CASE REPORT

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Seronegative Coeliac Disease Masquerading as Irritable Bowel Syndrome type Symptoms

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ABSTRACT

Coeliac disease affects 1% of the population but internationally delays in diagnosis are frequent. A relationship between irritable bowel syndrome type symptoms and coeliac disease is well established and most IBS guidelines recommend that patients presenting with IBS type symptoms should be tested serologically for coeliac disease. Seronegative coeliac disease accounts for 3-5% of all cases of coeliac disease and it is a diagnostic challenge which requires a high level of clinical suspicion and consideration of duodenal biopsies prior to confidently excluding this diagnosis. We report the first case of seronegative coeliac disease masquerading as IBS type symptoms. We suggest that if patients have evidence of haematinic deficiency, subsequent weight loss, features of malabsorption or a family history of coeliac disease, then a duodenal biopsy should be considered irrespective of negative serology.

Key words: coeliac disease – IgA deficiency – serology negative villous atrophy – tissue transglutaminase antibody – serology negative coeliac disease.

Abbreviations: CD: coeliac disease; EMA: Endomysial antibody; GFD: gluten free diet; IBS: irritable bowel syndrome; SNCD: seronegative coeliac disease; TTG: tissue transglutaminase antibody.

INTRODUCTION

Coeliac disease (CD) affects 1% of the population, but internationally delays in diagnosis are frequent[1]. In the United Kingdom a recent report suggests that only a quarter of cases are currently recognized [2]. A relationship between IBS type symptoms and coeliac disease is well established and most IBS guidelines recommend that patients presenting with IBS type symptoms should be tested serologically for CD [3, 4]. Seronegative coeliac disease (SNCD) accounts for 3-5% of all cases of CD [5]. This case explores the diagnostic dilemma of a female patient who was previously diagnosed as diarrhoea predominant IBS and on further investigation was found to have SNCD.

CASE REPORT

A 49-year old female presented with diarrhoea predominant symptoms in excess of 3 years. Bowel motions varied from 2 solid motions per day to passing loose stools within 5 minutes of each motion cycling several times daily. There was no nocturnal stool frequency or passage of blood per rectum; however, there was associated urgency with occasional incontinence and bloating with abdominal discomfort. Her symptoms fulfilled the Rome III criteria for diarrhoea predominant IBS. The patient maintained a normal appetite and had progressively gained weight. She described marked reflux particularly triggered with spicy and fatty foods, which was alleviated with omeprazole. She had not consumed any alcohol within the past 18 months and had stopped smoking 4 years previously. There was no family history of CD, colorectal cancer or inflammatory bowel disease.

Preliminary investigations showed a normal full blood count, urea and electrolytes, thyroid function, ferritin, folate, and C reactive protein, however, her B12 was 192ng/L (reference 197- 771) with negative intrinsic factor antibodies. Further investigations excluded exocrine pancreatic insufficiency with a faecal pancreatic elastase >500µg/l. Coeliac serology revealed a tissue transglutaminase antibody (TTG) level of 4.1 u/ml (normal range 0-7, ELIA Celikey, ThermoFisher,

Freiburg, Germany) and an IgA level of 1.48 g/l (normal range 0.8-4). Endomysial antibody (EMA) and stool cultures were also negative (Nova lite, ANOVA diagnostics). A SeHCAT scan for bile acid malabsorption was normal. She underwent a flexible sigmoidoscopy (with macroscopically normal views to the descending colon), biopsies showed no evidence of microscopic colitis or inflammatory bowel disease. Initially she was referred to gastrointestinal physiology for anorectal manometry and biofeedback and placed on follow-up with trials of loperamide and FODMAP adjusted diet and offered percutaneous tibial nerve stimulation.

Two years later she presented after one episode of possible melena with no other new red flag signs. She was noted to have folate deficiency (serum folate 2.1 µg/L lower limit of normal 3.9 µg/L). Despite her previously negative serology, due to her persistent unexplained symptoms and new folate deficiency she was booked for upper and lower endoscopy. The patient was on a normal (gluten containing) diet.

Duodenal biopsies revealed partial villous atrophy with crypt hyperplasia and increased intraepithelial lymphocytes. Concurrent coeliac serology showed a negative EMA and TTG of 1.6 u/ml. Random biopsies of the large bowel were within normal limits. Investigations were performed for serology negative villous atrophy (SNVA) including HIV serology, TB quantiferon and anti-enterocyte antibody, which were all normal. HLA typing showed the patient was DQ2 homozygous which is seen in patients with coeliac disease. Given the exclusion of other causes of SNVA she was placed on a gluten free diet (GFD) and her symptoms improved. Further supportive evidence occurred when her daughter presented with gastrointestinal symptoms and was tested and found to have a strongly positive EMA and TTG positive CD.

DISCUSSION

We believe that this is the first case reported of SNCD masquerading as IBS type symptoms. Coeliac disease is a small bowel enteropathy characterised by sensitisation with dietary gluten in genetically inclined individuals. Coeliac disease affects around 1% of the general population, but most cases are unrecognised, and diagnosis is often delayed considerably [1, 2]. Although CD can easily be misdiagnosed as IBS, international guidelines now recommend serological coeliac testing in patients with IBS type symptoms [3, 4]. It is now recommended to perform duodenal biopsies when symptoms persist and serology is negative [6].

A previous study (n=2000) demonstrated that SNCD only occurred in high risk cases; the symptoms delineated were weight loss, anaemia, or diarrhoea [6].

The commonest cause of SNVA is CD (accounting for ~30% of the cases) but there are many other causes and in some cases the villous atrophy may normalize in time whilst continuing on a normal gluten containing diet [7].

Seronegative CD accounts for 3-5% of all cases of coeliac disease [5]. The reasons for SNCD may be an IgA deficiency which can result in negative IgA TTG and IgA EMA. We would suggest that this is not SNCD because an IgG TTG may be elevated. Confusion and seronegative tests may occur if the patient has placed themselves on a GFD prior to testing or if the patient is on immunosuppressive therapy at the time of testing (for example azathioprine or budesonide). True SNCD occurs early in the disease [5], late in the disease particularly in refractory CD [8] or if the patient is a first degree relative of someone who has CD [9] (Table I). In hindsight our patient had evidence of haematinic (B12) deficiency at the first presentation and folate at the time of the second presentation.

Table I. Seronegative tests for coeliac disease

Associations with seronegative coeliac disease
Early in disease
Late in disease (refractory)
Dermatitis Herpetiformis
Family History: 1st degree relatives
Patients who may present with negative coeliac serology
Patient commenced a GFD prior to testing
IgA deficiency
Immunosuppressant's

GFD: gluten free diet

CONCLUSION

We recommend performing duodenal biopsies in patients presenting with IBS type symptoms with normal coeliac serology in the presence of haematinic deficiency, weight loss or a family history of CD.

Conflicts of interests: None to declare.

Authors' contribution: D.X.H. drafted and edited the case report. D.S.S.: conceived the paper, critical reviewed, approved the final version of manuscript. J.A.C., K.B., A.S.: critical reviewed, edited the report, approved the final version of manuscript.

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