

## Case Report

### A Case Report of Celiac Disease with Gitelman Syndrome: A Rare Combination

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#### Abstract

##### Background

The simultaneous presence of celiac disease and Gitelman syndrome is a rare combination. To the best of our knowledge this is the first case report of the two entities present together in a patient.

##### Case presentation

This is a case report of a 15 year old male child of Asian descent known case of celiac disease, presenting with weakness in all 4 limbs with severe electrolyte disturbance mainly hypokalemia and hypomagnesemia. On examination he had pallor, quadriparesis and absent deep tendon reflexes. Patient was diagnosed with celiac disease 4 years back on intestinal biopsy and then was kept on gluten free diet. We present a case of hypokalemic periodic paralysis in a patient with previously diagnosed celiac disease.

##### Conclusion

The correct diagnosis of our patient was based upon clinical suspicion, appropriate laboratory investigations and deliberation of possible differential diagnosis. The management of our patient was dependent on correct diagnosis of both the diseases.

**Keywords:** Celiac disease; Gitelman syndrome; Periodic hypokalemic paralysis

#### Abbreviations

CD: Celiac Disease

GS: Gitelman Syndrome

PHP: Periodic Hypokalemic Paralysis

#### Introduction

Celiac disease is an immune mediated enteropathy that is triggered when gluten containing diet (wheat, rice, barley) are ingested in genetically susceptible individuals. Majority of the times CD is

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associated with HLA molecule DQ2 subtype. However, it may also be associated with HLA-DQ8 in some cases [1].

Gitelman syndrome usually presents in or beyond adolescence [2]. GS is a rare autosomal recessive disorder which is caused by mutations in the SLC12A3 gene. This gene is responsible for encoding the thiazide sensitive sodium chloride co-transporter which is expressed in the distal convoluted tubule of the kidney and is therefore responsible for the reabsorption of sodium and chloride. As a result of mutation, there is defective reabsorption of these ions leading to hypokalemic metabolic alkalosis [3].

#### Case Presentation

An 11 year old male patient, Asian descent, had presented with recurrent episodes of diarrhea for past 5 months (4-5 episodes/day, semisolid, non-foul smelling) who had some pallor on examination. A full blood count revealed hemoglobin of 9g/dl with an MCV of 69. Suspecting malabsorption, workup was done for celiac disease. Anti TTG IgG and anti endomysial antibodies were negative however; an intestinal biopsy confirmed the diagnosis revealing partial villous atrophy, intra-epithelial lymphocytosis (50/100 enterocytes in duodenum) and crypt hyperplasia. According to the modified Marsh classification based on endoscopic findings, patient has type 3a disease patient was then kept on a gluten free diet.

Patient was doing well until now till the age of 15, when he presented with acute, non-progressive weakness of the upper and lower limbs for past two days, more marked in the lower limbs. There was no associated shortness of breath, dysphagia, visual disturbance, or altered level of consciousness. There was no history of diarrhea, vomiting, any drug or laxative abuse.

Patient has been having similar episodes of illness in the past for last 8 months. During each episode patient had documented low serum potassium levels which were replaced with I/V potassium. On two separate hospital admissions patient also had low serum sodium levels which were replaced with I/V sodium chloride.

However, birth history of the patient is unremarkable with all milestones achieved on time. Moreover, the parents of the child were found to be completely normal when specifically inquired for the presence of any autoimmune disease. Patient has 3 siblings, all of them are normal healthy individuals with no known medical disease or illness.

On examination, patient was vitally stable. Pallor was present. He was however conscious and well oriented to time place and person with intact memory and speech. Motor examination showed normal bulk of muscles with reduced tone in all four limbs. Powers were 0/5 in lower limbs and 1/5 in upper limbs. Superficial reflexes were normal however the deep tendon reflexes were absent in lower limbs and diminished in upper limbs. Planters were down-going. The sensory system and cranial nerves were intact. Sensibility examination was unremarkable with normal touch, pain, temperature, vibration and position sensation. No signs of cerebellar dysfunction were seen. Respiratory, cardio vascular and abdominal examinations were clinically normal.

Lab investigations showed hemoglobin 9.8g/dl with peripheral smear showing microcytic hypochromic anemia, MCV 70fl, TLC 6,000c/mm, ESR 40mm/h. Iron studies revealed serum iron to be 30µg/dl and serum ferritin 20ng/ml. creatinine 0.8 mg/dl, sodium 118meq/l, potassium 2meq/l, magnesium 1.0meq/l, serum calcium 8.5mg/dl. ECG showed hypokalemic changes. ABG's revealed metabolic alkalosis with pH of 7.45 and bicarbonate 33.3mmol/l. Total serum proteins were 6.9g/dl with albumin 2.5g/dl. Serum CPK levels were 50mg/dl. Thyroid profile of the patient was normal.

His urinary calcium was below normal (2mmol/l). Plasma renin levels were markedly elevated, >500 U/ml. Periodic hypokalemic paralysis was diagnosed on clinical and biochemical parameters. Hypokalemia causing periodic paralysis continued during the attack which was immediately corrected with I/V potassium chloride.

Diagnosis of recurrent PHP, most likely due to Gitelman syndrome, was made because of low serum potassium, sodium and magnesium levels along with metabolic alkalosis, hypocalciuria and hyperreninemia. Although the gold standard for the diagnosis of Gitelman syndrome remains the genetic analysis for the possible mutation, it could not be carried out due to its unavailability in our vicinity. Serum electrolytes became normal within 24 hours and quadriparesis improved in 2 days. The child was discharged with oral potassium, magnesium, ORS, calcium supplements and spironolactone (100mg/day). Follow up was advised after 2 weeks' time and the patient was counselled regarding long term follow ups concerning the electrolyte disturbances.

## Discussion

The symptoms of CD are that of malabsorption syndrome (classical features) [1]. Non-classical features include elevated transaminases and osteoporosis [4]. Many patients may have anemia at the time of diagnosis. Malabsorption of iron, folic acid or vitamin B12 (in case of extended disease) may give rise to anemia. Patient in our report was also found to have microcytic hypochromic anemia secondary to iron deficiency due to malabsorption of iron from the intestine. Patients with CD are also at a higher risk of developing Lymphoma, especially enteropathy associated T cell Lymphoma and B cell Lymphoma of the gut [5].

Closely associated with CD is Lactose intolerance, with both conditions occurring in the same individual in some cases [6]. Headache, neuropathy, behavioral changes and epilepsy are commonly identified neurological, extra intestinal manifestations of CD. However, a rare correlation of CD with pseudo tumor cerebrii has recently been reported recently [7].

CD is closely associated with other autoimmune diseases. One of them is type I diabetes mellitus. Diagnosis of CD may be simultaneous or subsequent to that of type I diabetes. Autoimmune thyroid disease may also be present in some patients with CD [8].

Another important association is with Addison's disease. Patients with Addison's disease are at a high risk of developing CD. Hence, it is important to screen for celiac disease in these patients [9].

Caused by hypersensitivity to gluten is a dermatological disease known as dermatitis herpetiformis characterized by formation of pruritic, vesicular and bullous skin lesions localized specially to the elbows, knees and buttocks [10].

CD can also occur with negative serology but positive histological findings at biopsy, as shown by Julian A. Abrams and Beverly

Diamond in their study [11]. Our patient also has seronegative CD and was diagnosed at intestinal biopsy.

CD is ideally diagnosed through a combination of serological and endoscopic findings. Serology includes antibodies to gliadin, endomysial and tissue transglutaminase. However, gold standard of diagnosis remains the endoscopy and small intestinal biopsy [12]. A strict life long gluten free diet is the mainstay of the treatment [13]. However, a refractory celiac disease may be treated with corticosteroids [14].

Gitelman syndrome is an inherited renal tubular disorder that is characterized by hypokalemic metabolic alkalosis. Bartter syndrome (classical type) is the closest possible differential diagnosis of Gitelman syndrome, from which it is differentiated by the presence of both hypocalciuria and hypomagnesemia, as suggested by M Patseadou and A Galli Tsinopoulou in their study [15]. Our patient also had the two findings in the lab reports with urine calcium and serum magnesium being less than the normal.

Gitelman syndrome can only present with persistent hypokalemia [16] or it may present with sudden onset of paralysis or quadriplegia with no other significant illness [17]. Our case report also deals with a patient who presented with weakness in all the four limbs at the time of admission and had persistently been having low serum potassium levels on previous hospital admissions.

GS can however present atypically with a systemic involvement. ACC Fu and KP Lee reported in their case of a child who presented with Pneumonia and was later diagnosed with Gitelman syndrome, when evaluated for severe hypokalemia [18].

A case report by Farhan Raza reports, for the first time, an association between GS and delayed puberty [19].

Diagnosis of GS including biochemical abnormalities are hypokalemia, metabolic alkalosis, hypomagnesemia, reduced urinary calcium excretion. Plasma renin activity and plasma aldosterone concentration are slightly elevated [20]. Our patient had metabolic alkalosis with bicarbonate 33.3mmol/l, hypokalemia with potassium 2meq/l, hypomagnesemia with magnesium 1.0meq/l and hypocalciuria with urinary calcium below 2mmol/l. Also plasma renin levels were elevated as mentioned earlier.

Treatment of GS is mainly symptomatic with potassium and magnesium supplements. High doses of magnesium may however cause diarrhea. Aldosterone antagonists may also be used to correct and maintain serum potassium level [18].

## Conclusion

When a young patient presents with quadriplegia or recurrent hypokalemia, a physician must keep in mind periodic hypokalemic paralysis or a renal tubulopathy.

## Consent

Written informed consent was obtained from the patient's legal guardian for the publication of this case report. A copy of written consent is available for review by the Editor-in-chief of this journal.

## Authors' Contributions

M. Ishaq was responsible for complete diagnosis, treatment and narration of the patient's history. M. Shariq conducted the examination, wrote the manuscript and is responsible for the correspondence. Ajeet, Ashok and Salma contributed in the revision of the final manuscript. All authors read and approved the final manuscript.

## Competing Interests

The authors declare that they have no competing interests.

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## References

1. Fasano A (2005) Clinical presentation of celiac disease in pediatric population. *Gastroenterology* 128: 68-73.
2. Mhasde DR, Gautam S, Zore RR, Nadeem S, Chole PV, et al. (2009) Gitelman's syndrome. *J Assoc Physicians India* 57: 211-212.
3. Simon DB, Nelson-Williams C, Bia MJ, Ellison D, Karet FE, et al. (1996) Gitelman's variant of Bartter's syndrome, inherited hypokalemic alkalosis, is caused by mutations in thiazide sensitive Na-Cl co-transporter. *Nat Genet* 12: 24-30.
4. Tavakkoli A, Lebwohl B (2013) Diagnosis of Celiac Disease. In: Rampertab SD, Mullin GE (eds.). *Clinical Gastroenterology*, Springer, New York, USA.
5. Halfdanarson TR, Litzow MR, Murray JA (2007) Hematologic manifestations of celiac disease. *Blood* 109: 412-421.
6. Samasca G, Bruchental M, Butnariu A, Pirvan A, Andreica M, et al. (2011) Difficulties in Celiac Disease Diagnosis in Children - A case report. *Maedica (Buchar)* 6: 32-35.
7. Rani U, Imdad A, Beg M (2015) Rare Neurological Manifestation of Celiac Disease. *Case Rep Gastroenterol* 9: 200-205.
8. Greco D, Pisciotta M, Gambina F, Maggio F (2013) Celiac disease in subjects with type I diabetes mellitus: a prevalence study in western Sicily (Italy). *Endocrine* 43: 108-111.
9. Betterle C, Lazzarotto F, Spadaccino AC, Basso D, Plebani M, et al. (2006) Celiac disease in North Italian patients with autoimmune Addison's disease. *Eur J Endocrinol* 154: 275-279.
10. Clarindo MV, Possebon AT, Soligo EM, Uyeda H, Ruaro RT, et al. (2014) Dermatitis herpetiformis: pathophysiology, clinical presentation, diagnosis and treatment. *An Bras Dermatol* 89: 865-877.
11. Abrams JA, Diamond B, Rotterdam H, Green PH (2004) Seronegative celiac disease: increased prevalence with lesser degrees of villous atrophy. *Dig Dis Sci* 49: 546-550.
12. Yasawy MI, Al-Quorain AA, Tamimi DM (2004) A typical adult celiac disease: report of cases and review of the literature. *Saudi J Gastroenterol* 10: 99-102.
13. Tack GJ, Verbeek WH, Schreurs MW, Mulder CJ (2010) The spectrum of celiac disease: epidemiology, clinical aspects and treatment. *Nat Rev Gastroenterol Hepatol* 7: 204-213.
14. Latorre M, Green PH (2012) The role of corticosteroids in celiac disease. *Dig Dis Sci* 57: 3039-3041.
15. Galli-Tsinopoulou A, Patseadou M, Hatzidimitriou A, Kokka P, Emmanouilidou E, et al. (2010) Gitelman syndrome: first report of genetically established diagnosis in Greece. *Hippokratia* 14: 42-44.
16. Cotovio P, Silva C, Oliveria N, Costa N (2013) Gitelman syndrome. *BMJ Case reports*.
17. Ahmed S, Qayyum M, Farooq F (2011) Quadriparesis in an adult--Gitelman syndrome. *J Pak Med Assoc* 61: 182-184.
18. Fu ACC, Lee KP, Tong LCT (2013) Gitelman's Syndrome: Asymptomatic Hypokalaemia in a Chinese Boy. *HK J Paediatr (New Series)* 18: 174-177.
19. Raza F, Sultan M, Qamar K, Jawad A, Jawa A (2012) Gitelman syndrome manifesting in early childhood and leading to delayed puberty: a case report. *Journal of Medical case reports* 6: 331.
20. Knoers NV, Levtchenko EL (2008) Gitelman syndrome. *Orphanet Journal of Rare Diseases* 3: 22.