



SCHIZOPHRENIA ASSOCIATED WITH CELIAC DISEASE: DIAGNOSTIC AND THERAPEUTIC DIFFICULTIES

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ARTICLE INFO

Article History:

Received 15th October, 2018

Received in revised form 7th

October, 2018

Accepted 13th December, 2018

Published online 28th January, 2019

Key words:

Celiac disease; Gluten; Schizophrenia.

ABSTRACT

Celiac disease (CD) is an enteropathy related to autoimmune diseases, induced by the ingestion of gluten in genetically predisposed individuals. The association between celiac disease and schizophrenia has been described in several studies. We report the clinical case of a patient admitted for delusional events with a progressive deterioration of general condition. On the basis of clinical and laboratory data, the diagnosis of schizophrenia associated with celiac disease was retained. This comorbidity raises the question of the pathophysiological basis for this association, and the diagnostic and therapeutic difficulties. The diagnosis of celiac disease in this population presents a challenge for the clinician, because most of them are not aware of their medical problems. On the other hand the suffering subjects with schizophrenia and celiac disease have difficulties to be active players in the treatment of their disease. Screening for celiac disease using serum dosage is legitimate before any call sign because the silent evolution of celiac disease expose to deadly complications. Psycho-education remains a key element in their care. The gluten-free diet changes the prognosis of celiac disease and schizophrenia.

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INTRODUCTION

Celiac disease (CD) is an enteropathy related to autoimmune diseases, induced by the ingestion of gluten in genetically predisposed individuals. HLA DQ2 and / or HLA DQ8 genetic markers are present in 95% of subjects with celiac disease, but have a low positive predictive value [1]. Its prevalence, all forms combined, is quite comparable from one country to another, around 0.7 to 2% [2]. The diagnosis of CD is based on a combination of clinical, serological, and histological criteria. The presentation of the disease is heterogeneous. Atypical forms, made of extradigestive or non-specific digestive symptoms, are the most frequent [3]. Anti-endomysial (AEM) and anti-transglutaminase (ATG) antibodies of IgA isotype are now the most sensitive and specific markers for the diagnosis and monitoring of celiac disease. Histological examination is essential to confirm the diagnosis before starting the gluten-free diet. The association between psychosis and celiac disease has aroused particular interest. In 1953, a published article described an increased incidence of celiac disease in children with schizophrenia [4]. Over the years, the comorbidity of celiac disease with schizophrenia has been described in many studies [5-7].

We report here the clinical case of a patient with schizophrenia associated with celiac disease. This comorbidity raises the question of the common physiopathological bases, the diagnostic and therapeutic difficulties encountered.

Clinical Case

First name, aged 22, single, unemployed, was admitted for delusional manifestations with a progressive deterioration of the general condition.

In his personal history, there was a tonsillectomy and fracture of the right arm in childhood, an irregular menstrual cycle and intermittent episodes of spontaneously resolved diarrhea reported by his surroundings. His family history was peculiar.

The psychiatric examination found an idle speech, poor and sometimes incoherent, an altered judgment, a cold affect, delusions of persecution associated with auditory hallucinations. The insight was negative, and this psychotic picture, evolved for 7 months, and settled very insidious and fluctuating intensity, which made that family tolerate it during all this time.

The clinical examination found a patient with lean fever, with a body mass index (BMI) of about 17.38 kg / m², pale, his general condition was slightly altered with edema.

An initial assessment made of a glycemia, a lipid balance, a blood count, a TP, a TCA, transaminases, a serum creatinine, a

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blood ionogram, an electrocardiogram, a test of pregnancy, a TSH us, a cerebral CT, a serology HIV, syphilitic serology and viral serology for hepatitis B and C, showed a malabsorption syndrome with hypochromic microcytic anemia (hemoglobin at 8 g / dL), hypocholesterolemia at 1.2 mg / L, hypoproteinemia at 53 g / L, hypocalcemia at 68 mg / L. The rest of the balance sheet was without particularities. The presence of signs of organic and organic appeal motivated the demand for a specialized opinion. Before the presence of an alteration of the general state and the presence of the stigmas of malabsorption, the assessment completed by the search for anti-transglutaminase autoantibodies (ATG), anti-endomysial autoantibody was found to be positive, an endoscopic exploration and subsequent duodenal biopsies showed subtotal villous atrophy (images 1 and 2)

On the basis of these clinical and paraclinical data, the diagnosis of schizophrenia associated with celiac disease was retained.

After a 1-year follow-up, under antipsychotic treatment (400 mg of amisulpiride) and gluten-free diet, the evolution of psychotic symptomatology was quickly favorable without recurrence. The patient gradually regained 4 kg of weight, anti-transglutaminase Ab disappeared, with more or less complete repair of histological lesions.



Image 1 Endoscopic exploration reveals an atrophic duodenal mucosa (Aspect compatible with celiac disease).

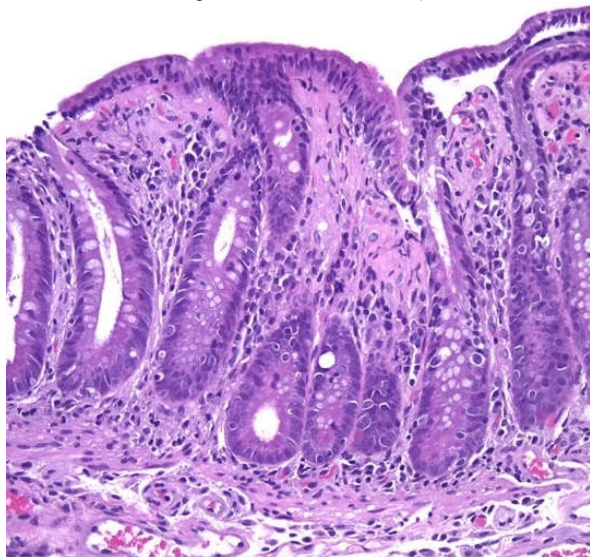


Image 2 Total villous atrophy with crypt hyperplasia.

DISCUSSION

The prevalence of celiac disease and autoimmune diseases in general in schizophrenia is higher than in the general population [8, 9, 23]. The incidence of neurological or psychiatric disorders during celiac disease is estimated at 22% [10].

In addition, neuropsychiatric disorders, such as schizophrenia, autism and depression, have been described in patients with sensitivity to non-celiac gluten. [11-13]. Comorbidity psychosis and celiac disease raises diagnostic and therapeutic difficulties. In the clinical case reported here, the diagnosis of celiac disease in our patient was guided by anamnestic and clinical elements, before being confirmed by serological and histological arguments.

Detection of somatic conditions in patients with schizophrenia remains too late. The diagnosis of celiac disease in this population presents a challenge for the clinician, as the majority of them are unaware of these medical problems. The silent evolution of celiac disease exposes to formidable complications. Its detection by means of a serum determination of anti-endomysium and / or anti-transglutaminase antibodies is legitimate before any sign of appeal. The precise mechanisms of the relationship between celiac disease and schizophrenia are not fully understood, the immunogenetic factor is the most studied.

Serological markers of celiac disease and gluten sensitivity have been investigated in patients with psychosis. IgG-AGA, IgA-AGA, IgA-ATG2, IgA-AGA (unspecified isotype) and anti-wheat Ig are all elevated during schizophrenia. In contrast, IgA-EMA, IgG-ATG2, IgG-DGP (deamidated gliadin peptides) and anti-gluten Ig are absent [14]. These markers have no specificity with respect to the nature of the symptoms (positive or negative) or the evolution of schizophrenia (first episode or recurrence) [5, 6]. Serological markers of gluten sensitivity are not all elevated in patients with schizophrenia. This indicates that the immune response specific to gluten in this population differs from that found during celiac disease [15]. The recent discovery, anti-TTG6 antibodies, directed against a transglutaminase mainly expressed in the brain, in patients with schizophrenia; suggests that these autoantibodies may be involved in the pathogenesis of gluten-related neuropsychiatric manifestations [16].

Other factors have been studied in celiac patients. Cerebral hypoperfusion has been demonstrated in untreated celiac patients, particularly in the upper and anterior areas of the frontal lobe and anterior cingulate cortex with gluten-free improvement, and similar changes have been reported in patients with schizophrenia [17]. In one case report, a patient with gluten ataxia and dementia had infiltration of CD8 + cells, perforin, and granzyme B. Activation of microglia in damaged areas of the brain was detected. This cytotoxicity may explain neuropathogenesis in celiac or gluten sensitive patients. [18]. In addition, the risk of developing non-affective psychosis has been high in children of women with high levels of IgG-AGA. The authors suggested that inflammation associated with the transplacental passage process of these immunoglobulins will have a deleterious effect on fetal development [19]. A second challenge for clinicians facing this comorbidity is that of care.

In the acute phase, the subjects suffering from schizophrenia and celiac disease have difficulties to be active actors in the treatment of their patients, indeed, it is noted the difficulties of compliance with the gluten-free diet in schizophrenics given the presence of judgment disorders. Family interventions and psychoeducation play a key role in starting and maintaining the gluten-free diet. The excipient of the antipsychotic chosen in celiac patients must be free of gluten and wheat starch [20].

Our patient adhered to the gluten-free diet and the antipsychotic treatment, which allowed a rapid improvement of the symptomatology. This trend is comparable to that reported by several studies that have shown the positive impact of the gluten-free diet on psychotic symptomatology [12, 21, 22].

CONCLUSION

A gluten-free diet changes the prognosis for celiac disease and schizophrenia. Some authors propose gluten sensitivity testing for subjects with schizophrenia who have clinical and biological signs of withdrawal, to determine which patients can benefit from a gluten-free diet, parallel to antipsychotic treatment. Although insight skills are low during schizophrenia, psychoeducation remains a key element in their care.

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