

Case Report

The Association of IgA Deficiency and Celiac Disease: What Hides Under the Iceberg

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To cite this article:

Hajar Saffour, Hassan Ouaya, Raihane Bahri, Fadoua Elfarssani, Karima Benjouad, Adil Aiterrami, Soufia Oubaha, Zouhour Samlani, Khadija Krati, Brahim Admou. The Association of IgA Deficiency and Celiac Disease: What Hides Under the Iceberg. *International Journal of Immunology*. Vol. 9, No. 1, 2021, pp. 13-15. doi: 10.11648/j.iji.20210901.13

Received: November 9, 2020; **Accepted:** November 20, 2020; **Published:** March 3, 2021

Abstract: Celiac disease is an autoimmune enteropathy, secondary to an allergy to gluten in genetically predisposed subjects, results in clinical polymorphism, with the presence of malabsorption syndrome, is a villous atrophy demonstrated using gastroscopy, which allows to biopsy the duodenal mucosa in order to demonstrate this atrophy at the histological level and also the demonstration of basal lymphocytosis, its associated clinical, endoscopic and histological abnormalities are positive for anti-ACs. IgA-type transglutaminase, the latter may be deficient, the chosen which is frequent in celiac patients compared to the general population, making sometimes the diagnosis is a challenge for the clinician. We report the case of an association between an IgA deficiency and celiac disease in a 20-year-old patient with no personal or family pathological history, revealed by diarrhea with signs of deficiency in connection with malabsorption and the presence of the sign suggestive at endoscopy. digestive system, with an analysis of the relationship between seronegative celiac disease (SNCD) and immunoglobulin A deficiency through a review of the literature on the main medical databases

Keywords: Celiac Disease, Selective IgA Deficiency, Diagnostic Trap, IgA-tTG, Intestinal Biopsy, Gastroscopy

1. Introduction

Selective IgA deficiency occurs in one of 39 to 57 patients with celiac disease (CD) [1]. This is much higher than the prevalence of selective IgA deficiency (IgA-D) in the general population, which is about 1 in 400 to 18 500, depending on ethnic background [2]. The prevalence of CD in patients with selective IgA deficiency ranges from 10% to 30%, according to series. On the other hand, the association of CD and IgA deficiency complicates the serological testing for CD [3]. Furthermore, gastrointestinal involvement is very common in IgA-D and patients with gastrointestinal symptoms in up to 50% of cases, which can complicate the diagnosis of CD in primary Ig-D [4]. Generally Most laboratories offer IgA-based assays only for performing CD serological testing. If IgA-D not excluded, the doctor may

overlook false negatives. Thus, patients with IgA-D and CD will not detected by standard IgA-based serological tests unless IgA concentrations assessed simultaneously [3]. In the current narrative, we report the case of an association between IgA deficiency and celiac disease as we analyze the relationship between seronegative celiac disease (SNCD) and immunoglobulin A deficiencies throughout a literature review on the main medical databases.

2. Case Report

A 20 year-old female patient, without a notable medical history, presented in our institution for etiological assessment, of an ongoing watery chronic diarrhea. The patient reported 8 to 10 stools per day, day and night for over 4 years, without mucus or blood, associated to intermittent minimal intensity

abdominal pain. Our patient also reported a significant weight loss estimated at 5 kg in 6 months, with conserved appetite. There were no other digestive manifestations associated nor extra digestive signs. The clinical examination was normal.

Laboratory tests showed an iron deficiency anemia at 9.8 g/dl, with a ferritinemia at 8 IU, blood ionogram and hepatic balance were normal. Etiological biology tests revealed negative inflammatory markers with ESR = 3 and C-reactive protein = 0.32. Normal endocrine tests: TSH = 0.41; T4 = 12.2; Glycaemia = 0.88. Lymphoma markers were negative with LDH = 210, β_2 microglobuline normal. Tuberculosis tests were also normal: negative BK sputum and Quantiferon and normal chest x-ray. HIV serology was negative. Copro-parasitological examination of stools was normal.

Celiac disease serology revealed: negative IgA TG: <1.9 CU and positive IgG TG: >2560 CU. IgA serum levels were low <0.02 (N: 0.71–4.07)

Gastroscopy showed erythematous and atrophic pan-gastritis aspect and mosaicism and fold scalloping in duodenum.



Figure 1. mosaicism and fold scalloping in duodenum (gastroenterology department CHU Mohamed VI Marrakech).

The pathology study of duodenum biopsies revealed: Subtotal villous atrophy with lymphocytic exocytosis of 48 Lymphocytes / 100 epithelial cells; Compensatory hyperplasia of the crypts classified stage 3b according to modified Marsh.

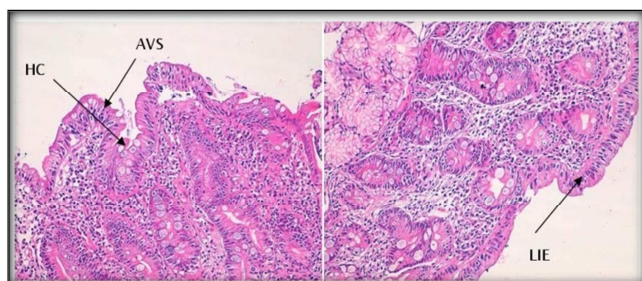


Figure 2. Subtotal villous atrophy with lymphocytic exocytosis.

3. Discussion

The ID universe is an impressive field in immunology

because of the variability of clinical and autoimmune characteristics. Gastrointestinal involvement is common and sometimes resembles primary digestive disorders like CD. Additionally, the shortage of immunoglobulin production often accounts for the absence of serological markers of CD. For this reason, ID could mask CD, and the diagnostic of the frequent association between Celiac disease and ID could be a challenge for the clinicians, the endoscopist, and the pathologist. Except for gluten-related disorders, indeed, a condition of villous atrophy or duodenal lymphocytosis may be linked to other disorders like alimentary atopy, inflammatory bowel disease, parasitic or viral infections and medicines like olmesartan. [5, 5–7].

Selective IgA deficiency is that the foremost typical primary ID, with a prevalence of 1/300–700 individuals. It is defined as serum IgA levels less than 0.07 g/L with normal IgM and IgG levels in people >4 years old [4, 8]. The pathogenic hallmark may be a defective regulation of the terminal maturation of B-lymphocytes into IgA-secreting plasma cells [9]. sIgAD becomes clinically evident in childhood, due to recurrent respiratory and gastrointestinal infections. Moreover, sIgAD may frequently be associated to atopic or autoimmune disorders like inflammatory bowel disease, nodular lymphoid hyperplasia, malignant anemia and CD [10]. The association between CD and sIgAD could also be explained by a shared genetic susceptibility. sIgAD, like CD, is strongly related to with the major histocompatibility complex (MHC) region and, particularly, with the human leukocyte antigen (HLA)-B8, DR3, DQ2 haplotype. HLA-DQ/DR is that the major immunoglobulin A locus [11]. Up to 45% of selective IgA deficiency patients have a minimum one copy of this haplotype, compared to 16% within the general population. The prevalence of CD in sIgAD is far quite within the general population, starting from 6.7%–20.6%. On the opposite, sIgAD is more common in celiac patients, with a prevalence of 1:39 [4]. The frequency of selective DI association with IgA and intestinal malabsorption is rare. Hillemand collected 40 cases within the literature up to 1981. The common age of diagnosis was 35 years (extremes of 3–65 years) with a female predominance (67%). Crabbé and Hermmans disease associating a selective deficiency in IgA and a complete villous atrophy described in 1966 by these 2 authors shares with celiac disease the clinical, radiological and biological aspect, and even the antigen of 'HLA B8 histo-compatibility. It also sometimes associates a microbial proliferation, and / or a lamiasis [12]. Like celiac disease, it responds to the diet which improves villous atrophy and leaves intact the definitive IgA deficiency. It should be noted that in CD there ana rise in plasma cells secreting IgA unlike Crabbé and Hereman's disease [12]. Primary IgA deficiency is taken under consideration to be a delayed maturation within the IgA system, and the residual capacity of antigen-specific IgA responses in patients with celiac disease.

The study of Kumar and col strongly suggest that PIGAD doesn't affect the diagnostic sensitivity of IgA-tTg. Confirmation of this finding in multicenter studies has avoided unnecessary exploration in asymptomatic people,

because of family history of CD, and in people undergoing CD assessment evaluation for non- GI symptoms. This may avoid unnecessary delay and expense in diagnosis of the particular underlying etiology of their symptoms.[13]

According to the study of McGoing and col, ordering physicians inappropriately managed 1 in 6 negative IgA-EMA patients with IgA deficiency. Others have demonstrated that the speed of intestinal biopsy increased from 18% to 80% after the introduction of a commenter commending biopsy for positive celiac disease testing results [14]. To enhance patient care, positive IgG-tTG test ends up in IgA-deficient patients will include the subsequent comment: “Your patient is IgA deficient. There is an increased risk of celiac disease in individuals with IgA deficiency. An IgG-tTG is positive in your patient. This is suggestive of celiac disease and we recommend your patient be referred for an intestinal biopsy. Treatment without biopsy is not recommended, and initiating a gluten-free diet before biopsy interferes with results. The diet for CD is complicated, expensive and has to be followed for life.” For IgA-deficient patients with a negative IgG-tTG, the following comment will be included: “Your patient is IgA deficient and screens negative for celiac disease with testing of the IgA-deficient patient. False-negative celiac disease screens can occur. If you still suspect celiac disease or another gastro-intestinal disease, your patient should be referred to a gastro-enterologist for further evaluation.”[3]

False negative serology without classical digestive symptoms in the pulpart of CD patients within the SIgAD makes CD more difficult to detect. Pallav et al reported that a minority of CD patients with SIgAD tested positive for IgA-tTG, showing the power of tTG-2 to activate a strong B-cell response. Factors determining CD involvement with SIgAD can be seropositive or seronegative is unclear. PIgAD is a common phenomenon both in people watched for gastrointestinal disorders and in the healthy population and has not occupied the diagnostic performance of IgA-tTG serology within the detection of CD [13].

4. Conclusion

IgA deficiency creates challenges within the management of patients undergoing evaluation for CD. We suggest that IgA deficiency and CD occur more commonly when employing a case-finding strategy to test for CD compared with testing the general population. Furthermore, many physicians who test patients for celiac disease are unaware that additional testing is required to exclude CD in patients with IgA deficiency. Patients with gastrointestinal symptoms and IgA deficiency frequently have gastrointestinal pathology, and endoscopic evaluation must be considered. Testing algorithms and comments designed by clinical laboratories to address these issues will likely improve the detection of CD in the clinic.

Disclosure Statement

No potential conflict of interest was reported by the author(s).

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