

Inflammatory bowel disease-like colitis in a young Turkish child with glycogen storage disease type 1b and elevated platelet count

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SUMMARY: Saltık-Temizel İN, Koçak N, Özen H, Yüce A, Gürakan F, Demir H. Inflammatory bowel disease-like colitis in a young Turkish child with glycogen storage disease type 1b and elevated platelet count. Turk J Pediatr 2005; 47: 180-182.

Inflammatory bowel disease (IBD)-like colitis is a known entity in glycogen storage disease (GSD) type 1b patients. The mean age of the reported cases with IBD-like colitis was 12 ± 5 years, and all had absolute neutrophil count (ANC) less than 1,000 cells/ μ l. We report a three-year-old girl with GSD type 1b that was diagnosed by mutation analysis. The patient was hospitalized with fever, diarrhea, and perioral and anal ulcers. Colonoscopy was performed and IBD-like colitis was diagnosed. The patient had elevated platelet count beyond the age of three months, but IBD-like colitis was diagnosed at three years of age. An elevated platelet count may be a warning sign for the IBD-like colitis in young patients with GSD type 1b.

Key words: glycogenosis, inflammatory bowel disease, neutropenia, platelet.

Inherited metabolic diseases, including glycogen storage disease (GSD), are frequently seen in Turkey due to the high consanguinity rate¹, but the distribution of various types of GSD is unknown. The frequency of type 1a in GSD presenting with hepatomegaly was determined as 45%², but the frequency of GSD type 1b is unknown in our country. GSD type 1b (MIM # 232220) is caused by the deficiency of the microsomal membrane translocase system for glucose-6-phosphate (G6P) in the liver³. Hypoglycemia, hepatomegaly, growth retardation, hyperlipidemia, hyperlactacidemia, and hyperuricemia are the common features of GSD type 1, while neutropenia and neutrophil dysfunction are specific to GSD type 1b³. Although the pathogenesis and the course of the neutropenia remain undefined, it was reported in 64% of cases before the age of one year. Most of the reported patients had intermittent neutropenia, but a clear cyclical pattern could not be defined⁴. Recently, the cloning and characterization of the GSD type 1b gene locus on chromosome 11q23 enabled the identification of the mutations⁵. In addition

to recurrent infections and perianal and/or perioral infections, inflammatory bowel disease (IBD)-like colitis has been occasionally reported^{4,6,7}. The mean age of the reported cases with IBD-like colitis was 12 ± 5 years (range 5 to 21), and all had absolute neutrophil count (ANC) less than 1,000 cells/ μ l^{6,7}. We report a three-year-old girl with GSD type 1 that was diagnosed by mutation analysis.

Case Report

A 36-month-old girl was hospitalized with fever, diarrhea, and perioral and anal ulcers. She was the first child of a consanguineous family and had been followed up with GSD since three months of age. Genetic analysis of G6P translocase gene revealed that she had a homozygous mutation (c.1211-2delCT) that confirmed the diagnosis of GSD type 1b. Despite frequent feedings and uncooked corn starch meals, she had been hospitalized five times with respiratory and urinary tract infections and metabolic decompensation. She had bilateral nephrocalcinosis on ultrasonographic examination, and angiotensin converting enzyme inhibitor (captopril) was administered to prevent renal

complications⁸. The results of complete blood count and blood smear at different times are shown in Table I. On last admission, the patient presented with multiple oral and perianal ulcers, fever and diarrhea. Physical examination revealed height of 93 cm (25 percentile) and weight of 13 kg (25 percentile), and liver was palpable 8 cm below the costal margin. ANC was normal (Table I). The C-reactive protein level was 56 mg/dl (normal 0-0.8). Stool culture was negative for pathogenic bacteria and stool contained occult blood. Immunologic tests including serum immunoglobulin levels, neutrophil chemotaxis, nitroblue tetrazolium (NBT) dye test for phagocytic function, T-cell subpopulations and CH₅₀ assay for complement defects were all normal. Colonoscopy was performed and showed only decreased vascularity. Histologic examination revealed non-specific colitis without granulomatous lesions. IBD-like colitis was diagnosed. Patient was treated with antibacterial agents and local supportive treatment for anal and oral ulcers. No improvement was observed, so per-oral steroid (1 mg/kg/day) and mesalazine were added to therapy. Within a three-month period, oral and perianal lesions improved and steroid dose was decreased and stopped. At 39 months of age, due to new oral ulcers, granulocyte colony-stimulating factor (G-CSF) (5 µ/day for 2 days) was administered. One month after G-CSF treatment, oral lesions resolved.

The mean age of the reported IBD-like colitis cases was 12 years and all had neutropenia⁶. If protracted diarrhea, perioral and perianal infections are considered to be early manifestations of IBD, the prevalence of the IBD-like colitis increases up to 77% in GSD type 1b patients⁴. In our patient, IBD-like colitis was diagnosed at the age of three years, earlier than the reported cases. The ANC of our patient was not detected below the 500/mm³ that is considered severe neutropenia. In fact, the measured ANC levels of our patient were normal except on one occasion. It may be due to the intermittent, fluctuating neutrophil counts that we could not detect severe neutropenia. Another important finding was the elevated platelet counts of our patient. Although platelet dysfunction is a known feature in GSD type 1³, there are few reported data on elevated platelet counts in patients with GSD type 1b^{9,10}. A platelet count of 740x10⁹/L was reported in a patient with Crohn's-like colitis and GSD type 1b⁹. Similarly, elevated platelet counts were reported in 14 of 17 patients with GSD type 1b¹⁰, but no cause or pathogenesis was discussed. An elevated platelet count is well recognized as a marker of IBD especially for Crohn's disease^{11,12}. It may be speculated that the elevated platelet counts in patients with GSD type 1b may be an early

Table I. Complete Blood Count and Blood Smear Results of the Patient at Different Admissions to Hospital

Age*	WBC	ANC	Platelets	Hg	ESR	Diagnosis	Acidosis	Glucose
3	3,300	891	718,000	9.4		Hypoglycemia	+	Low
4	16,400		758,000	10		Hypoglycemia	+	Low
6	13,200		556,000	10.4	33	Pneumonia	-	N
12	7,700	1,694	607,000	10.6		UTI	-	N
21	11,400	2,280	744,000	12.6		UTI	+	Low
22	18,500	13,320	593,000	12.3		UTI	+	Low
24	10,800	6,372	597,000	11.9		Pneumonia	-	N
27	9,300		840,000	9.7	70	Lymphadenitis	-	N
36	12,000	5,880	801,000	6.9	76	IBD-like colitis	-	N
39**	5,400	1,780	942,000	11		Oral ulcers	-	N

* month, **granulocyte colony-stimulating factor was administered, WBC: white blood cell count (/mm³), ANC: absolute neutrophil count (/mm³), Hg: hemoglobin (mg/dl), ESR: erythrocyte sedimentation rate (mm/hour), UTI: urinary tract infection, N: normal, IBD: inflammatory bowel disease.

Discussion

Neutropenia/neutrophil dysfunction in GSD type 1b seems to be a cause of IBD-like colitis and reported cases with neutropenia and history of recurrent infections have supported this suggestion. But the pathogenesis of IBD-like colitis in GSD type 1b patients is still unclear^{4,6}.

marker for IBD-like colitis, as in our case. The G-CSF therapy is efficacious in the management of neutropenia and neutrophil dysfunction associated with GSD type 1b¹³. Although the duration was short, treatment with G-CSF in our patient was also effective. In conclusion, our first patient with GSD type 1b and IBD-like

colitis was younger than the reported patients, and had no prominent neutropenia. She did have thrombocytosis, however which may be a warning sign for the IBD-like colitis in young GSD type 1b patients.

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