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Case Report Open Access

Celiac Disease in South Jordan: The Typical and the Atypical

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Abstract

Celiac disease is an autoimmune enteropathy in genetically susceptible individuals triggered by exposure to wheat gluten. Celiac disease presented classically with malabsorption related symptoms. The term "atypical" celiac disease is used to describe patients presenting with extraintestinal symptoms, positive serology and typical small intestinal changes. Few studies had addressed atypical or silent CD in the Middle East. In this case series we are presenting the first cases of CD diagnosed at our new service at South Jordan. The small number limits any statistical conclusions, but it shows that the non-classical presentations are not uncommon in our rural community.

Keywords: Gluten sensitive enteropathy; Gluten; Gluten-free diet

Introduction

Celiac Disease (CD) is an autoimmune enteropathy in genetically susceptible individuals triggered by exposure to wheat gluten (Gliadins) [1]. The previously considered rare disorder is now one of the most common genetic disorders in the West with a prevalence of 1%-2.67% [2].

The true prevalence of the disease in our area of the world is underestimated due to the unawareness of the atypical presentations of the disease [3]. Previous report from Jordan reported an incidence of celiac disease as 1 in 2800 live births, with estimated point prevalence of 7:100 000 [4].

Celiac disease presented classically (typically) with malabsorption related symptoms (diarrhea, abdominal bloating, weight loss, muscle wasting, and nutritional deficiencies), within weeks to months of gluten exposure. The term "atypical" celiac disease is used to describe patients presenting with extraintestinal symptoms, positive immunological workup and typical small intestinal changes [2].

Few studies had addressed atypical or silent CD in the Middle East [3]. Jordan reported a high prevalence rate of short stature in celiacs [4]. In this case series we are presenting the first cases of CD diagnosed at our new service at South Jordan. The small number limits any statistical conclusions, but it shows that the non-classical presentations are not uncommon in our rural community. Our aim is to increase the awareness of pediatricians and general practitioners of the diverse clinical presentations, and specific at risk population.

Case Reports

Case 1

A 2.5-year-old girl, with abdominal distention and chronic diarrhea, on physical exam, she was severely malnourished. Her investigations showed iron deficiency anemia (IDA), prolonged PT, rickets (Chemical and abnormal wrist X-ray) and hypoalbuminemia. Stool routines were negative for ova and parasites, but positive for fat droplets. Anti-tTG IgA was > 200 units (normal <12 units). She was started on Gluten-Free Diet (GFD) and vitamins supplementation without Esophagogastroduodenoscopy (EGD). After starting the GFD, she developed Refeeding Syndrome. Her condition was controlled by cutting back the caloric intake and supplementation of minerals and vitamins. Gradual increment in her caloric intake was tolerated later. On follow up; she is adding weight and her hematological abnormalities corrected.

Case 2

A 12-year-old boy, known case of chronic headache, referred to our clinic with recurrent abdominal pain and early satiety to role out abdominal migraine. His school performance deteriorated over the last few months. Physical exam showed pallor and a height on the 5th centile. His investigations showed Iron Deficiency Anemia (IDA). Occult blood loss and Hemoglobinopathies were excluded. Anti- tTG IgA was 72 units (normal <12 units). EGD done, his small intestinal biopsies showed subtotal villous atrophy and crypt hyperplasia (Marsh III b). On GFD, his headache and abdominal pain improved. His school performance became better. His anemia resolved.

Case 3

A 4-year-old boy, known case of Down syndrome, presented to our clinic with failure to thrive. His growth parameters were far below 3rd centile. He had recurrent aspiration episodes due to GERD but no congenital heart disease, or gastrointestinal symptoms. His workup showed dimorphic anemia, rickets (chemical and abnormal wrist X-ray) and prolonged PT. Anti-tTG IgA >100 units (normal<12 units). Patient was scoped outside our facility and his biopsies showed a total villus atrophy with marked crypt hyperplasia (Marsh IIIc).

He was started on GFD, multivitamins and anti-reflux measures. On follow up; anemia and coagulopathy corrected and the patient started to add weight. High caloric, gluten-free formula was added to his nutritional plan.

Case 4

A 4-year-old boy, referred to our clinic with poor appetite and persistent IDA. He had no abdominal pain, vomiting, diarrhea or blood in stool. His physical examination was normal except for being pale. His anemia persisted despite Iron supplementation.

His Hb-electrophoresis was normal. His stool workup showed no ova or parasite and negative heme-occult. His anti-tTG IgA was >100 units (normal<12 units). Upper Endoscopy showed no ulcers or signs of inflammation. His small intestinal biopsies showed chronic

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inflammatory infiltrate; unfortunately the surface was lost during fixation. Condition discussed with the family and agreed on trying GFD. After 3 months of GFD; he added 2 Kgs, his Hb, MCV, MCH and RDW normalized.

Case 5

An 8-year-old girl, referred with early satiety and short stature. She had no abdominal pain, diarrhea or vomiting. Her height was below the 5th centile. Rest of physical exam was normal. Her endocrine work-up was normal. Anti tTG IgA was negative, but her serum IgA was undetectable (Normal level for age 34-305 mg/dL). EGD was done. Small intestinal biopsies showed complete villous atrophy with significant crypt hyperplasia (Marsh III c).

Case 6

An 8.5-year-old girl, known case of IDDM on insulin, had no gastrointestinal symptoms. Her physical exam was normal except for using hearing aids. Anti tTG IgA was >100 units (normal < 12 units). Patient scoped outside our facility. Her intestinal biopsies showed mild villous atrophy with crypt hyperplasia (Marsh III a). Patient started on GFD, follow up Anti tTG IgA was negative. Summary of patients` demographics, clinical presentation and investigations appear in Table 1.

Discussion

Celiac disease is a genetically determined autoimmune enteropathy triggered by exposure to gluten and related proteins. CD can present at any age [1]. Unlike other autoimmune disorders there is a known trigger, avoidance of which produces remission in the vast majority of cases. Clinical presentation varies according to many factors: age, sensitivity to gluten, and the amount of gluten ingested in the diet, as well as other unknown factors.

Younger age groups present with classical (typical) picture [2,5]. In our case series typical CD was seen in one case (case 1). In case of severe growth failure and malnutrition, Refeeding Syndrome is a real concern. Refeeding syndrome is the result of metabolic and physiological consequences of the depletion, repletion and compartmental shifts and inter-relationships of minerals, glucose metabolism, vitamin deficiency and fluid resuscitation. As these minerals shift to the intracellular space, serum levels drop and the intracellular extracellular fluid balance jeopardized [6].

Some of these changes such as severe hypophosphatemia and severe hypokalemia are potentially fatal. Treatment depends on cutting back caloric intake and correcting electrolyte imbalance.

Malabsorption in celiac disease can lead to multiple nutritional deficiencies. Fat soluble vitamins (K, D, E and A), iron, Vitamin B12 and zinc are commonly encountered [7]. In our facility, vitamins levels are unavailable. In cases 1 and 3, prolonged (PT, INR), chemical rickets and wrist X-ray used to diagnose Vitamin K and D deficiencies.

The proximal small intestine is the predominant site of inflammation and the site of iron absorption. The frequency of iron deficiency anemia in celiac disease varies from 12% to 69% [8]. The association of celiac disease and refractory iron deficiency anemia is well established. In our small series most of our children were iron deficient (Cases 1, 2, 3& 4).

IDA resolves with adherence to GFD, although normalization of the iron stores may require longer duration. The NASPGHAN guidelines recommend testing children with unexplained persistent IDA not responsive to treatment for celiac disease [9].

The fact that Vitamin B12 being absorbed from the ileum, which is relatively spared in celiac disease leave the mechanism of Vitamin B12 deficiency unclear. Coupling of Iron and Vitamin B12 deficiency in celiacs gives the classical dimorphic anemia seen in celiacs (as in case 3). The incidence of vitamin B12 deficiency in untreated celiac patients ranges from 11% to 41% [7,8].

Atypical presentation of CD is more common in older children. Children with atypical presentation may have either unusual intestinal (recurrent abdominal pain, nausea, vomiting, bloating or constipation), or extraintestinal manifestations (Table 2) [10].

It is well-established that short stature (case 5) can be the only presenting clinical feature of CD. Previous study from Jordan reported a prevalence rate of 12% [4]. In the Middle East and North African countries, short stature was the presenting symptom in 7.7% to 53% of patients [3]. The pathogenesis is still unclear. A significant increase in height velocity is often noticed; especially within one year of GFD. The target height is usually reached within 2 to 3 years. However, the catch–up growth is not always complete, probably because of the marked acceleration in bone maturation that parallels rapid growth velocity [11]. In case 5, due to short period of follow up the growth velocity could not be assessed.

Neurological and psychiatric disorders including depression, anxiety, irritability, peripheral neuropathy, epilepsy, cerebellar ataxia and migraine have all been reported in Celiac Disease [12]. There are few studies specifically addressing the association between headache and CD [13]. In patients with migraine, CD was found in 4.4 % compared with 0.4 % in blood donors [13]. In case 2, headache improved on GFD.

An increased frequency of Celiac disease is found in specific risk groups. First degree relatives of celiacs, patients with autoimmune disorders (IDDM (case 6), thyroiditis), Down syndrome (case 3), Turner Syndrome, Williams Syndrome, and IgA deficiency patients (case 5) all were reported to have higher rates. There is no consensus on screening all these groups. While the NIH guidelines from 2004 recommends screening Down syndrome and Williams Syndrome patients but not the asymptomatic IDDM patients [14].

The NICE guidelines suggest screening both adults and children with IDDM, IBS, Dermatitis herpetiformis and autoimmune thyroid

Case no.	Age at diagnosis	Sex	Presentation	Serology Anti-tTG IgA Nl. < 12 units	Biopsy (Marsh classification)
1	2.5 years	Female	Chronic diarrhea and malnutrition	>200	Not done
2	12 years	Male	Headache, Abdominal pain	72	Marsh III b
3	4 years	Male	Down Syndrome, FTT	>100	Marsh III c
4	4 years	Male	Poor appetite, persistent IDA	>100	Not confirmatory *
5	8 years	Female	Early satiety, Short stature	- ve	Marsh III c
6	8.5 years	Female	IDDM, asymptomatic (using hearing aids)	>100	Marsh III a

*The surface lost during fixation

Table 1: Patients` Demographics, presentations and investigations.

Neurological disorders such as depression, epilepsy, migraine, ataxia, occipital calcification
Dermatitis herpetiformis
Enamel defects
Overweight
Elevated liver enzymes, liver failure
Infertility
Stomatitis
IgA Nephritis
Myocarditis
Idiopathic Pulmonary Hemosiderosis
Arthritis
Intestinal Lymphoma in subjects with untreated celiac disease
Pancreatitis
Sensorineural hearing loss

Table 2: Atypical manifestations of Celiac Disease.

disease [15]. Coupling the recommendations of those major health guidelines expected to identify higher number.

IgA anti-tTG testing has now become the test of choice for identifying celiacs and monitoring their dietary compliance. Total serum IgA level should be determined to assess for selective IgA deficiency. Complete IgA deficiency will cause false negative IgA anti-tTG results (case 5) but on the same time should alert the specialist for the increased risk of CD in the patient. If IgA deficiency is found, then depending upon the clinical presentation, IgG serology or even duodenal biopsy is recommended [16]. In our series one patient (case 6), had a follow up Anti-tTG level, and not the rest of our patients due to financial reasons.

The association between hearing impairment and celiac disease is well established [17]. In case 6; the patient has a long standing hearing impairment; long-term follow up on GFD should determine the relation to celiac disease.

Since the recognition of CD the diagnosis was based on villous atrophy on small intestinal biopsy [18]. Despite substantial changes in the mode of presentation and the availability of new diagnostic tools, small bowel mucosal biopsy has remained the gold standard for CD diagnosis until now [19]. The number and the site of biopsies, the orientation of the biopsy during fixation and the experience of the pathologist especially in nonatrophic lesions should be in mind while interpreting the pathology report [19]. (Case 1) was not scoped due to unavailability of appropriate size scope. Based on the ESPGHAN guidelines patients with classical presentation and an Anti-tTG more than 10 times the normal, confirmed with Anti-endomysial Ab. or HLA typing, intestinal biopsies can be omitted [20]. In our case Antiendomysial Ab. and HLA typing were not available.

Adherence to gluten-free diet remains the mainstay of therapy for CD. Detection and correction of nutritional deficiencies is also important. Symptoms resolve in most cases following compliance to GFD. Follow-up is important to ensure compliance and enforce it. The main cause of non-compliance in our population is unavailability of GFD and financial restrains.

Conclusion

This small series describing our first consecutive cases diagnosed with CD pointing that we are sharing the world the changes in epidemiology of CD. The awareness and knowledge about the variable clinical presentations will lead to early detection, appropriate intervention in affected children.

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