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Case report

A difficult diagnosis of coeliac disease: Repeat duodenal histology increases diagnostic yield in patients with concomitant causes of villous atrophy

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ABSTRACT

Villous atrophy in absence of coeliac disease (CD)-specific antibodies represents a diagnostic dilemma. We report a case of a woman with anaemia, weight loss and diarrhoea with an initial diagnosis of seronegative CD and a histological documented villous atrophy who did not improve on gluten-free diet due to the concomitant presence of common variable immunodeficiency (CVID) and Giardia lamblia infection. This case report confirms that CD diagnosis in CVID patients is difficult; the combination of anti-endomysial antibodies (EmA-IgA), anti-tissue transglutaminase antibodies (tTG-IgAb) antibodies and total IgA is obligatory in basic diagnostic of CD but in CVID are negative. Furthermore, the typical histological aspects of the intestinal mucosa in CVID (absence of plasma cells and switch to the IgD immunoglobulins), cannot rule out a concomitant CD diagnosis. HLA typing in this setting has a low positive predictive value but should be considered. Histological response to a gluten-free diet on repeat biopsy and the concomitant treatment of other causes of villous atrophy leads to a definite diagnosis of CD.

Introduction

Duodenal villous atrophy in absence of the positivity of the coeliac disease (CD)-associated serum antibodies (anti-tissue transglutaminase: anti-tTG- and/or anti-endomysial: EmA-) can be defined as sero-negative villous atrophy (SNVA). Although SNVA can be part of the clinical spectrum of coeliac disease (CD) with a prevalence up to 39% [1], many other causes must to be considered and excluded before to making a diagnosis of CD. In this paper we show the case of a "difficult diagnosis" of sero-negative CD as multiple causes of SNVA concurred in the same patient and suggest a diagnostic approach based on repeated intestinal histology evaluation.

Case report

A 40 years old woman with a ten-years clinical history of autoimmune thyroiditis, and iron deficiency anaemia treated with oral iron courses and folic acid supplementation without clinical recovery, was referred to our hospital, a tertiary gastroenterology center, because of chronic diarrhoea. She reported 5 bowel motions per day of liquid stools without blood, and weight loss of 8 kg in the last 2 months.

Two years before (January 2013), the patient had been hospitalized elsewhere for the same reason and had received a diagnosis of CD, based on the following histological characteristics: Marked chronic inflammation with glandular epithelial lymphocytosis and severe flattening of the villi – grade B2 according to Corazza and Villanacci classification. [2] However, CD serologic markers (anti-tTG IgA and IgG and EmA Ig A antibodies) were negative. Accordingly, she had started gluten free diet (GFD) but, for the persistence of the gastrointestinal symptoms despite GFD, a medical reassessment was performed in January 2014. Stool cultures and

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search for ova and parasites were negative; laboratory examinations showed persistent negative CD markers, but also low serum levels of all the immunoglobulin (Ig) classes: immunoglobulin IgA < 6.67 mg/dl (ref. 9–450 mg/dl), IgG 119 mg/dl (ref. 751–1560 mg/dl), IgM < 4.17 mg/dl (ref. 40–274 mg/dl).

Abdominal ultrasound examination demonstrated only mild splenomegaly (Dt max 13 cm). The oesophagogastroduodenoscopy (EGDS) showed on the duodenal mucosa, nodules of various sizes, up to 5 mm. Duodenal histology confirmed the persistence of severe villous atrophy, nodular lymphoid infiltration of the lamina propria, no evidence of plasma cells, and showed also the presence of many spheroidal morphology forms compatible with Giardia lamblia (GI) (Fig. 1A and B); CD5, CD3 and CD38 glycoprotein expression were positive (as a markers of intraepithelial T lymphocytes), (Fig. 2A–D) whereas CD20 glycoprotein expression was negative (B-lymphocytes absent) (Fig. 2E); there was also a switch on

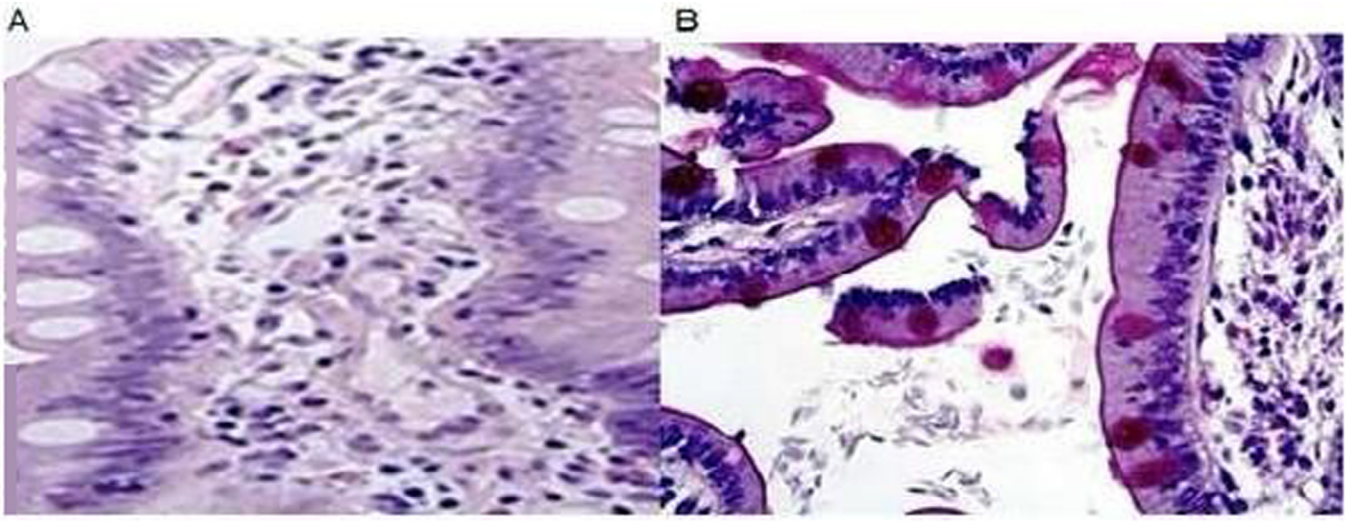

Fig. 1. A. Giardia lamblia, haematoxylin and eosin (×25), B. Giardia lamblia, PAS (×40).

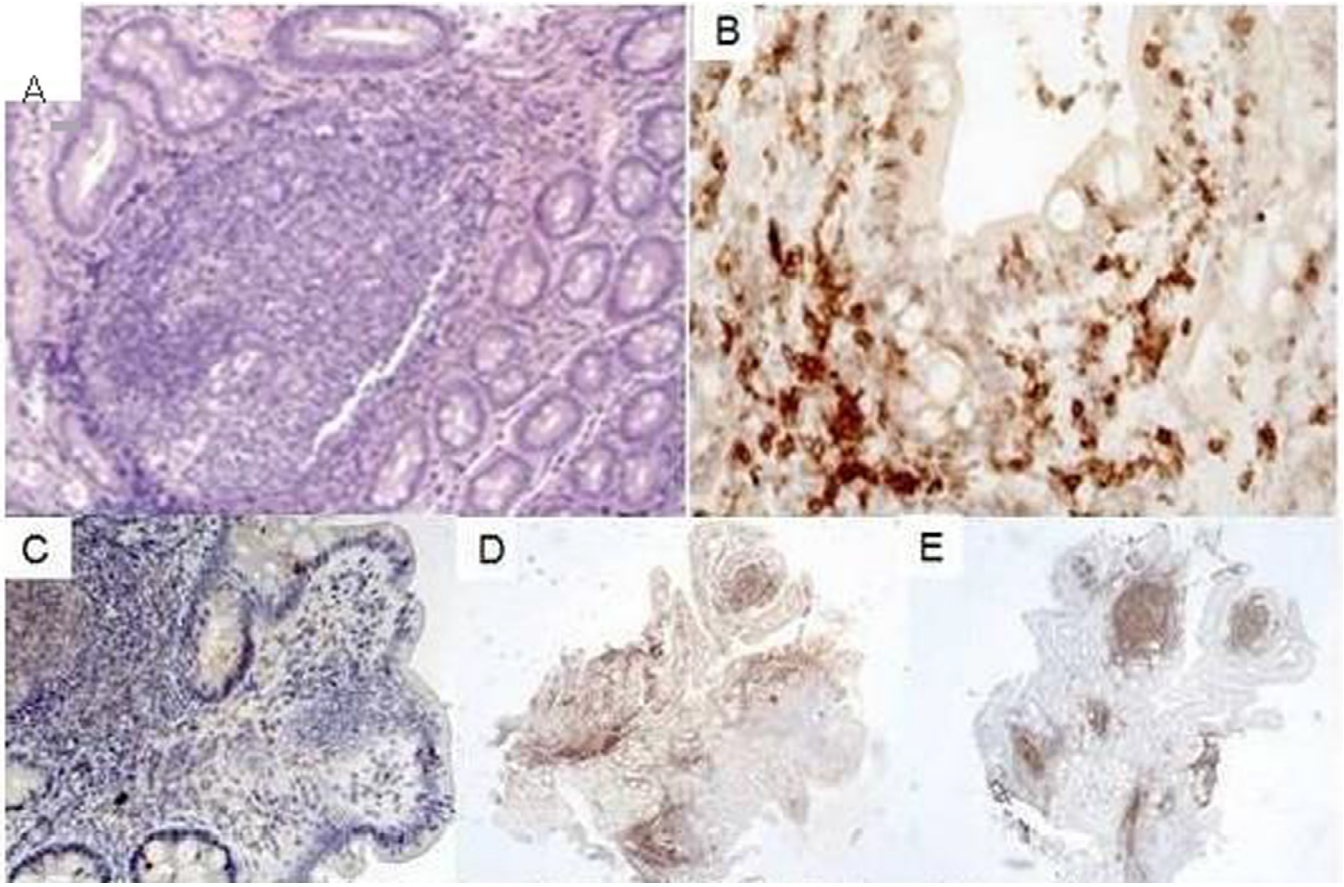

Fig. 2. A. Haematoxylin and eosin (×10), B. CD3 (×25), C. CD38 (×25), D. CD5 (Original magnification ×4), E. CD20 (×4).

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