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A Case of Gitelman Syndrome Diagnosed with Anorexia Nervosa in a Psychiatry Clinic

Gökçe KAVAK SİNANOĞLU[1], Memduha AYDIN[2]

SUMMARY

Anorexia nervosa is a disorder that is characterized by excessive preoccupation with body weight and shape, and conscious attempts to stay in low weight due to fear of weight gain. Vomiting, one of the methods used by anorexia nervosa patients to stay in low weight, is one of the most important causes of hypokalemia. Diuretics and diarrhea are other common causes of hypokalemia. If hypokalemia is chronic and resistant to treatment, eating disorders and other metabolic conditions should be investigated. One of the rare causes of hypokalemia, an electrolyte imbalance that can cause fatal outcomes, is Gitelman syndrome. Gitelman Syndrome is a genetically inherited disease of the distal tubules which causes hypokalemia, metabolic alkalosis, hypocalcemia, hypomagnesemia and vomiting. It is a syndrome usually diagnosed during adolescence, however it sometimes remains asymptomatic throughout life. Severe symptoms such as tetanus, rhabdomyolysis, and paralysis can also be seen. A case of Gitelman syndrome which was diagnosed as anorexia nervosa due to physical appearance of the patient, low body mass index (BMI), and frequent vomiting and in which the other medical pathologies have not been adequately investigated is presented in this article. Assessments to exclude the medical conditions that may be associated with symptoms are necessary before a diagnosis of a psychiatric disorder is made.

Keywords: Anorexia nervosa, hypokalemia, Gitelman syndrome

INTRODUCTION

Anorexia nervosa (AN) is a disorder that is characterized by excessive mental preoccupation with body weight and shape, fear of weight gain and conscious attempts to maintain low weight. Although AN was first described by William Gull in 1873, there are records that holy anorexics self starved to achieve sainthood in the Hellenistic period (Yucel et al. 2013). On grounds of rarely made medical consultations by members of the public and low prevalence in populations, clear information on its incidence cannot be quoted. Regarding those who seek treatment, a yearly incidence 270 individuals out of 100,000 has been reported (Smink et al. 2012). AN patients attempt to reduce body weight by methods such as restricted food intake, vomiting, laxative use, and diuretic abuse. Vomiting can lead to tooth decay, salivary gland duct dilation, gastroesophageal reflux disease, and electrolyte imbalance. Vomiting or laxative abuse may cause fatal arrhythmias by causing hypokalemia (Sato and Fkudo 2012). When hypokalemia is chronic and resistant to treatment, it should be investigated for diarrhea, diuretic dependence, eating disorders and other metabolic complications. The presented case, previously diagnosed with severe AN due to impaired body image, low body mass index (BMI=13.8), and frequent vomiting, had been treated accordingly. Gitelman syndrome was diagnosed after subsequent medical examinations. It is emphasized that other possible medical conditions should be well investigated in patients consulting psychiatric clinics, especially before somatic complaints are based on psychogenic origins.

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[1]Assist., [2]Assist. Prof., Selçuk University Department of Psychiatry, Konya, Turkey.

e-mail: *drgokcecicek@gmail.com*

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CASE

The 22-year-old female patient, second sibling of her family, was a university graduate who had discontinued working after 1.5 months. She currently lived with her family after having previously lived in different provinces due to her father's vocation. She had been married for 3.5 months but lived apart from her husband who worked outside the city limits.

Her first complaints of abdominal pain and cramps began when she prepared for the high school entrance exam nearly 8 years previously. She had fainted with exam anxiety when seeing the exam premises. Since her complaints repeated when preparing for university entrance examinations, she consulted an outpatient psychiatric treatment center, but could not benefit from the treatment protocol and had to abandon it. Residing with her parents when continuing evening classes at the university, she had progressive complaints of nausea, vomiting and abdominal pain after ingesting food. When she consulted the department of internal medicine for her complaints, medical reasons explaining her symptoms were not found and she was referred to the psychiatry clinic. At our inpatient clinic she was given olanzapine and clomipramine teatment as a final resort. She also drank the herbal tea of Achillea millefolium, but did not benefit from it. She attended psychotherapy sessions at different intervals for nearly two years in a private psychotherapy center. Eating avoidance behaviors started because of vomiting after almost all meals in the last one year. Secondary amenorrhea started when her weight had decreased from 60 kg to 45 kg one year previously. She further lost 7 kg in the last one year. When she applied to our clinic, her body weight and height were, respectively, 37 kg and 164 cm.

Her complaints at admission to our clinic were postprandial nausea and vomiting, weakness, fatigue, convulsions, dizziness, fainting, chest pain, and weight loss. She often said that "Everyone called me anorexic, I was not anorexic, although they thought I consciously vomited, I wanted to gain weight". She also said that she couldn't express herself and was misunderstood. Her family relationships deteriorated during this process. She also complained of increased irritability and reactive behaviors to family members and physicians.

Detailed laboratory tests were requested initially for possible electrolyte imbalance and metabolic disorders. It was explained that she should be an inpatient for close follow-up and preparation of a treatment plan. Although not happy with treatment on an inpatient basis, she was hospitalized in the gastroenterology clinic as the laboratory test results showed severe hypokalaemia (K: 2.3 mEq/L; normal range: 3.7 mEq/L-4.9 mEq/L) and she was given potassium replacement therapy. Upper gastrointestinal system endoscopy was performed to investigate aetiology. Biopsy material was examined by a pathologist. She was investigated for coeliac disease. Medical reasons were not found to explain the hypokalaemia. She was referred to the psychiatry clinic after it was concluded that the low potassium level was caused by malnutrition and vomiting.

She was hospitalized with the preliminary diagnoses of eating disorder and generalized anxiety disorder. The mental status examination showed that she was conscious, fully-oriented, and cooperative. Her memory and executive attention processes were normal. Her physical appearance was quite cachectic (BMI=13.8). She looked tired and exhausted. She had prominent eyeballs and collapsed cheeks. She communicated well with someone and made eye contact. She had a slow speech rate and a hoarse voice. She seemed anxious. Her perception was normal. She had normal thought processes and health status concerns in her thought content. Although she has seeked treatment for a long time, she said that her health condition got worse, she continued to lose weight, she wanted plump cheeks as before, and she wanted to gain weight. Her anxiety and irritability escalated while trying to express herself during the examination. She felt angry because others thought that she vomited intentionally. In particular, her family relationships had deteriorated. She had a good appetite but chose not to eat anymore because she was afraid of vomiting. She had a disturbed sleep pattern. She had blood-injury phobia. Therefore, she was reactive and anxious during phlebotomy for blood potassium level measurement. Her vital signs were stable and blood pressure (BP) was generally within the normal limits of 90/60 mm Hg, and rarely lower at 70/40 mm Hg, during inpatient treatment.

According to first laboratory results, serum potassium was 2.81 mEq/L (3.7-4.9 mEq/L), chloride level was 71 mmol/L (101-109 nmol/L), sodium level was 129 mEq/L (137-144), haemoglobin level was 11.5 g/dl (12-15.5 g/dl), and hematocrit level was 33.6% (34.8-44.5%). Urinalysis did not show any pathology other than low urine density of 1.009 (normal range: 1.015-1.025). Electrocardiography (ECG) revealed increased P-wave amplitude and T-wave flattening. This result was considered to be compatible with chronic hypokalaemia. The QT interval was prolonged to 0.47 seconds (normal range: 0.36-0.44 sec).

She did not observe calorie restriction and was not afraid to gain weight. She did not give great importance to her body weight and shape. She did not make herself vomit and use laxatives or diuretics. Considering the prelimiary diagnoses of generalized anxiety disorder, psychogenic vomiting and anger attacks, she was started on escitalopram (5 mg/day) and risperidone (0.25 mg/day), these dosages being titrated to 20 mg/day and 1 mg/day, respectively, during the follow-up

period. Hyoscine-N-butylbromide and medazepam HCL were administered 3 times daily.

Consultation was seeked with the Department of Nephrology for low potassium level obtained after the initial evaluation. Potassium replacement therapy was started. The number of calories needed each day was calculated by a dietitian. Nutritious supplementary foods (liquid formulae) were added to her diet to meet her daily intake need of about 2000-2200 calories. Some recommendations were made to prevent vomiting after meals. She was an inpatient of the psychiatry clinic for approximately 1 month. Potassium replacement therapy was given to maintain the potassium level in blood within the normal range with the recommendation from the nephrology department. During the first two weeks of hospitalization, the frequency of vomiting was significantly reduced, and although occurring daily vomiting immediately after eating could be delayed for a long period. Potassium level was decreased after vomiting resulting in contractions occurred in the hand and feet muscles due to low potassium level. She willingly complied with the recommended treatments, not rejecting pharmacotherapy, dietary supplement use, increased food d intake or observation of vomiting after eating. On the third week of hospitalization, she did not vomit and was well nourished for three days. Serum electrolyte values during this period were 2.9 mEq/L (3.7-4.9 mEq/L) for potassium, 133 mEq/L (137-144) for sodium, 81 mmol/L (101-109) for chloride and 1.51 mg/dL (1.9-2.7) for magnesium.

When her family had been informed about treatment-resistant hypokalemia and the results of her blood tests, her mother remembered that a general surgeon, at the hospital she had consulted years ago for her initial complaints, had warned that her potassium level was low; but that further examinations had not been made. Since the patient's potassium level remained low despite regular feeding and absence of nausea, another underlying medical condition was suspected. The relevant departments were consulted for further investigations on the aetiology of hypokalaemia. The 24-hour urinary electrolyte levels, blood electrolyte levels and venous blood gases were examined. After the serum potassium level was increased above 4 mEq/L by intravenous potassium replacement, plasma renin and aldosterone levels were found to be, respectively, 4.44 ng/ml/h (0.51-2.61 ng/ml/h) and 11.8 ng/dl (1-16 ng/dl). Also, ACTH level was 21.97 pg/ml (7.2-63.3 pg/ml); cortisol level was 18.41 ug/dl (0-10000 ug/dl); FSH level was 1.08 U/L (0-10000 U/L); LH level was <0.1 U/L (0-10000 U/L); and estradiol level was <5 ng/L (0-10000 ug/dl). On venous blood analysis, pH level was 7.479 -log(H) (7.32-7.42 -log(H)); potassium level was 3.1 mEq/L (3.4-4.5 mEq/L) and bicarbonate level was 32.8 mmol/L (22-26 mmol/L). The 24-hour urine analysis results indicated a calcium level of 15.96 mg/day (100-300 mg/day), chloride level of 18.6 mmol/g (24-250 mmol/g), and phosphate level of 46.5 mg/day (400-1300 mg/day). She was diagnosed with Gitelman syndrome by the internal medicine department on the basis of frequent vomiting and muscle contractions, not gaining weight despite adequate nutrition, and the laboratory test result of hypocalciuria associated with resistant hypokalemia. Oral magnesium and potassium supplementation was recommended.

During her psychiatric interviews, she had mentioned that she was affected by family relationships and and that the frequency of vomiting increased during periods of high anxiety especially concerning the employment of her father and husband. She indicated that she would like to continue psychiatric drug therapy since it helped her cope with high anxiety, physical complaints, irritability, and anger management problem. Treatment with escitalopram and risperidone were continued for anxiety symptoms and the anger management problem together with supportive interviews at the psychiatric outpatient clinic. During outpatient follow-up visits, it was learned that she vomited less frequently but could not gain weight. She was referred to the nephrology department for close follow-up of Gitelman syndrome and to the genetics department for genetic counselling. Genetic tests could not be made as she stayed outside the city for long periods for family reasons.

DISCUSSION

This case report explained the diagnostic process on the many symptoms of Gitelman syndrome in a patient who was previously diagnosed with AN and treated with various medications. Clinical information including physical appearance, low BMI, anxious personality traits, frequent vomiting and further increase in vomiting frequency due to stressful life events have caused psychiatrists and psychologists to conclude on AN diagnosis for a long time. Inability to gain weight and involuntary vomiting were considered as misleading symptoms to be seen in AN patients. In the case of the patient discussed here, her complaints at first examination, her past medical history, and clinical observations and measurements were adequate to make us diagnose AN. Previous unsuccessful treatment experiences, inability to understand her, being misunderstood by her and her attitudes in the examination room due to mistrust in her treatment supported these prejudices. The necessity of inpatient treatment due to both low BMI and hypokalaemia gave a good chance for the appropriate clinical observation. The preliminary diagnosis of AN was cancelled after the first days of hospitalization. Her medical history, family relationship problems, increased vomiting and physical symptoms after interfamily discussions, complaints of fainting and hand numbness, and exacerbation of these complaints due to high anxiety revealed that the patient needed to be assessed

in terms of eating disorders, anxiety disorders, somatization disorder and related disorders.

The first remarkable findings in our patient were persistent vomiting and hypokalemia. When patients presenting with vomiting are aetiologically examined, it would be appropriate to evaluate them under seven main headings including central nervous system diseases, gastrointestinal diseases, infectious diseases, medications, toxic substances, metabolic diseases, and psychogenic vomiting (Scorza et al. 2017). The central nervous system diseases were eliminated as the patient did not have clinical findings including blurred consciousness, severe headache and high fever related to vomiting, and brain imaging techniques did not reveal evidence of vomiting. The patient was hospitalized and treated in the gastroenterology clinic shortly before admission to our clinic. Endoscopic biopsy did not reveal evidence for vomiting. Infectious diseases were eliminated since the patient did not have acute onset vomiting and clinical features suggestive of infectious diseases; and the inflammatory markers were within the normal reference range. According to information given by her and her family, our patient did not take any medications and did not have any contact with any toxic substance that could cause emesis. Therefore, we focused on metabolic abnormalities and psychogenic causes. It was vital that our patient had hypokalaemia accompanied by vomiting which occurred every day after almost every meal. Therefore, we ascribed importance to the cause of hypokalaemia.

The most common causes of hypokalaemia are vomiting, diuretic use, and diarrhea. Hypokalaemia and metabolic alkalosis can be seen in diuretic and laxative abusers and in patients who vomit covertly. Urinary sodium, potassium and chloride excretion is higher in diuretic abuse (Akcakaya et al. 2009). Hypokalaemia and metabolic acidosis are often seen in frequent and repeated use of laxatives. Our patient had severe vomiting, but clinical observations and laboratory findings did not support laxative or diuretic abuse. As in this case, Gitelman and Bartter syndromes (familial hypokalaemic alkalosis) should be considered in the differential diagnosis of adult patients with metabolic alkalosis, hypokalemia, and normal blood pressure, besides diuretic/laxative abuse and chronic vomiting.

Gitelman syndrome is an autosomal recessive disorder characterized by renal potassium loss, hypokalemia, metabolic alkalosis, hypocalciuria, and hypomagnesaemia (Cruz et al. 2001, Enríquez et al. 2010). It is a rare cause of hypokalaemia with a prevalence estimated to be approximately 1 in 40,000. The prevalence of heterozygotes is estimated to be approximately 1% in the white population (Levtchenko and Knoers 2008). It is caused by mutations in the genes encoding the sodium-chloride and magnesium carriers in the thiazide-sensitive segments of the distal tubule. The genetic defect has been described in the gene SCL12A3 on the short arm of chromosome 16 (Ji et al. 2008). This disease can sometimes be asymptomatic throughout life and may cause symptoms such as muscle weakness, malaise, fatigue, cramps, or carpopedal spasms in adolescence as in our case. However, it has been reported that severe symptoms such as tetany, rhabdomyolysis, and paralysis may also occur (Gjate et al. 2007) Our patient had previously experienced anxiety because she had taken exams and had been separated from her father on account of his vocation. This anxiety led to the fact that ambiguous symptoms which began in adolescence and were considered as anxiety disorder. The increased complaints in the following periods were associated with stressful life events. Although the patient's family problems, test anxiety, fatigue, weakness, muscle spasms, irritability, involuntary contractions, and sleep disturbance may be considered as symptoms related to generalized anxiety disorder, some of these symptoms overlap with the muscular weakness and contractions seen in Gitelman syndrome.

Gitelman syndrome can be frequently confused with Bartter syndrome type 3, another hereditary renal tubular dysfunction, with concurrent occurrence of metabolic alkalosis and hypokalemia. Although Bartter syndrome type 3 often occurs before the age of two years, the diagnostic process may extend to puberty because most patients have a good prognosis. Growth retardation can occur due to delayed diagnosis and treatment. Bartter syndrome can be separated from Gitelman syndrome with developmental delays at an early age. Although there are some differences between these two syndromes, such as hypomagnesemia and hypocalciuria common in Gitelman syndrome but rare in Bartter syndrome, the differential diagnosis between them is quite difficult since they have the same phenotypic variants (Shibli and Narchi 2015). Our patient was diagnosed with Gitelman syndrome because she was considered to be in early adulthood and hypomagnesaemia and hypocalciuria coexisted. However, she was thought to have comorbid generalized anxiety disorder when considering the fact that she had weakness, fatigue, irritability, restlessness, sleep problems and muscle spasm on the mental status examination. There was also an increase in the frequency of vomiting after stressful life events and a decrease in the frequency of vomiting with suggestions, such that she benefited from supportive psychotherapy and psychopharmacologic treatment with escitalopram (20 mg/day) and risperidone (1 mg/day). In the clinical follow-up, it was observed that fainting and hand contractions occurred after vomiting and that these contractions disappeared with potassium replacement therapy. The diagnosis of somatization disorder and related disorders were eliminated. Although the patient was considered to have psychogenic vomiting due to anxiety symptoms as well as vomiting attacks triggered by psychosocial stressors, it was observed that her anxiety

and stress levels decreased but vomiting occurred during periods when she felt more comfortable. This situation was interpreted as increased level of anxiety in the patient with tendency to vomit due to triggering of pre-existing complaints by Gitelman Syndrome.

Vomiting, fatigue, and muscle spasms are symptoms that can be seen in many diseases and should firstly bring to mind the medical condition of electrolyte imbalance. Hypokalaemia is an important electrolyte disorder that may have fatal consequences. Therefore, the underlying causes should be clarified in patients with resistant hypokalaemia. While at times the clinicians at psychiatry clinics remain within the psychiatric diagnostic criteria and overlook the other medical problems of the patients, clinicians of other disciplines remain within the framework of a preexisting psychiatric condition while evaluating medical conditions of the patients. Attributing most of the complaints by patients to a predetermined diagnostic pattern can narrow the viewpoints of clinicians in their practice and delay diagnostic and therapeutic approaches.

CONCLUSION

As clinicians, we can demonstrate in detail the medical and psychological factors that cause complaints by taking a detailed clinical history from patients and their relatives and by performing a careful physical and medical examination.

This case report is important in having emphasized the importance of follow-up and observation related to examination and diagnostic processes in psychiatry as well as by demonstrating that medicine is a multidisiplinary approach.

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