CASE REPORT

β-thalassemia minor, carbohydrate malabsorption and histamine intolerance

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1. Introduction

β-thalassemia minor is a heterogeneous autosomal recessive hereditary anaemia characterized by reduced β-haemoglobin chain synthesis [1]. In Northern Europe β-thalassemia is a rare disease but the number of patients is, due to mobility and migration, significantly growing [2]. Gastrointestinal (GI) malabsorption is caused mainly by carbohydrates (lactose and fructose), biogenic amines (e.g., histamine), and proteins (gluten), and shows nonspecific abdominal symptoms [3]. In two patients with β-thalassemia minor we tested GI malabsorption, and diagnosed carbohydrate and histamine malabsorption. Both patients with nonspecific abdominal complaints due to carbohydrate and histamine malabsorption recovered with an individual diet free of symptom triggering carbohydrates and histamine.

2. Case discussions

2.1. Case 1

A 60-year-old male, white patient presented with continuing nonspecific abdominal complaints. His symptoms were bloating, semifluid stools, and diarrhea up to 3 times/day. Anamnesis showed that he migrated from Southern Romania and physical examination revealed a bloated abdomen. Red blood count (RBC) was 5.78 T/L (normal 3.5–5.7), mean corpuscular volume (MCV) 66.8 fl (normal 85–98), mean corpuscular haemoglobin (MCH) 20.5 pg (normal 27–34) and reticulocytes were 23% (normal 4–15). Measurement of the haemoglobin fractions with cellulose acetate electrophoresis revealed HbA 92.7% (normal >96,3), HbF 1.3% (normal <0.5), and HbA2 6.0% (normal <3.2). The peripheral blood smear in this patient demonstrated RBC morphologic changes with anisocytosis, microcytosis, poikilocytosis, and hypochromia.

Elevated laboratory parameters were fasting blood glucose 122 mg/dl (normal <110) and low-density lipoprotein (LDL) cholesterol 103 mg/dl (normal <100). The hydrogen breath test (Gastrolyzer, Bedfont Scientific Inc., Kent, England) was performed with a drink containing 50 g lactose dissolved in 200 ml water, the end-expiratory exhalation of H2 was measured every 30 min for a period of 150 min. The result was an H2-value increasing from the baseline 9 up to 130 parts per million (ppm) (normal: <20) [4]. An additionally performed lactase gene (LCT) C/T-13910 polymorphism genotyping revealed the congenital lactase deficiency C/C genotype (Amplifluor Genotyping System, Chemicon, Merck, Germany). In a similar breath test with a drink containing 25 g fructose load dissolved in 200 ml water the end-expiratory exhalation of H2 was <20 ppm. Using a radio extraction assay for the determination of diamine oxidase (DAO) in serum (Sciotec Diagnostic Technologies, Tulln, Austria) the DAO value in serum was normal, and antibodies against tissue transglutaminase were not found. All the
other routine laboratory parameters, including glycated haemoglobin A1C, were within normal limits. Abdominal sonography revealed no abnormalities. Gastroscopy with biopsies demonstrated absence of Helicobacter pylori infection or other abnormality, and a colonoscopy revealed no abnormalities.

2.2. Case 2

A 33-year-old female, white patient presented with bloating, postprandial fullness and diffuse abdominal pain. Anamnesis showed Turkish origin and physical examination was normal. Abdominal sonography revealed a slightly enlarged spleen at 15 × 8 cm (normal 14 × 7). RBC was 5.85 T/L (normal 3.5–5.7), Hb 11.2 g/dl (normal 12.1–17.2), MCV 73.9 fl (normal 85–98), MCH 18.8 pg (normal 27–34) and reticulocytes were 15% (normal 4–15). Cellulose acetate electrophoresis showed HbA 92.7% (normal >96.3), Hbf 1.3% (normal <0.5), and HbA2 6.3% (normal <3.2). Peripheral blood smear demonstrated anisocytosis, microcytosis, poikilocytosis, hypochromia, and target cells.

In the H2-breath test with a drink containing 25 g fructose load dissolved in 200 ml water the end-expiratory exhalation of H2 increased from baseline 3 to 24 ppm (normal <20) and fructose malabsorption was diagnosed. The diagnosis of histamine malabsorption was made because the DAO value was 4.3 U/ml (normal >10) and more than two gastrointestinal symptoms described for HIT were present [5]. All the other routine laboratory parameters were within normal limits. During the breath test with a drink containing 50 g lactose, the end-expiratory exhalation of H2 was <20 ppm [4]. Antibodies against tissue transglutaminase were not found, and a gastroscopy with biopsies was negative for Helicobacter pylori infection or other abnormality.

A registered dietitian developed an individually tailored diet for both patients and this dietary intervention resulted in the improvement of symptoms. We obtained written informed consent for all procedures, which were in accordance with the Declaration of Helsinki and the recommendations of the local ethics committee.

3. Discussion

β-thalassemia minor is a heterogeneous autosomal recessive hereditary anaemia characterized by reduced β-haemoglobin chain synthesis. Due to mobility and migration, haemoglobinopathies have spread from the Mediterranean, Africa, and Asia, where they can appear endemic, to Northern European Alpine regions, too [2]. There are poor data on the precise prevalence, overall burden, and trends of these diseases in Europe. Although β-thalassemia minor sometimes causes mild anaemia, carriers of disease are usually clinically asymptomatic [6].

Carbohydrates (mainly lactose and fructose) and biogenic amines (e.g., histamine), or proteins (gluten) may cause GI malabsorption. These food components are not absorbed and digested properly during GI passage, and then unabsorbed food results in symptoms due to bacterial metabolism and fermentation in the colon. Recently various combinations of malabsorption/intolerance syndromes in patients with GI malabsorption were reported [3].

Lactose intolerance is related to lactase deficency and causes nonspecific GI complaints with the ingestion of dairy products [7]. Fructose malabsorption is caused by limited absorption capacity of the GLUT-5 protein, the major fructose transporter in enterocytes of the small intestine [8]. Histamine intolerance is a disproportionate amount of histamine in the body caused by the consumption of histamine-containing food or drinks, and/or a reduced ability of enzymes to catalyse histamine. Within the GI tract, diamine oxidase (DAO) is the primary enzyme for the digestion of histamine [9]. Due to the variability of symptoms observed in multiple organs, the diagnosis of histamine intolerance is generally difficult. Usually, the diagnosis of histamine intolerance is based on a diamine oxidase value <3 U/ml and can be assumed with a DAO <10 U/ml in serum. In the patient described here the diagnosis of this condition was a diamine oxidase value <10 U/ml and more than two GI symptoms belonging to histamine malabsorption [5].

Written information on lactose intolerance in case 1, and on fructose malabsorption and histamine intolerance in case 2, was handed out to the patients on the day of diagnosis. This information included patient-friendly knowledge on malabsorption/intolerance and a specific list of foods covering the symptom triggering carbohydrates and histamine. Lactose-free products have widespread availability for patient 1, but patient 2 with the combined malabsorption was advised to provide a detailed food protocol over the time period of two weeks before a conversation with a registered dietitian. The dietitian then developed an individually tailored diet for each patient. The result was that patient 1 was asymptomatic within three days and patient 2 had a very good improvement of symptoms within 10 days. The congenital lactase deficiency in patient 1 demonstrated the independent co-occurrence of lactose intolerance and β-thalassemia minor. Due to the improvement of GI symptoms with a diet free of triggering carbohydrates and histamine, we assumed that the complaints in both patients with usually asymptomatic β-thalassemia minor were caused by concomitant GI malabsorption/intolerance.

4. Conclusion

Nonspecific abdominal symptoms in these patients with β-thalassemia minor were due to carbohydrate
and histamine malabsorption, and were treated effectively with an individually tailored diet. Because of the increasing number of patients with β-thalassemia minor in Northern Alpine Europe we want to increase awareness on β-thalassemia minor and demonstrate that nonspecific GI complaints in β-thalassemia minor patients may be caused by GI malabsorption.

Disclosure statement

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