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CASE REPORT

Transient non-coeliac gluten sensitivity (NCGS) with markedly reduced villous height/crypt depth ratio

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ABSTRACT

There is no confident evidence in the current literature to show or demonstrate that non-coeliac gluten sensitivity (NCGS) exclusively presents with mild or nearly normal duodenal mucosal abnormality. Gluten sensitive patients with negative serology and severe mucosal changes are labelled with the term seronegative coeliac disease (SNCS). There might be at least some overlap between NCGS and SNCD. Transient gluten sensitivity with severe mucosal changes without CD have been previously reported like in our case.

Keywords: Non-coeliac gluten sensitivity, Coeliac disease, Histology.

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Introduction

The histology of NCGS has been a matter of debate and there is no clear consensus on the spectrum of mucosal changes in this group of patients. A positive HLA DQ2/DQ8 and more severe duodenal mucosal abnormality has been used to endorse a diagnosis of SNCD versus NCGS patients who may present with positive or negative of these alleles of the HLA in a 50% ratio. In this case report we show that gluten may induce severe enteropathy without a diagnosis of coeliac disease or appropriate HLA association.

Case report

A 76 years old woman with a background of B12 deficiency and lymphocytic colitis was referred to gastroenterology with a history of 17 kg weight loss over four months and symptoms of decreased appetite, severe nausea and occasional loose bowel motions. Initial investigations in primary care found a normal complete blood count (Hb, MCV WCC, and platelets), normal ferritin, thyroid screening test and she had negative serial faecal occult blood results. No infective organisms were detected on stool culture including giardia or H pylori. Faecal calprotectin was also negative. She had a normal IgA level and coeliac disease (CD) serology were negative during full gluten containing diet. Further investigation including HIV screening and imaging were negative. She was not on any regular medication or analgesics like NSAID except Omeprazole as PRN. She underwent a CT chest, abdomen and pelvis for weight loss investigation which did not reveal any underlying malignancy. The patient and family were very concerned about possible malignancy as a cause for her progressive weight loss and lack of other explanation or diagnosis. As the next step, she underwent an upper gastrointestinal endoscopy (UGE) that was reported unremarkable. However, the duodenum biopsies revealed clear decrease of villous height/crypt depth ratio with markedly increased intraepithelial lymphocytes consistent with Marsh III appearance (1, 2) (see Figure 1). Following UGIE and the finding of a flat duodenal mucosa, the patient was recommended to start with a strict gluten-free diet (GFD) under dietitian's guidance as she was

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highly suspicious for seronegative coeliac disease. With this intervention, she gained dramatic improvement of symptoms and impressively regained the 17 kg of weight loss over the following 6 months post GFD. Her symptoms of nausea and loose bowels reoccurred following a short period of gluten challenge. Given the histological findings and impressive response to a GFD, her HLA DQ2/DQ8 status was assessed and interestingly her HLA DQ2/DQ8 similar to her CD serology came back negative. Patient underwent a gluten challenge again when she fully recovered and interestingly she tolerated gluten again without experiencing any of her previous symptoms. Her weight remained stable and she remained asymptomatic based on last telephonic follow up nearly a year after normal diet.

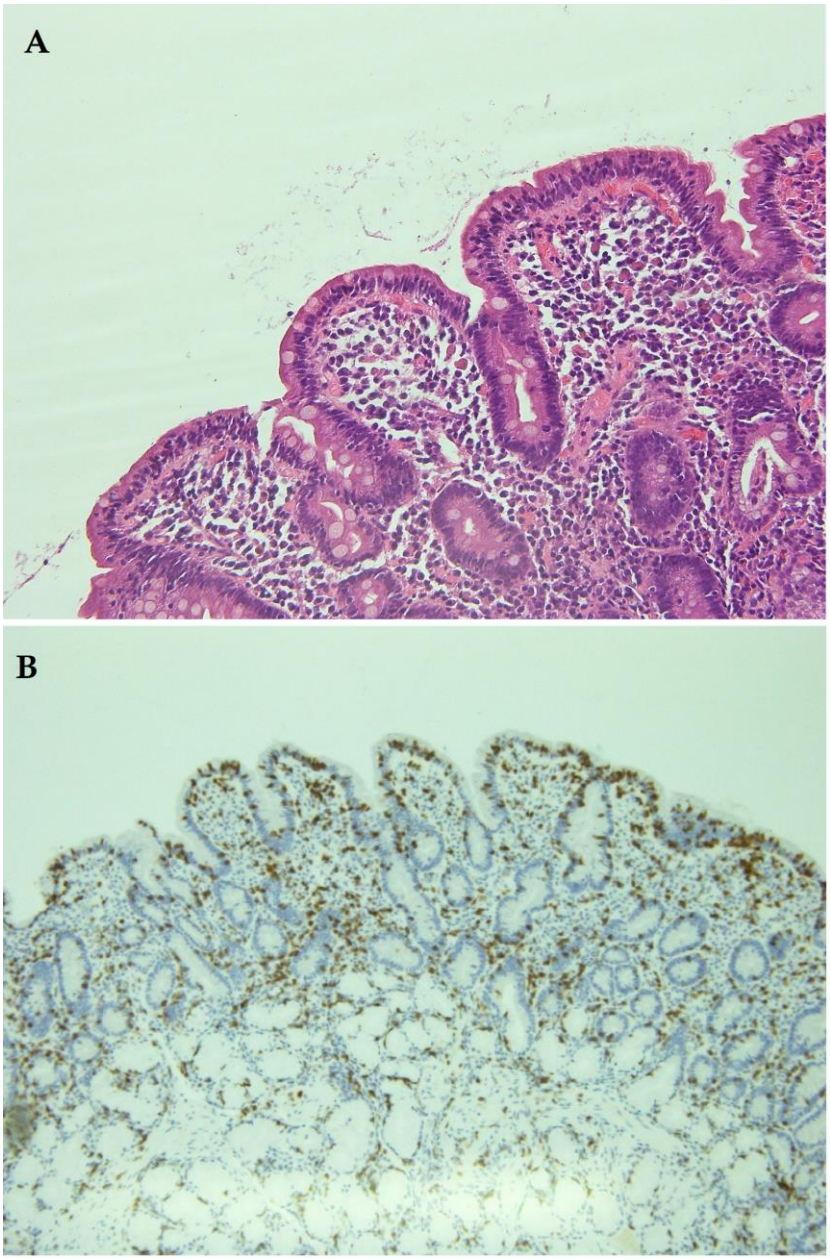

Figure 1. A) Duodenal biopsy specimen showing flattening of the villous architecture increased lymphocytes in the surface epithelium (H&E Stain 100x magnification). **B)** CD3 stain of the duodenal biopsy specimen highlighting the showing a clear decrease in villous height/crypt depth ratio and marked intraepithelial lymphocytosis, exceeding 25IEP/100EC at the tips of the remaining villi (CD3 stain 100x magnification).

Discussion

The negative HLA, immune-allergy and clinical presentation made a diagnosis of seronegative coeliac disease (CD) or wheat allergy unlikely. She was not taking any medication than omeprazole PRN and she was not on analgesics like NSAIDs. Her immuno-globulins were normal that excluded common variable immunodeficiency (CVID) and IgA deficiency. Her dramatic improvement and response to GFD, made a diagnosis of conditions like idiopathic or autoimmune enteropathy very unlikely. In this equation, in light of a negative HLA, negative coeliac serology (both EMA and tTG), normal IgA level, negative culture and microscopy for infections, non-coeliac gluten sensitivity (NCGS) (3-6) was considered the most likely diagnosis as the GFD appeared to be the ultimate therapeutic intervention that impressively and successfully treated her symptoms. As this patient tolerated gluten again and remain asymptomatic, it raise the suspicion for possible transient NCGS (7). NCGS can be defined as a clinical entity induced by the ingestion of gluten causing intestinal and/or extraintestinal symptoms that improve on GFD (3). Traditionally the main differential diagnosis of the flat mucosa in patients sensitive to gluten is CD or seronegative CD, even-though the systemic immune activation may induce enteropathy in NCGS (3-4). There is no confident evidence in the current literature to show or demonstrate that NCGS should not present with more severe mucosal abnormality like in this case. In contrast, transient gluten sensitivity with severe mucosal changes without CD have been reported (7, 8). Since immune activation is demonstrated in NCGS mucosa, there is no a good reason why we should not believe the range and degrees of enteropathy in NCGS in permanent or transient forms could be variable similar to CD and other causes of mild to severe enteropathy. Many gluten sensitive cases with negative serology are labeled incorrectly as seronegative CD without clear HLA compatibility (4). Even-though the severe mucosal changes might be less common in NCGS, this presentation is bringing to light a broader spectrum of enteropathy for NCGS even in transient form.

Conflict of interests

Authors have no conflicts of interest to disclose.

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