Stenosis due to inflammatory bowel disease in patient with glycogenosis Ib-therapeutical options

Tamara Alempiev\textsuperscript{1,2}, Ivan Jovanovic\textsuperscript{1,2}, Miodo Stulic\textsuperscript{2}, Danica Pejkovic Stamenkovic\textsuperscript{1}, Predrag Milic\textsuperscript{4}, Biljana Mili\textsuperscript{2}, Marijan Micev\textsuperscript{4}, Dragan Popovic\textsuperscript{1,2}, Srdjan Mijatovic\textsuperscript{2}, Slobodan Krstic\textsuperscript{1,3}, Aleksandar Karamarkovic\textsuperscript{1,2}

\textsuperscript{1}School of Medicine, University of Belgrade, Serbia
\textsuperscript{2}Clinical for Gastroenterology and Hepatology, Clinical Center of Serbia, Belgrade, Serbia
\textsuperscript{3}Clinic for Endocrinology and Metabolic disorders, Clinical Center of Serbia, Belgrade, Serbia
\textsuperscript{4}Clinic for Haematology, Clinical Center of Serbia, Belgrade, Serbia
\textsuperscript{5}Center for anaesthesiology and reanimation, Clinical Center of Serbia, Belgrade, Serbia
\textsuperscript{6}Department for pathology, Clinical Center of Serbia, Belgrade, Serbia
\textsuperscript{7}Clinic for Emergency Surgery, Clinical Center of Serbia, Belgrade, Serbia

CASE REPORT

A 28-years old female patient started her gastroenterological investigation because of prolonged diarrheal syndrome. In her early childhood she was diagnosed with glycogenosis type Ib, so she was regularly controlled by an endocrinologist and haematologist. Upper and lower endoscopy was performed because of prolonged diarrheal syndrome. The upper endoscopy revealed normal. By colonoscopy diffuse inflammation with ulceration were seen, with a relative stenosis in the ascending colon, and based on pathological examination inflammatory bowel disease- was diagnosed. Because of her underlying disease, immunosuppressive treatment was not introduced, and treatment was started with metronidazol for 10 days, aminosalicylates and probiotics. Initially, there was an adequate clinical and biochemical response, but after 6 months she was admitted in the Emergency room department because of profound vomiting, bloating, abdominal pain and absence of stool discharge. The laboratory values indicated inflammation with elevated white blood cells (to 5.9x10\textsuperscript{9}/L), normally around 2x10\textsuperscript{9}/L), platelets 509x10\textsuperscript{9}/L, sedimentatio rate 110mm/h, fibrinogen 8.07 g/L and CRP 25mg/L, as well as normocytic anaemia and hypertrygliceridaemia. On a plain abdominal X-ray image, hydroaeric levels were seen. After placement of a nasogastric tube and introduction of deep enemas, the symptoms resolved, but exploration of the digestive tract was planned again. The upper endoscopy revealed without pathological remarks, but the stenosis in the ascending colon exacerbate, and the lumen was about 5 mm diameter. The mucosa in this part of the colon was inflamed with ulcerations. In other parts of the colon were no signs of inflammation. This time, the pathologist diagnosed a pseudo-Crohn’s chronic colitis. Because of the

INTRODUCTION

Glycogenosis type Ib (GSD Ib) (McKusick 232220) due to glucose-6-phosphatetranslocase (G6PT1) deficiency results in fasting hypoglycaemia, hyperlactataemia, hyperlipidaemia and hyperuricemia. Poor metabolic control associated with intercurrent illness can cause impaired growth. Patients also have neutropenia and neutrophils from GSD-Ib patients have been shown to possess a variety of functional defects including variable degrees of neutropenia,1, chemotactic abnormalities\textsuperscript{2,3}, inability to elevate cytosolic free calcium\textsuperscript{4}, and abnormal glucose transport and utilization\textsuperscript{5}. That cause recurrent infections Crohn-like colitis is very rarely encountered in patients with GSD-Ib, and its occurrence is associated with longstanding low-grade bowel infection\textsuperscript{6}. Establishing a link between neutrophil abnormalities and the initiation and persistence of inflammatory bowel disease (IBD) could provide new insights into the pathogenesis and therapy for other forms of IBD, such as idiopathic CD.

The occurrence of inflammatory bowel disease in patients with glycogen storage disease Ib is rare (GSDIb). We present the case of a young woman with the diagnosis of GSD-Ib Crohn-like colitis developed at age 27. She was under regular medical control because of severe malnutrition, secondary amenorrhea, leukopenia, neutropenia, hyperlipidaemia, dysfunctions of phagocytosis, and a subtotal stenosis of the ascending colon. Several months after diagnosing Crohn-like colitis, symptoms and signs of ileus developed, and she was admitted in the Emergency room department. Baloon dilatation with local corticosteroid injection was used for treatment. Clinical status of the patient markedly improved after this intervention. As far as we know, no similar cases with this kind of treatment are published.

Key words: glycogen storage disease Ib, Crohn-like colitis, endoscopic baloon dilatation
underlying disease, there was no possibility for further step-up conservative approach, neither to surgical treatment. So, the decision was to perform a balloon dilatation, using a CRF balloon diameter 16mm, stepwise dilation up to 3 atm for 60s -90s. In the region of stenosis 20mg od metilprednisolone was injected. No complications were observed. Six months after this procedure, the patient reports no complaints, and the lower colonoscopy revealed a relative stenosis in the ascending colon, but the diameter of the lumen was around 20mm.

DISCUSSION

Our case patient was a 28-yr-old woman with the diagnosis of GSD-Ib, confirmed by physical and biochemical examinations. Our patient developed Crohn-like colitis about t the age of 27, confirming the hypothesis that long-lasting low-grade bowel infection, resulting from neutrophil deficiency, may predispose such patients to chronic inflammation\textsuperscript{9,10}. The severity of bowel inflammation and the degree of bowel stenosis resulted in marked catabolic state, manifested as a severe reduction in BMI, central hypothalamic hypofunction, and secondary amenorrhea.

The occurrence of Crohn-like colitis disease in patients with GSD-Ib is rare and mostly presented as case reports \textsuperscript{6,7}. The minimum incidence of GSD-1b in United States patients was 1 per 2.5 million births presented in 2002\textsuperscript{8}.

Crohn-like IBD is associated with primary neutrophil deficits, and, conversely, various disorders of the oxidative metabolism of neutrophils are linked to Crohn disease\textsuperscript{9,10}. These observations suggest that neutropenia and neutrophil dysfunction in patients with GSD-Ib predispose to the development of IBD\textsuperscript{11}. Visser et al.\textsuperscript{12} further demonstrated a variety of neutrophil functional defects in subset of their patients. A causal connection between neutropenia or neutrophil dysfunction and CD in these cases is further suggested by: (1) a lack of association between the GSD-1a and CD, (2) preliminary evidence that treatment with agents that stimulate qualitative and quantitative neutrophil function (G-CSF) may result in improvement or resolution of intestinal inflammation, and (3) the association between a CD phenotype and other diseases associated with qualitative and quantitative neutrophil dysfunction\textsuperscript{13}. Based on this indicated that G-CSF is indicated of treatment.

A North American survey revealed that G-CSF was generally well tolerated and was associated with decreased gastrointestinal disease activity\textsuperscript{5}. An unexpected finding in this study was the lack of individuals with IBD born after 1990. The mean age of diagnosis of patients with IBD was 8.7 years. Therefore, it can be expected several individuals to have already developed IBD in this cohort. This change may coincide with the availability of G-CSF in the United States in February 1991, which was widely applied to treat neutropenia associated with GSD-1b. These results suggest that G-CSF may prevent or delay expression of IBD in GSD-1b. One potential mechanism may have been the correction of neutropenia in G-CSF treated GSD-1b patients.

In case that this way of treatment fails or is unavailable, next step would be immunosupression and surgical treatment, and a a case report presenting this way of treatment was published \textsuperscript{14}.

In the literature we could not find further therapeutic measurements used. Despite lack of data, based on her medical history we decided to use endoscopic treatment, as a less invasive medical procedure. Tack ing into account positive effects of our therapeutic approach, we encourage introducing endoscopic treatment in this patients.

SAŽETAK


Ključne reči: glikogenoza Ib, Kronu sličan kolitis, endoskopska balon dilatacija
REFERENCES


