ANEMIA RESISTANT TO THE GLUTEN-FREE DIET IN CELIAC DISEASE PATIENTS: IS IT JUST A MALABSORPTION PROBLEM?

Short Title: ANEMIA RESISTANT TO GFD IN CD PATIENTS

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ABBREVIATIONS USED IN THIS CORRESPONDENCE

CeD: Celiac Disease

GFD: Gluten-Free Diet

IDA: Iron Deficiency Anemia

Dear Editor,

We read with great interest the paper of Roldan G. et al. about anemia in Celiac Disease (CeD), recently published in the AJG[1].

The study addressed the hot topical question regarding the presence, of anemia in patients with CeD, often due to iron, vitamin B12 and folate deficiency, and chronic disease. The authors demonstrated that out of 572 adult patients (75.3% females) with a recent diagnosis of CeD, about 25% presented with mild anemia, mainly characterized by iron deficiency anemia (IDA). Within 1 and 2 years of gluten-free diet (GFD), hemoglobin levels normalized in respectively 81% and 89% of patients. Moreover, the laboratory parameters associated with anemia showed a tendency to improve on GFD.

We would like to contribute on this topic, as recently we assessed the frequency, severity, morphological features and pathogenic factors of anemia in 159 adult patients (females 81.1%) of the "Sicilian Regional Network of Celiac Disease" (Italy)[2], and analyzed the causes of anemia persistence after 1 year on a strict GFD (assessed by the Biagi Score)[3].

On the basis of our data, we think that some points of Roldan G. et al.'s paper should be highlighted and analyzed.

Anemia prevalence in our population at CeD diagnosis was consistently higher (54.7% vs 25%), but this result is in line with the previous literature reports[4,5]. However, it is possible that the high prevalence of anemia observed in our CeD population depended on the very high percentage of females (92%) in fertile age in the whole group. This could also explain the different frequency of persistent anemia after the GFD: in the US study, 19% and 11.3% of patients were still anemic (with normocytic features), after 1 and 2 years on a GFD respectively; in our population, anemia (with hypochromic, microcytic features) persisted in 46% of the anemic patients after 1 year on GFD. We hypothesize that menstrual losses could, partially, explain this difference. Indeed, we showed that a large percentage of women with persistent IDA on strict GFD presented poly/hypermenorrhea at diagnosis (40.0% in persisting anemic *vs* 20.2% in non-anemic patients, P=0.02), suggesting that, unlike in the US survey, IDA might be more often due to iron loss rather than malabsorption, or to the coexistence/overlap of the two. Furthermore, the increased loss of iron as a cause of anemia is in agreement with the hypochromic, microcytic features and anisopoikilocytosis which characterized our

population, whereas the US authors reported a normocytic anemia. Thus, the morphological features in the US population seem to differ from the typical features of IDA (hypochromic, microcytic anemia), suggesting a frequent multifactorial etiology, which was not so common in our Sicilian population, characterized by the typical IDA features.

To our knowledge, no studies have focused on poly/hypermenorrhea as a cause of blood loss and anemia persistence in CeD women, thus in view of these preliminary data it could be useful to perform a prospective study analyzing gynecological disorders in CeD patients as a possible cofactor of anemia onset and persistence after a GFD.

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