoepidermal junction, a rapid resolution of lesions when adopting the GFD.

The physiopathology is currently unknown, and there are no valid biomarkers to help with the diagnosis. NCGS is an inflammatory condition supported by innate immune mechanisms, including high level of CD3 T cells and TLR2 on the mucosa in patients with NCGS compared to controls ⁵. A study researched the expression levels of selected miRNAs in duodenal biopsies collected from newly diagnosed patients with NCGS and, as controls, from patients with CD and gluten-independent gastrointestinal problems. They identified 7 miRNAs with higher expression in the intestinal mucosa of patients affected by NCGS ⁶.

This syndrome is often criticized by the lack of strong studies and the subjective nature of the end points that may be linked to the placebo effect of a GFD on digestive symptoms ⁷.

However, NCGS has been reported to induce skin reactions in 29 % of 486 patients in a prospective study and up to 65,6% of the patients in some cohorts ^{2,8}. We could therefore rely on the response of these skin manifestations to the GFD to be less subjective than digestive symptoms. The different type of lesions found were : eczematous dermatitis, generalized itching, psoriasiform lesions, or dermatitis herpetiformis like, with important pruritus, on the extensor surfaces of limbs, bottom, and trunk as in our case ^{4,8}. The histological analysis showed granular

or microgranular C3 deposits at the dermoepidermal junction in 82% of cases. In all these patients, the GFD lead to the disappearance of the lesions in less than a month. The diagnosis should be confirmed by double-blind, placebo-controlled food challenge ⁹.

The GFD has been reported to be beneficial in multiple sclerosis too, which could be helpful for our patient ¹⁰.

It seems that NCGS and the use of GFD, even though it has been criticized as an entity, has been an answer to a growing population of patients seeking care. Further larger series of patients would be interesting, to better characterize the different skin presentations.

Figures : see separate file.

Figure 1 : NCGS, 1A - Papulo-vesicular rash on the hands before Gluten Free Diet (GFD) and 1B - after GFD

Figure 2 : NCGS, Direct immunofluorescence technique (DIT) showing granular C3 deposits on the dermoepidermal junction

Abbreviations

Non-Celiac Gluten Sensitivity (NCGS)

Celiac Disease (CD)

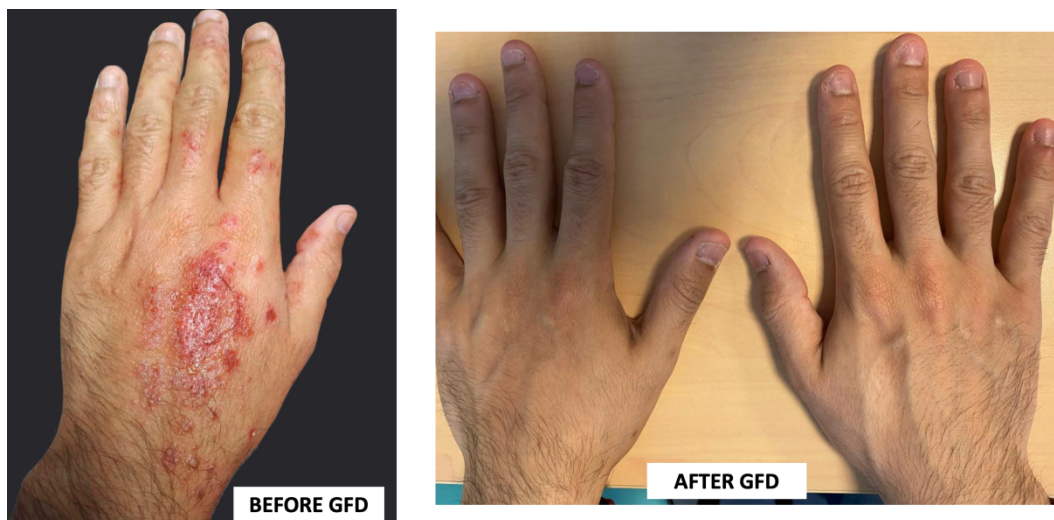
Dermatitis Herpetiformis (DH)

Direct immunofluorescence technique (DIT)

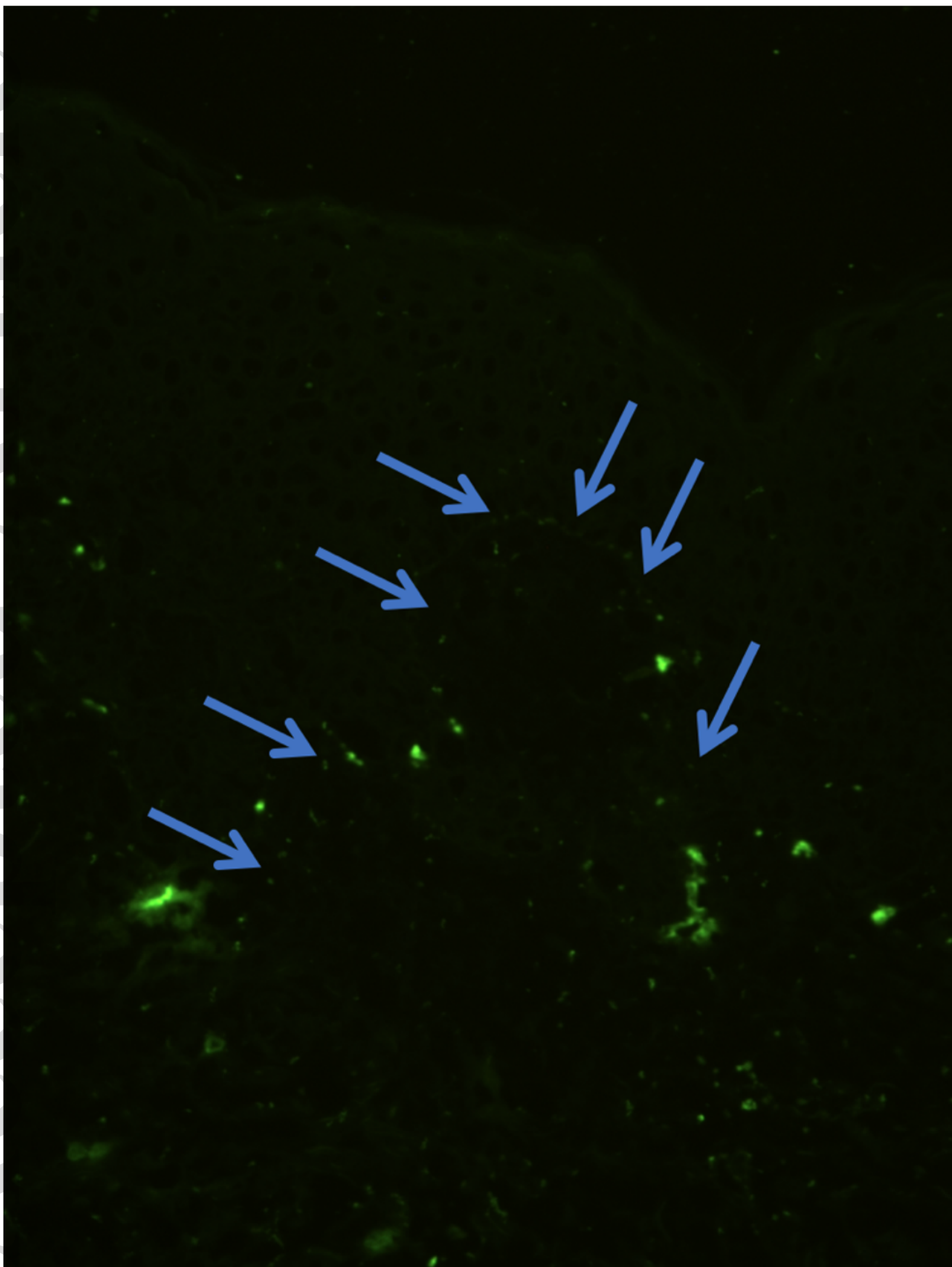
Gluten Free Diet (GFD)

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