Microangiopathic Anemia without Thrombocytopenia and Kidney Disease in a Child with Diarrhea Caused by Shiga Toxin–Producing *Escherichia coli*

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A child with a history of diarrhea presented with transient anemia, reticolucytosis, and red blood cell fragmentation. Blood pressure and levels of blood platelets, creatinine, and urea were normal, as were results of urinalysis. *Escherichia coli* harboring genes for Shiga toxin were detected in stool specimens. It is concluded that extraintestinal diseases caused by Shiga toxin–producing bacteria sometimes present without any renal involvement.

Diarrheal diseases caused by Shiga toxin–producing *Escherichia coli* are sometimes complicated by the appearance of hemolytic uremic syndrome, a severe disease characterized by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and renal insufficiency [1]. Some patients, however, present with minimal extraintestinal disease, mostly mild kidney disease with minimal or no hematologic disturbances [2–5].

We describe a pediatric patient with hemolytic anemia and RBC fragmentation but without thrombocytopenia and acute kidney disease in the context of a diarrheal disease caused by non-O157:H7 *E. coli* harboring genes for Shiga toxin.

Case report. On 2 May 2003, a 14-month-old Swiss boy—the son of a stockbreeder—was referred because of the appearance of pallor. He had history of watery diarrhea for 4 days. Body weight was 9.32 kg, rectal body temperature was 37.5°C, blood pressure was 94/50 mm Hg, and heart rate was 146 beats/min. On examination he appeared mildly ill and pale. Other findings of the physical examination did not contribute to the diagnosis. Laboratory values were as follows: hemoglobin, 81 g/L (reference range, 100–150 g/L); RBC count, 2.98×10^{12} cells/L (reference range, 3.70×10^{12} cells/L to 5.30×10^{12} cells/L); reticulocyte count, 670×10^9 cells/L (reference range, 20×10^9 cells/L to 80×10^9 cells/L); platelets, 440×10^9 cells/L (reference range, 150×10^9 cells/L to 450×10^9 cells/L); WBC count, 15.4×10^9 cells/L (reference range, 3.0×10^9 cells/L to 12.5×10^9 cells/L); C-reactive protein, 3 mg/L (reference range, ≤5 mg/L); sodium, 139 mmol/L (reference range, 132–145 mmol/L); potassium, 5.1 mmol/L (reference range, 3.6–5.4 mmol/L); creatinine, 50 μmol/L (reference range, 25–67 μmol/L); urea, 5.3 mmol/L (reference range, 2.1–8.0 mmol/L); total bilirubin, 9 μmol/L (reference range, ≤22 μmol/L); lactate dehydrogenase, 1149 U/L (reference range, ≤850 U/L). A polyspecific direct Coombs test yielded a negative result. A blood film revealed a severe RBC fragmentation and a moderate polychromasia. Urinalysis failed to disclose pathological proteinuria, erythrocyturia, and pyuria on 3 occasions.

A stool specimen was processed as described elsewhere [6]. Diarrheagenic non-O157-H7 *E. coli* harboring genes for Shiga toxin types 1 and 2 were detected. In contrast, the gene encoding for intimin was not detected.

The subsequent acute course of disease was uneventful: the hemoglobin level decreased further (to 71 g/L) but spontaneously recovered, and plasma creatinine and urea levels were stable. At follow-up 6 weeks later, the child was healthy. The hemoglobin level was 112 g/L, the plasma creatinine level was 52 μmol/L, the urea level was 4.8 mmol/L, and results of urinalysis were normal.

Discussion. The demonstration of hemolytic anemia and RBC fragmentation in the son of a stockbreeder with a history of acute diarrhea suggests the possible diagnosis of hemolytic uremic syndrome. In our patient, however, thrombocytopenia and, more importantly, signs consistent with some renal involvement, including arterial hypertension, pathological urinalysis, and increased creatinine and urea levels, were not found, therefore excluding the diagnosis of hemolytic uremic syndrome.

The history of diarrhea, the stool culture result, the negative results of the direct Coombs test, and the benign, self-limiting course of the hematologic disturbances indicate that the acute disease noted in our patient was caused by a Shiga toxin–producing strain of *E. coli* [1]. Diarrheagenic strains of *E. coli* isolated in typical postdiarrheal hemolytic uremic syndrome mostly produce the gene encoding initimin, a pivotal virulence factor [1]. The failure to find this gene in our patient likely accounts, at least in part, for the very benign disease course.

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It is well recognized that Shiga toxin–producing strains of *E. coli* sometimes cause isolated anemia in the absence of thrombocytopenia and deterioration of renal function, as indicated by normal plasma and urea levels [3, 5]. However, in these patients, urinalysis discloses the features of a glomerulonephritic syndrome, including hematuria, RBC casts, and pathological proteinuria [3, 5]. In conclusion, we believe that this is the first report of microangiopathic anemia caused by Shiga toxin–producing *E. coli* in which there was no thrombocytopenia and, more importantly, no signs of renal involvement. This report is a reason to rethink the traditional explanation for hemolytic anemia—namely that the RBCs are fragmented as they pass through largely occluded, fibrin strand–filled glomerular vessels—and suggests the possibility that Shiga toxin may sometimes directly damage the RBC membrane [7].

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