Case Report

Celiac disease presenting as hypocalcemic tetany: Report of four cases

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ABSTRACT

Celiac disease (CD) is a lifelong gluten-sensitive autoimmune disorder of the small intestine. These patients present with gastrointestinal symptoms, extra-gastrointestinal symptoms or no symptoms. Adult patients rarely present with malabsorption. The removal of the offending antigen in the diet leads to complete resolution of the clinical condition. Diagnosis is usually suggested by the presence of highly sensitive and specific serological tests but established by biopsy of the small intestine. Many cases of CD have been reported to have hypocalcemia but symptomatic hypocalcemic tetany is not common. We describe here four patients with such presentations. (Rawal Med J 2014;39:349-353).

Keywords: Celiac disease, hypoglycemia, tetany.

INTRODUCTION

Celiac disease (CD) is a lifelong gluten-sensitive autoimmune disorder of the small intestine.[1] It is one of the most common genetic disorders in the West with prevalence of 1-2.67% and recent studies showed a prevalence of 0.59-0.9% in the North Africa and Asian Areas.[2] Approximately 97% of individuals with CD have genetic markers on chromosome 6p21 called class II human leukocyte antigen (HLA). HLA DQ2 predominates occurring in 90-95% of patients and HLA DQ2 occurs in the remainders.[1,2] CD is known to be associated with variety of autoimmune conditions and endocrine abnormalities.[2,4]

CD can be asymptomatic, however, it commonly presents with gastrointestinal symptoms. The classic symptoms include diarrhea, abdominal pain, steatorrhea and weight loss and in adults, rarely features of malabsorption. About 50% patients attend different clinics with anemia, osteoporosis, dermatitis herpitiforme, neurological problem and dental enamel hypoplasia.[1,2] The wide spectrum of clinical picture is reflected in the age of onset, extent of mucosal injury, dietary habits and gender. Late presentations, mostly relates to malabsorption include profound vitamin D deficiency, vitamin K deficiency and iron and folate deficiency presenting as rickets, osteomalacia, hypocalcemia, tetany, coagulopathy[3,4] and anemia.[2-4] Many cases of CD have asymptomatic hypocalcemia,[5] but many present with symptomatic hypocalcemia.[6-9] We report four patients with such presentations.

CASES

CASE 1. A 29 year old female patient complained over the last 2 years of frequent attacks of muscle spasms. Attacks worsened after thyroidectomy for a large goiter, done 6 months earlier and she developed recurrent corpopedal spasms, peri-oral and peripheral numbness and tingling. Her past history included nonspecific abdominal cramps and watery voluminous -malodorous diarrhea with occasionally sticky stool.

Table 1. Clinical characteristics and examination of patients.

	CASE 1	CASE 2	CASE 3	CASE 4
AGE	29 yrs old	27 yrs old	42 yrs old	45 yrs old
SEX	FEMALE	FEMALE	FEMALE	FEMALE
HEIGHT	156cms	160cms	158cms	
WEIGHT	42kgs	49kgs	48kgs	
B.P	110/70 mmHg	110/60 mmHg	100/60-90/50 mmHg	130/80 mmHg
PULSE	80 bpm	84bpm	86bpm	80bpm
HEART	NAD	NAD	NAD	NAD
CHEST	NAD	NAD	NAD	NAD
ABDOMEN	No organomegally, Hyper active bowel movements		Distended abdomen, Active bowel motion	Soft, lax
LL	No edema	No edema	Mild petting edema	No edema
NEUROLOGY	Power normal reflexes +1	Normal power +1 reflexes	Power 3/5, proximal muscle weakness and none tenderness	Normal

NAD: No abnormality is detected

Clinical examination and the results of investigations are showed in Tables 1 and 2. Diagnosis was established by intestinal biopsy (Table 3). She was managed by gluten-free diet and supplementation of calcium and one-alfa. A month later, all her symptoms resolved and she gained 7kg of weight and lab investigations were normal. Two months later, she developed nausea and vomiting and found to have of hypercalcaemia of 3.5 mmol/L. She recovered after the calcium supplements were stopped.

CASE 2. A 27-yr-old female developed two episodes of carpopedal spasm over one month before presentation. Few months prior to presentation, she had persistent diarrhea with malodorous loose and watery stool. Other symptoms included nausea, vomiting, epigastric pain and intolerance to meals. Clinical examination and investigations showed in Tables 1-3. She was treated with gluten-free diet, in addition to supplementation of calcium, ferrous and one alfa. After 4 months, she was in good general condition with complete resolution of her symptoms and increased 5 kg weight. Her laboratory results were normalized and PTH decreased from 336 to 167 pg/ml with the same Hb 10.5g/dL and low MCV 66. Her further management included continuation of gluten-free diet and HB electrophoresis to be done to rule out Thalassemia.

CASE 3. A 42-yr-old female was admitted to Surgical Ward to rule out malignancy because of six months history of persistent diarrhea, abdominal pain and 20kg weight loss. During preparing for endoscopy, she developed severe carpopedal spasm with severe hypocalcemia and hypokalemia. Her symptoms started 2 years ago, mostly in a form of persistent diarrhea, up to 10 motions daily, offensive watery with no blood. She had nausea, vomiting and food intolerance. She gave history of mouth ulcers, scalp hair loss and bone and muscle pain all over and cholecystectomy.

Table 2. Laboratory results of the patients.

Investigation	Case 1	Case2	Case 3	Case 4
HB (g/dl)	11,5	9,7	10,5	9.4
PCV%	37	34.9		
MCV mcm3	89	59,2	60	73.9
PLT 103/mcl	244.000	546.000	545.000	715.000
MCH pg/cell	26,5	16,5	19.8	5100
MCHCg/dl		27.8	32	
ESRml/h	22	15	25	
WBC 103/mcl	7000	7900	7500	
Glucose mmol/L	5.3	5.6	4.1	6.6
NA+ mmol/L	138	145	142	141
K+ mmol/L	3,98	3,3	2.3	3.5
UREA mmol/L	2,3	1,2	2,4	3.6
Creatinine mcmollL	41	37	45	52
Cholesterol mmol/L	3,6	3,7	1.0	
Triglyceride mmollL	1,1	0,7	1.4	
CA++ mmollL(2-2,6)	1,8	1,7	1,6	1.7
P04+mmollL(0,8-l,6)	0,7	0,7	0.4	0.9
ALP lUll (UP 198)	149	235	981	107
Total protein g/l	65	65	57	
Albumin g/l	44	39	19	30
AST IUll(uP to34)	27	25	60	
ALT IU/I(up to31)	22	57	53	
PT,PTT,INR			Normal	
Serum iron (10-27)		1,9		
TIBC (44-71)		55.8		
TSH mIU/l	1.2		1.4	
FT4 ngldl	1		0.9	
TPO-Abs IU/ml			Positive	
TG-abs IU/ml			Positive	
PRL ng/ml	18			
iPTH pg/ml	248	363	272	107
25(OH)VIT.D ng/ml	3.7 (8.9-46. 7)	1,3(25-80)	7.9(25-80)	

Clinical features and investigations results are shown in Tables 1-3 and Fig. 1. During hospitalization, she developed severe hypocalcemia, muscle spasm and hypokalemia with ECG changes, which was corrected with intravenous electrolyte replacement. She was given steroid for 10 days to control severe symptoms. Gluten free diet and oral supplement of calcium and one alfa were started. She was given alendronate for osteoporosis. Two months later she recovered completely and had normal laboratory investigations.

CASE 4. A 45 years old female patient admitted to the medical ward with complaints of peri-oral and all limbs numbness and had bilateral carpopedal spasm. She had 2 weeks history of nausea, vomiting and diarrhea. Clinical examination and investigations are showed in Tables1-3. Diagnosis was established and she was treated with gluten free diet, calcium, iron and one alfa supplements.

Table 3. Radiological, serological and histopathological results.

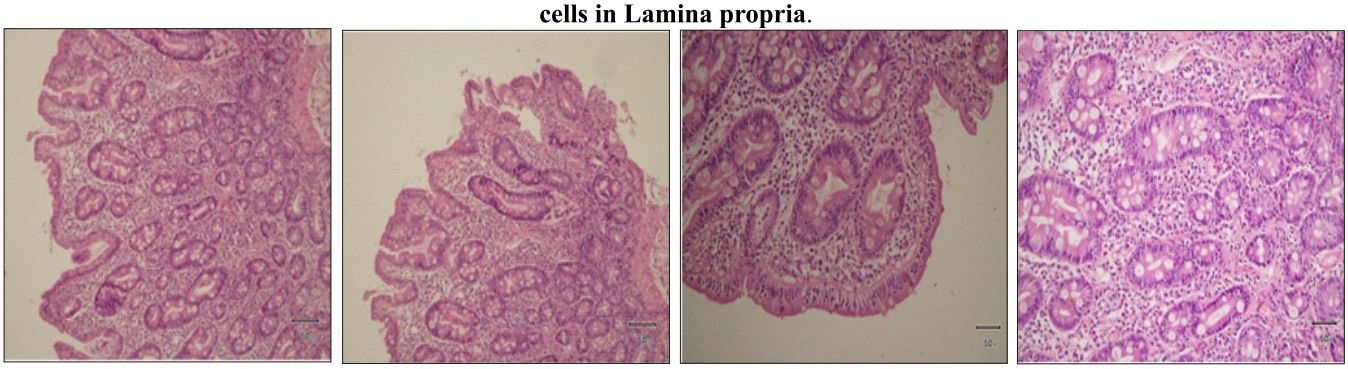
	CASE I	CASE2	CASE 3	CASE 4
RADIOLOGY	Normal skeletal bone survey DEXA - not done	Normal bone survey DEXA - Not done	Bone survey - osteopenia DEXA - severe osteoporosis T Score - 2.6	Bone survey - not done DEXA - not done
Anti-Gliadin Abs	Positive	Positive	Positive	.
Anti-Endomysial TGAbs	Positive	Negative	Negative	
BLOOD FILM			Poikylocytosis target cells and fragmented RBCS	
STOOL			Negative for parasites.	Negative for infection and parasites.
BOIOPSY	Subtotal villous atrophy with increased number of mononuclear cells in the surface epithelium and lamina propria including large number of plasma cells.	Duodenal mucosa with flattened mucous membrane and one short broad villous only seen. Lamina propria is heavily infiltrated with lymphocytes and plasma cells.	Villous atrophy with increased Lymphocytes intra epithelial and increased inflammatory cells in Lamina propria. Figure	Complete atrophy of villi Surface epithelium is columnar with fat globules in many cells and infiltrated with lymphocytes increased vascularity below basement membrane. Lamina propria heavily infiltrated with Lymphocytes and plasma cells

She was admitted few years ago with vomiting and watery diarrhea but had no carpopedal spasm at that time. Clinical examination was unremarkable. Laboratory investigations showed hyponatremia (129meq/L), hypokalemia (k+ 2.8meq/L), hypoalbuminemia (22g/l) with high liver enzymes and marginal hypocalcemia (Ca++ 2.0 mmol/L). She was treated as gastroenteritis. Intravenous fluids were given and electrolyte disturbances were corrected. Suspicion of malabsorption was raised and intestinal biopsy showed doudenal mucosa with partial laceration of mucous membrane, lamina propria showed moderate lymphocytic cellular infiltrate.

DISCUSSION

Celiac disease is a common genetic disorder induced by ingestion of gluten. Factors like infection, gluten overload and gastric surgery can trigger CD in abrupt manner.[1] CD was traditionally thought to be a disease affecting primarily children and uncommon in adults. Multiple studies in the last few decades have showed that it may present at any age in life and 20% of patients are older than 55 years at the time of diagnosis.[1,4] CD develops classically in early years of life when gluten containing cereals are introduced, with subsequent development of diarrhea, abdominal bloating, wasting and both nutritional and vitamin deficiencies.[10] Adult CD presents usually with fewer digestive manifestations and displays atypical forms characterized by common extra-intestinal complaints and various accompanying conditions which render diagnosis more challenging.[1,2,4,10] The combination of history, physical examination and diagnostic tests (chemistry, serologic results and biopsy findings) can help in establishing the diagnosis.[1-4,10]

Fig.1. (A, B, C, D). Villous atrophy with increased Lymphocytes intra epithelial and increased inflammatory cells in Lamina propria.



In the 4 cases described here, clinically presented with hypocalcemic tetany, which was the trigger factor to investigate thoroughly the patients and establish the diagnosis of CD. The clinical picture described in these patients was mostly due to Vitamin D deficiency in association with secondary Hyperparathyroidism. It's mostly related to malabsorption of vitamin D and calcium.[11]

CD presentations as hypocalcemia, osteopathy, osteoporosis, osteomalacia, have been reported[5,11-15] but not common presentation with symptomatic hypocalcemia.[6-9,16] CD was not suspected in these 4 patients until development of symptomatic hypocalcemic tetany manifested as recurrent carpopedal spasm. This clinical picture initially was explained as consequence of postsurgical and/or idiopathic hypoparathyroidism in first and second case. No provisional causes were for 3rd and 4th cases. The combination of careful clinical history, physical examination and laboratory investigations raised the possibility of CD, which was confirmed by serological and intestinal biopsy results.

Hypocalcemia in CD may be associated with osteomalacia, osteoporosis, which was seen in third case. Osteoporosis and osteopenia are highest in newly diagnosed CD or in the patient not in remission. The low vitamin D is usually present in CD patients with low BMD. Secondary to pain and decreased physical activity, secondary hyperparathyroidism and hypocalcemia also contribute to low BMD.[6] The development of hypocalcaemia in CD may be due to negative calcium balance because of intestinal villous atrophy and impairment of active intestinal calcium transport mechanisms. Low vitamin D also contributes to decreased calcium absorption.[6,7,11,14]

Other 3 cases had normal skeletal bone survey. This may be due to early detection of CD involvement of the proximal intestine despite obvious clinical picture of malabsorption and second hyperparathyroidism.[14] The third patient, in addition to hypocalcaemia, osteomalacia, osteoporosis, developed symptomatic hypokalemia and lower limbs weakness with ECG changes and that actually was keeping with celiac crisis, which is reported mostly in children[18] and may developed in adults.[19,20] Celiac crisis may be due to acute exacerbation of underlying mucosal inflammation leading to severe diarrhea, dehydration and significant metabolic disturbances. This includes hypokalemia, hyponatremia, hypocalcemia, hypomagnesemia and metabolic acidosis. Underlying malabsorption state would predispose to hypoalbuminemia, as in our case and decreased effective arterial volume. This may explain resistanance to usual treatment until steroids were given.[19,20]

First patient had post surgical hypothyroidism. She had anti-thyroglobulin (Tg) antibodies and thyroperoxidase antibodies (TPO Abs). This is suggestive picture of Hashimoto autoimmune thyroiditis which is associated with CD.[4] The 3d patient had elevated liver enzymes, which normalized after gluten free diet. This was due to autoimmune hepatopathy, which may be associated with CD.[4] First intestinal biopsy of 4th patient did not confirm CD in her first admission; however, 3 years later intestinal biopsy showed frank histological picture of CD. This may be explained by slow progression of latent CD.[1,2]

CONCLUSION

CD is commonly encountered disorder in children and adults, which has variable clinical pictures far from classical picture of malabsorption. It is important to remember that patients with CD are at risk of developing secondary endocrine abnormalities such as symptomatic hypocalcaemia and bone mineralization defects.

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