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Case Report Open Access

Our Cases with Sucrase Isomaltase Deficiency

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Abstract

Objectives: Individuals affected with sucrase isomaltase deficiency are unable to digest sucrose-containing foods. Primary symptoms include watery diarrhea, abdominal discomfort and vomiting. Secondary symptoms include retarded growth and malnutrition. Nonspecific symptoms may lead to lengthy delays in diagnosis. The objective of this report is to describe the clinical presentation, diagnosis and treatment of five Turkish children with sucrase isomaltase deficiency.

Methods: This is a series of three male and two female patients that presented to the Department of Pediatric Gastroenterology, Hepatology, and Nutrition at Ege University between 2008 and 2014.

Results: Patient ages ranged from 6 months to 9 years and symptoms began after the introduction of food or formula into the diet at 1 week to 6 months of age. Presenting symptoms included growth retardation, decreased weight gain, watery diarrhea and vomiting. Four patients were previously misdiagnosed with GERD, celiac disease, lactose intolerance and food allergy but they did not respond to standard treatment. Routine clinical laboratory assessments including hematology, renal, thyroid and hepatic function, renal tubular function were normal. A detailed history revealed the association between the onset of illness and dietary changes leading to the diagnosis of congenital sucrase isomaltase deficiency. All five patients responded to treatment with sacrosidase oral solution.

Conclusion: This is the first case series of pediatric patients with sucrase isomaltase deficiency in Turkey. The actual prevalence of the disease in Turkey is unknown, probably due incorrect diagnoses. Four of our patients were previously misdiagnosed with other gastrointestinal disorders leading to delayed treatment. We suggest that sucrase isomaltase deficiency should be considered in pediatric patients presenting with chronic watery diarrhea.

Keywords: Sucrase-isomaltase deficiency; Watery diarrhea

Introduction

Sucrase isomaltase deficiency is a small bowel disease characterized by OR transitive, rare, osmotic diarrhea, meteorism and weight loss. Due to differences in specified different mutations, residual enzyme activity carbohydrate intake, gastric emptying and small intestine transit time, this disease may occur at different ages and in different clinical manifestations. Prevalence ranges from 0.05% to 3%. What are important in diagnosis are patient complaints, clinical presentation, age-related changes observed and the amount of carbohydrates received, and the gold standard is the measurement of disaccharidases enzyme activity in small intestinal biopsy tissue. However, as measuring enzyme activity is also not possible in Turkey, in the event of clinical suspicion, by loading sucrose-isomaltose, diagnosis is provided by the emergence of symptoms within hours. Sucrase-isomaltase enzyme extract is used in therapy.

Case Report

4 patients including 2 boys, 2 girls were diagnosed as sucrase isomaltase deficiency between the years 2008-2014 in Pediatric Gastroenterology Hepatology and Nutrition branch of Ege University.

The ages of the patients applied were between 5 months and 5.5 years, the age of onset of complaints ranged from 15th day to 6 months. Reference symptoms were growth retardation, decreased weight gain, plenty of watery diarrhea, vomiting. 4 patients had previously applied to in health care organizations several times and they were followed by GERD, celiac, psödobartt, the lactose intolerance, and food allergy diagnosis but they did not respond to treatments. 4 patients also underwent upper gastrointestinal endoscopy. Esophagitis and gastritis were present in one patient, another biopsy results were normal. One of the cases had B12 and iron deficiency and in one of theme, hypocalcemia was found. Routine biochemistry, hemogramme, sweat test, the CF mutation, IgA, fx5, SPT, stool examination of cases were normal. When the cases were examined in conjunction with beginning of complaints, diarrhea histories, and diet anamnesis, it was found to be a significant relationship between the intake of foods containing sucrose and isomaltose and complaints. Thereupon, in cases began to be fed with the sucrose-free foods, dramatically decreased complaints and the weight gain was observed. Thereupon, treatment began by bringing sakrosidaz enzyme extract from abroad; it was observed that after carbohydrate restriction is removed, there was no recurrence of symptoms.

Result

Congenital sucrase isomaltase deficiency is a disease of which true prevalence is unknown with the diagnostic challenge in the entire world. We presented these cases as this is the first case series diagnosed and treated with enzyme in Turkey and in order to contribute to the literature. The diagnosis of sucrase isomaltase deficiency is put first by knowing disease and clinically suspecting. In cases presenting with chronic diarrhoea symptoms, detailed content of the diet should be queried, in the event of clinical symptoms, the diet should primarily be regulated and in responsive patients, enzyme replacement therapy should be applied.

Sucrase-Isomaltase Deficiency

Sucrase-isomaltase deficiency is the most common congenital disaccharides deficiency. Sucrose isomaltase deficiency is transitive congenital intestinal disease that was first described in 1960 by Weijers et al. [1-3]. Disease prevalence ranges from 0.05 to 0.2%i n North America and Europe but in the natives of Greenland, in Alaska and Canada, the rate is as high as 3% to 10%. (4.5) As no case is not reported in Turkey, the prevalence is not known yet. There are known two activity of the sucrase-isomaltase enzyme complex; sucrose hydrolyses alpha-1,2 and 1,4 glycoside bond, isomaltase degrades the alpha 1,6 linkages.

The classic presentation of the disease includes, after exposure to starch and sucrose, severe aqueous diarrhoea, protrusion, abdominal distention, malabsorption, weight loss and growth retardation [4,5]. However more rarely the disease can be seen with an atypical presentation such as hypercalcemia, renal stones, medullary nephrocalcinosis, metabolic acidosis, In patients with sucrase isomaltase deficiency, sucrose, maltose, oligomers of short alpha 1-4 glucose, dextrin and starch cannot be hydrolyzed [6].

It has been identified by Chantret et al. in 1992 that the sucrase isomaltase gene were in Chromosome 3 (3q25-26), and there were 25 different mutations affecting the synthesis of the enzyme. The event that the disease is seen with different clinical symptoms even in the same family is connected to this genetic heterogeneity [7-9]. Furthermore; residual enzyme activity, the amount of carbohydrates taken, gastric emptying and small intestinal transit time, the amount of carbohydrates that cannot be absorbed to be fermented by the colonic bacteria and absorptive capacity of the colon affects clinical heterogeneity.

It may be diagnosed late or misdiagnosed as it can cause the same clinical findings CSID, celiac disease, cystic fibrosis, food allergy, or to other chronic diarrhea causes. Therefore, in recognition of the disease the most important step is to know the disease and to suspect. Another important step is to be able to notice the changes in the patient's complaints and clinical findings due to age and nutritional content [10-12]. The gold standard of diagnosis is the measurement of disaccharides enzyme activity in intestinal biopsy sections. However, since this is not possible in developing countries, sucrose tolerance test helps to recognize [12,13]. In patients diagnosed with CSID, lifelong sucrose restriction is a treatment option. However, as sucrose tolerance can vary, the quantitative restrictions should be determined according to the complaint of patients. Saccharomyces cerevisiae may increase sucrase and to a lesser extent isomaltase and maltase activity. Sakrosidase or invertase (sucraid)produced from S.cerevisiae can be used successfully in patients with CSID. We aimed in this article to present patients came with different clinical presentations and sucrose-isomaltase deficiency diagnosed and treated with enzyme treatment, to contribute to the literature and to raise awareness of the disease.

Case 1

5 years old female patient. 35 weeks c / s and a history of premature delivery are available. 15 cases followed as intubated for 21 days in the NICU unit and with no relationship between the parents and family history were initiated premature food per day. The cases suffering from watery diarrhea from the day 15 and with metabolic alkalosis in blood gas, hypocalcemia, hypokalemia and hyponatremia have been followed with the diagnosis of neonatal barter. Cases suffering from diarrhea previously examined by external centers referred to our center as the complaints were still available. On physical examination, weight: 16.6 (75-90p, -1.01 SDS), Height: 97 cm (<3p, -2.52 SDS), blood pressure was normal, other systemic examinations were normal. In received routines, electrolytes, LFTs, renal function, thyroid function tests, ferritin, lipid profile, growth hormone levels, renal tubular function, blood count, stool analysis, sweat test was normal, Cystic fibrosis mutation, celiac serology, IgE, SPT, fx5 were negative. Underwent upper gastrointestinal endoscopy and biopsy were normal. When deepening the history of diet of patients, it was understood that diarrhea was obvious especially after the sucrose and starchy foods. The amount of faeces of the patient from whom dietary sucrose and starch were removed was regressed from 1500 g / 24 h up to 100 g and solidified.

Case 2

5 years old male patients were born with NSVD 3850 g at term. 1st degree cousin marriages are present among parents. In brief personal histories, the baby food began to be used and watery diarrhea started in 2.5 months. They had crawled 1 year old and walked 3 years old. In family history, diarrhea started in family's 1st child after the start of complementary foods at 6 months and become ex when 8 months of age with diarrhea and dehydration statements. On physical examination, weight: 7 kg (<3 p, -11.7 SDS), Height: 80cm (<3 p 6:25 SDS), blood pressure was normal, turgor was decreased, other systemic examinations were normal. In received routines, electrolytes, LFTs, renal function, thyroid function tests, lipid profile, renal tubular function, blood count, stool analysis were normal. The sweat test was normal, cystic fibrosis mutation, celiac serology, IgE, SPT, fx5 were negative. B12: 115, Ferritin: 13. Underwent upper gastrointestinal endoscopy and biopsy were normal. When deepening the history of diet of patients, it was understood that diarrhea was obvious especially after the sucrose and starchy foods. The patient had chronic diarrhea for a long time that had not yet diagnosed. Cases only fed with protein from hospitalization could tolerate only a small amount of bread and quince. Together with the resumption of sugary foods in diet, diagnosis of cases whose diarrhea has started was confirmed. It was thought that pituitary insufficiency can be seen in patients with marked growth retardation; however, this diagnosis was ruled out in cases grown up 4 cm in 4 months with the introduction sucraid. After you start using Sucraid enzyme treatment, diarrhea was not seen in cases with diet.

Case 3

3 years old male patients were born as 2200 g with 36 weeks C7S. There is no relationship between the parents. In brief personal histories, the baby food began to be used and watery diarrhea started in 6 months. In family history, chronic diarrhea was not diagnosed in

father. On physical examination, weight: 10 kg (<3 p, -4.08 SDS), Height: 87cm (25 p, -2.45 SDS), blood pressure was normal, abdomen was distended appearance, X-thousand deformity was present and other systemic examinations were normal. In received routines, electrolytes, LFTs, renal function, thyroid function tests, lipid profile, renal tubular function, blood count, stool analysis were normal. The sweat test was normal, cystic fibrosis mutation, celiac serology, IgE, SPT, fx5 were negative. Ferritin was found to be 7. Underwent upper gastrointestinal endoscopy and biopsy were normal. When deepening the history of diet of patients, it was understood that Aptamil formula was started to be used at 6th month, and diarrhea was obvious especially after the sucrose and starchy foods. The diarrhea of case from whose sucrose and starch were removed was decreased and weight gain started. After you start using Sucraid enzyme treatment, diarrhea was not seen in cases with diet.

Case 4

6 month old female patients were born 3300 g at term with NSVD. There is no relationship between the parents. In brief personal histories, they have started to be fed with baby food at 15th days and then complaining of vomiting was started, Supplement food was started at 6 months and complaining of watery diarrhea started 7-8 times a day. In his family history, his mother's cousin was exe 1.5 years old due to chronic diarrhea. On physical examination, weight: 6840 g (25 p, -1.12 SDS), Height: 64cm (50 p, - 0.67 SDS), blood pressure was normal, abdomen was distended appearance, other systemic examinations were normal. In received routines, electrolytes, LFTs, renal function, thyroid function tests, lipid profile, renal tubular function, blood count, stool analysis were normal. The sweat test was normal, cystic fibrosis mutation, celiac serology, IgE, SPT, fx5 were negative. Ferritin was normal. Underwent upper gastrointestinal endoscopy and biopsy were normal. Lactose intolerance and GERD was considered at the forefront in patients. Meanwhile, concentrated carbohydrate product containing maltodextrin was added to enteral product with high soluble fiber ratio and maltose ratio intake in order to increase the amount of calories in the diet due to the emerging malnutrition. Then, copious, foul-smelling, watery diarrhea was observed in patient at a level that requires immediate fluid therapy. As a result of this experiment, sucrase-isomaltase deficiency was suspected due to carbohydrate malabsorption in patient taken maltose and sucrose and enteral products in dietary and osmotic type of diarrhea was observed with intensive maltodextrin addition. By starting carbohydrate-free formulant and with removal of sucrose from dietary, diarrhea was resolved completely and preliminary data was obtained to support a diagnosis. In the medical history received from mother, we learned that diarrhea and abdominal distension increased especially after eating grapes, apples, green beans, pinto beans, potatoes. After you start using Sucraid enzyme treatment, diarrhea was not seen in cases with diet.

Case 5

9 years old male patients were born 3120 g with NSVD at term; there is no relationship between the parents. In brief personal histories, diarrhea began in the 1st week in the patient fed with formula from the neonatal period, congenital chloride diarrhea was diagnosed in patients previously hospitalized in other centers due to diarrhea and treatment was started. Patient admitted to our outpatient clinic because of watery diahhroea close to 2 liters per day and short stature. On physical examination, weight: 23g (3-10 p, -1.27 SDS), Height: 118 cm (<3p, -1.86 SDS), blood pressure was normal, abdomen was distended appearance, other systemic examinations were normal. In received routines, electrolytes, LFTs, renal function, thyroid function tests, lipid profile, renal tubular function, blood count, stool analysis were normal. The sweat test was normal, cystic fibrosis mutation, celiac serology, IgE, SPT, fx5 were negative. Ferritin was normal. Underwent upper gastrointestinal endoscopy and biopsy were normal. Sugary foods were removed from the diet by thinking of sucrase isomaltase deficiency to be in line with clinical experience previously experienced by patients and the dietary history from the mother. In tests, the amount of stool decreased up to 150 g, the patient suffering from sucreid was discharged to come for control.

Discussion

CSID is a rare, genetic disease occurring as a result of mutation in sucrase isomaltase gene. Sucrase-isomaltase deficiency is the most common congenital disaccharides deficiency [1,2]. The real prevalence of the disease is not yet fully known. In Turkey, these patients are either omitted or incorrect diagnoses are made for the treatment, therefore there are no cases that have yet been reported. We suspect the lack of sucrase isomaltase in cases who admitted to Ege University Pediatric Gastroenterology, Hepatology and Nutrition department between the years 2008-2013 with symptoms of watery diarrhea, failure to thrive, malabsorption and previously followed by different diagnostic, and here we present 4 cases diagnosed. Our recommendation is that SCID should be investigated in patients come with chronic watery diarrhea.

CSID is an OR inherited small intestine disease. Disease may lead to different clinical conditions even within the same family depending both on genetic heterogeneity and residual enzyme activity, the amount of carbohydrate taken, gastric emptying and small intestine transit time, the amount of carbohydrates that cannot be absorbed to be fermented by the colonic bacteria and absorptive capacity of the colon. Symptoms of the disease in our patients and the severity of these symptoms vary. Gastrointestinal symptoms associated with the disease usually arise as a result of encounters with sucrose or starch after feeding with breast milk. Weight loss, watery diarrhea, and abdominal distension, growth retardation symptoms were present in our cases in transiting to the food and after the use of food containing maltodextrin. The presence of different clinical presentations delays the diagnosis and causes patients with different diagnoses; such as monitoring toddler diarrhea, food allergies, celiac disease, and diarrhea predominant irritable bowel syndrome. In our patients, diagnosis such as reflux, lactose intolerance, and celiac disease were followed but failed to respond to conventional therapy.

In diagnosis, necessarily sucrase isomaltase enzyme activity of the small intestine mucosa samples should be studied. Sucrose tolerance test or C 13 sucrose breath test from noninvasive tests may also be helpful in diagnosis [10,11]. But in our country C 13 sucrose test or sucrase isomaltase enzyme activity measurements cannot be made. This deficiency explains the lack of diagnosis in Turkey to an extent. 3 cases series reported from China had been diagnosed by applying sucrose tolerance test 2014 [11]. After obtaining a detailed dietary history of our cases the diagnosis was confirmed by applying sucrose loading test. In addition, our diagnosis was supported by onset of watery diarrhea after sucrose loading in 4 hours, diarrhea decline after elimination of sucrose and diarrhea emerging by a diet containing sucrose in the history.

CSID treatment is lifelong starch and sucrose elimination. However, it is observed that the use of enzyme replacement therapy including sakrosidase is much more effective and the quality of life and nutrition of patients has improved significantly [14-16]. Sucrose and starch restricted diet was administered until available enzyme in our patients and also a significant clinical improvement was observed in four patients. Treatment was started in 3 cases that enzymes obtained, the dietary was opened and patients whom diarrhea, weight loss, bloating symptoms are not observed were going to be followed-up of who recur.

As a result, the disease being an important cause of chronic diarrhea emerges after initiating to the food but even during the neonatal period may give evidence by formula intake. After initiating the supplementary foods, the intake of sugary and starchy foods have increased, the elimination of responsible food is difficult. Sucrose isomaltase deficiency is more common than lactose intolerance but cannot get a diagnosis. Diagnosis is more difficult because adults develop a diet over time without being aware of how. As is the first case series published in our country, although we cannot comment on the prevalence of structures, as consanguineous marriages are much, frequency is expected to be higher. Although there must be the cases 50-100000, we report the first case series diagnosed and enzyme treatment given in Turkey.

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