Case Report

Seronegative celiac disease: a case report

Amita Surana*, Vaishali Chaudhari, Shefali Patel

Department of Pediatrics, SMIMER Hospital, Umarwada, Surat, Gujarat, India

Received: 28 November 2016
Accepted: 13 December 2016

*Correspondence:
Dr. Amita Surana,
E-mail: amigheewala.as@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

In this article we report a case of 17 years old male with short stature, severe anaemia and delayed puberty. After extensive workup and in spite of being seronegative for celiac antibodies, he was diagnosed as an atypical case of celiac disease based on duodenal biopsy report suggestive of CD. The patient is put on gluten free diet along with other nutritional supplements. Long term consequences like short stature, infertility can be prevented by higher clinical suspicion and early diagnosis. Intestinal biopsy should be performed if there is strong clinical suspicion. The relevant literature has been reviewed and discussed in brief.

Keywords: Celiac disease, Delayed puberty, Intestinal biopsy, Serology

INTRODUCTION

Celiac disease (CD) is an immune mediated systemic disorder elicited by gluten and related prolamines in genetically susceptible individuals and is characterised by presence of variable combination of gluten dependent clinical manifestations, CD- specific antibodies, HLA-DQ2 or HLA-DQ8 haplotypes and enteropathy. It is one of the most common causes of chronic malabsorption.1 This condition can manifest with a previously unsuspected range of clinical presentations, including the typical malabsorption syndrome (chronic diarrhea, weight loss, abdominal distention) and a spectrum of symptoms potentially affecting any organ or body system.2 The availability of screening test has resulted in picking up of many cases of CD. However many a times lack of gastrointestinal symptoms results in delayed diagnosis. Hereby we present a case of such delayed diagnosis.3,4

CASE REPORT

A 17 years old male patient was admitted with complaints of short stature and not attainment of puberty. On examination his weight was 18 kg (<3rd percentile) and height was 123 cm (<3rd percentile), BMI 11.89 kg/m^2 (severe under nutrition), US/LS ratio 0.8. Height age was 8 years and bone age was 7 years. Patient had severe pallor, bilateral pedal oedema upto knees with periorbital puffiness and mild ascites. His SMR staging was 1 (preadolescent), stretched penile length was 4 cm. On asking patient gave history of poor appetite, abdominal fullness (bloating) and infrequent history of diarrhoea.

His CBC showed severe anaemia (Hb 5.5 gm%) of microcytic hypochromic type. ESR was normal. Renal profile and thyroid function test was normal. Stool examination was negative for ova/cyst. Stool culture was negative. HIV, HBsAg, HCV, ANA, RA factor tests were negative, MT was negative. XRC was normal.

Liver function tests showed normal liver enzymes, total serum proteins 4.2 g/dl, serum albumin 1.8 g/dl and serum globulin 2.4 g/dl. His lipid profile showed total lipid 243.91 mg%, TG 52 mg%, HDL 16mg%, LDL 11mg%, cholesterol 37mg%. Serum vitamin D3 <3ng/ml, serum vitamin B12 – 578pg/ml, His USG abdomen showed fatty liver grade 1,USG scrotum showed testicular volume of 0.5 ml, serum FSH 3.38mIU/ml (N 1.27-19.3mIU/ml), serum LH 0.456mIU/ml (N 1.24-
8.6mIU/ml) suggestive of hypogonadotropic hypogonadism.

In the view of severe malnutrition, severe anaemia, short stature and delayed puberty, screening test for CD was done which showed serum iTG IgA 4.9AU/ml (N less than 12 AU/ml) and serum IgA 4.01G/L (N 0.61 - 3.48 G/L). In spite of seronegativity, on the ground of strong clinical suspicion of CD, intestinal biopsy was done from duodenum which showed focal and partial villous atrophy, prominent crypt hyperplasia, and focal decrease in villous: crypt ratio with intraepithelial lymphocytosis, suggestive of celiac disease. After biopsy report, patient was put on gluten free diet and nutritional supplements were started. During hospital stay his oedema subsided in two weeks. Patient was discharged after 3 weeks. Owing to seronegativity for CD, genetic testing for HLA DQ2 & DQ8 was planned, but due to the unavailability of this investigation at our centre it could not be done.

Our patient presented at 17 years with short stature, severe malnutrition, severe anaemia and delayed puberty. Lack of gastrointestinal symptoms could be the reason for not suspecting CD by treating physician earlier. Extensive diagnostic workup to rule out other causes and Marsh type of lesions on intestinal biopsy helped to confirm the diagnosis in our case.

**DISCUSSION**

Celiac disease (CD) is an intestinal chronic inflammatory and autoimmune disease that develops as a result of interplay between genetic, immunologic, and environmental factors. The current global prevalence is 0.5 to 1.26 % and Makharia et al. reported the prevalence of 1.04% in northern India. The low reported prevalence of CD is due to underdiagnosis and clinical CD represents only tip of iceberg. The reasons for underdiagnosis are lack of awareness in treating physician, presentation with non-classic symptoms or failure by pathologist to recognise early features of CD.

The classic CD presents with gastrointestinal symptoms. While the individuals with atypical CD can also have gastrointestinal symptoms, approximately 70% of them are diagnosed based on extra intestinal manifestations like iron-deficiency anaemia, dermatitis herpetiformis, unexplained short stature, neurologic symptoms and delayed puberty. The age of diagnosis is extremely variable. In India 80% of children with CD have classical presentation. Non-classic CD usually presents in later childhood or adulthood.

A diagnostic test for CD specific antibody detection is the first tool used to identify patient with signs and symptoms suggestive of CD for further workup. Initial testing is IgA class anti-tTG or EMA antibody for IgA competent subjects. Although combination screening by anti-TTG and anti-EMA offer high sensitivity; seronegative celiac disease does occur. Different studies have shown prevalence of seronegative CD 6.4%, 12%, 15%. It is believed that, the presence of related CD antibodies correlates with the degree of villous atrophy and possibly the mode of presentation of the disease. If CD suspicion is high with persistently negative tests, individuals must perform typing for HLA and, if positive, they must perform duodenal biopsy or alternatively perform biopsy directly.

However a recent guideline by ESPGHAN has proposed that it may be possible to avoid intestinal biopsy in children meeting criteria like characteristic symptom of CD, iTG IgA level >10x upper limit of normal and positive HLA DQ2/DQ8. But in India diagnosis without intestinal biopsy is still not recommended as reliable HLA testing, EMA estimation is not widely available.

All patients with confirmed diagnosis of CD should be put on gluten free diet i.e., foods that contain ≤20 ppm of gluten. Oats are considered safe; however 5% of patient may be sensitive to oats.

**CONCLUSION**

Atypical CD with negative serology is a diagnostic dilemma. Intestinal biopsy still should be carried out with strong clinical suspicion. Genetic testing if available offers additional support to the diagnosis.

**Funding:** No funding sources  
**Conflict of interest:** None declared  
**Ethical approval:** Not required

**REFERENCES**


