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# Non-Coeliac Gluten Sensitivity and Autoimmunity: A Case Report

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**Abstract**

*Introduction, objective:* To present a case report in which the finding of non-coeliac gluten sensitivity was decisive for the treatment of a complex autoimmune disease.

*Materials and methods*: A 43-year-old woman with polyarthritis, psoriatic features, anti-SSA/Ro and anti-cyclic citrullinated peptide antibodies, with refractory course, was evaluated for gluten sensitivity despite negative serology for coeliac disease.

*Results:* The patient carried the HLA DQ2 haplotype and duodenal biopsy showed lymphocytic enteritis. A gluten-free diet resolved the clinical picture and permitted tapering of immunosuppressive therapy.

*Conclusion*: Non-coeliac gluten sensitivity can be associated with autoimmunity despite the absence of the specific autoantibodies of coeliac disease.

**Keywords:** Coeliac disease, gluten sensitivity, autoimmunity

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**Introduction, objective**

The existence of gluten sensitivity without the characteristic diagnostic features of coeliac disease (CD) is recognized as an entity included in the spectrum of gluten-related disorders. It is a condition in which CD and wheat allergy are excluded, but the patient responds to a gluten-free diet and relapses after gluten exposure. The current proposed definition lists CD and non-coeliac gluten sensitivity as distinct diseases: CD is an autoimmune condition, in contrast to non-coeliac gluten sensitivity, in which there is no autoimmunity [1, 2]. Despite this concept, the limits between CD and non-coeliac gluten sensitivity are often poorly defined [3, 4].

Here we report the case of a woman with a complex autoimmune condition in which the finding of non-coeliac gluten sensitivity had a critical treatment role, showing that non-coeliac gluten sensitivity can be associated with autoimmunity despite the absence of the specific autoantibodies of coeliac disease.

**Materials and methods**

In April 2010, a 43-year-old woman with a 5-year history of chronic polyarthritis presented at our rheumatology department. She was receiving treatment with methotrexate 17.5 mg weekly and prednisone 5 mg daily. Although there was no active arthritis at clinical examination, she had persistent severe polyarticular pain and asthenia refractory to previous increases in corticosteroid dose. She had a clear personal history of dactylitis and a brother with psoriasis. She had been diagnosed with irritable bowel syndrome but had no gastrointestinal complaints at consultation.

Laboratory tests showed positive ANA (1/320), positive anti-cyclic citrullinated peptide antibodies (55 U/mL) and positive anti-SSA/Ro antibodies (58 U/mL).

Rheumatoid factor, anti-thyroglobulin and anti-TPO antibodies were positive with low titres. Erythrocyte sedimentation rate, C-reactive proteins and thyroid function were normal. X-rays showed narrowing of the joint space at the left elbow, which had been affected with chronic joint effusion, without alterations in other joints.

Thus, there was an overlap of different diseases, and arthritis treatment did not achieve relief of severe polyarticular pain and asthenia. At our unit, there is high awareness of gluten sensitivity and further studies were performed.

Screening tests for anti-transglutaminase and anti-deamidated gliadin peptide antibodies, immunoglobulin A (IgA) and IgG were negative. HLA typing showed the haplotype DQ2 (DQA1*05 – DQB1*02). Fibrogastroscopy showed no alterations. Duodenal biopsies showed normal length of villi, normal crypts and intraepithelial lymphocytosis with up to 40 intraepithelial lymphocytes per 100 enterocytes on haematoxylin–eosin-stained sections and 55 in sections stained with anti-CD3 (Marsh 1 type lesion or lymphocytic enteropathy). CD was ruled out based on negative serology and absence of villous atrophy in duodenal biopsy. Still, gluten sensitivity was suspected and a gluten-free diet was started.

**Results**

Remission of all the patient's symptoms was achieved in 3 months. Medication was very slowly tapered. At follow-up, after 3 years of a gluten-free diet, she was still in complete remission, without arthritis, musculoskeletal pain or asthenia,

taking only methotrexate 7.5 mg every other week. Occasional inadvertent low gluten ingestion had been followed by diarrhoea. Anti-cyclic citrullinated peptide antibodies and ANA remained positive. Anti-SSA/Ro and anti-thyroid antibodies were negative. After her diagnosis of gluten sensitivity, a niece was diagnosed with CD with positive anti-transglutaminase IgA antibodies and villous atrophy in the duodenal biopsy, and a daughter was diagnosed with CD with villous atrophy in the duodenal biopsy and the HLA DQ2 haplotype, despite negative serology for CD.

**Discussion**

CD is an autoimmune disorder linked to other autoimmune diseases with a shared genetic background [5]. Non-coeliac gluten sensitivity is recognized as a condition which mimics CD in the absence of coeliac-specific antibodies and villous atrophy, and is included in the spectrum of gluten-related disorders. Lymphocytic enteropathy in the duodenum is a feature of CD. Enteropathy caused by gluten with only lymphocytic enteropathy without villous atrophy has been demonstrated in patients that have HLA DQ2/DQ8 susceptibility for CD. This condition resembles CD, challenging the boundaries between CD and non-celiac gluten sensitivity to the point that this condition has been termed Marsh 1 CD[4] In this patient, gluten-induced disease classifiable as non-coeliac gluten sensitivity or Marsh 1 CD is supported by the negative serology for CD, absence of villous atrophy, response to a gluten-free diet, relapse of diarrhoea after gluten ingestion, HLA typing, Marsh 1 type lesion in the duodenum and relatives with CD.

CD and non-coeliac gluten sensitivity can present with extraintestinal manifestations such as musculoskeletal pain and asthenia, and may lack gastrointestinal symptoms. We have reported fibromyalgia associated with non-coeliac gluten sensitivity [5]. In this case, non-coeliac gluten sensitivity was found because of high awareness of this condition. There were no gastrointestinal symptoms and no known coeliac relatives at the time of diagnosis. Maybe gluten sensitivity associated with autoimmunity is not a rarity, it is just not looked for. As there is no diagnostic tool for gluten sensitivity, we suggest this should be suspected in patients with severe untreatable asthenia associated with autoimmune disease, particularly if there are gastrointestinal symptoms or a relative with CD. HLA typing and duodenal biopsy, although not specific, help in reaching a diagnosis.

This case shows the poorly defined limits between non-coeliac gluten sensitivity and CD, that non-coeliac gluten sensitivity can be associated with autoimmune manifestations and, more importantly, that the finding and treatment of non-coeliac gluten sensitivity can be critical for the management of an otherwise refractory patient.

**Learning Points**

- Negative serology for coeliac disease does not rule out gluten sensitivity.
- Severe asthenia and musculoskeletal pain can be due to non-coeliac gluten sensitivity despite the absence of gastrointestinal symptoms.

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