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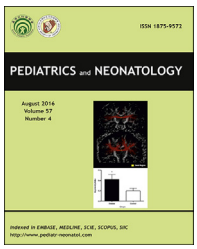

Letter to the Editor

Hypoplastic crisis in hereditary spherocytosis associated with Kawasaki disease

To the editor:

Hereditary spherocytosis (HS) is one of the most common congenital hemolytic anemias. Infections aggravate clinical and subclinical hemolysis in patients with HS. On the contrary, aplastic crisis (AC) occurs in patients with human parvovirus B19 (B19V) infection. No other specific causes of severe anemia have been recognized in patients with HS. Herein, we report severe anemia in a patient with HS during the course of acute Kawasaki disease (KD). The comparison of iron profiles and serum hepcidin levels in this patient between KD and B19V infection indicated that KD-associated severe anemia occurred as an episodic hypoplasia. This is the first report of KD-driven hypoplastic crisis in a patient with HS.

A 5-year-old boy with HS was admitted to our hospital because of a high-grade fever lasting 6 days and severe anemia without anti-B19V-IgM elevation (0.46 index). He presented with prolonged jaundice and anemia (minimum hemoglobin, 7.4 g/dL) at birth and was diagnosed with non-severe HS because of spherocytosis and undetectable haptoglobin without family history. Although active, he had 10—11.5 g/dL of hemoglobin concentrations, mild splenomegaly, and jaundice and did not require regular oral folic acid, iron, or red blood cell (RBC) transfusion. On day 9 of fever, he was diagnosed with KD due to fever, conjunctival injection, lip erythema, extremity changes, and slightly dilated coronary arteries. Intravenous immunoglobulin (IVIG) at 2 g/kg and oral administration of aspirin 30 mg/kg/day led to a prompt defervescence on the next day. Coronary artery lesions regressed within 1 month. Hemoglobin concentration showed a nadir of 6.6 g/dL on day 11 of KD, which gradually improved without RBC transfusion. Approximately 17 months after KD, he was re-admitted due to fever and severe anemia and was diagnosed with AC with anti-B19V-IgM elevation (11.47 index). He required an RBC transfusion on day 3 of AC.

Iron profiles monitored during KD were compared with those during AC (Fig. 1). Serum hepcidin-25 levels were measured using liquid chromatography/mass spectrometry (Medical Care Proteomics Biotechnology, Ishikawa, Japan). The reference range of serum hepcidin-25 levels in healthy adult controls was 7.8 $\pm$ 7.0 ng/mL.[1] His serum hepcidin level reached a maximum of 28.5 ng/mL on day 9 of KD and 162 ng/mL on day 3 of febrile AC in B19V infection. The serum hepcidin level peaked at the nadir of hemoglobin concentration and declined with improved symptoms.

Hepcidin is the key iron-regulating peptide synthesized and released by hepatocytes. Iron overload and interleukin (IL)-6 induce hepcidin secretion that suppresses iron metabolism and reduces hematopoiesis. Infection or non-infectious systemic inflammation raises serum IL-6 levels. Previous reports have shown that hemoglobin levels in patients with KD were 1.9 and 1.3 g/dL lower than those in healthy and febrile controls, respectively.[2,3] Considering the slight decline in reticulocyte counts and indirect bilirubin levels along with hepcidin-iron profiles, not hemolysis but suppressed hematopoiesis triggered by prolonged inflammation of KD was the main cause of severe anemia in this patient. Inflammation control with IVIG effectively reduced hepcidin levels, resulting in rapid anemia recovery. On the contrary, during AC, the iron burden from RBC transfusion and prolonged inflammation might lead to a more delayed reduction of serum hepcidin levels than during KD. This first reported case of KD-driven hypoplastic crisis in a patient with HS was less severe than B19V-induced AC, but the pathophysiology shared suppression of hepcidin-mediated iron metabolism.

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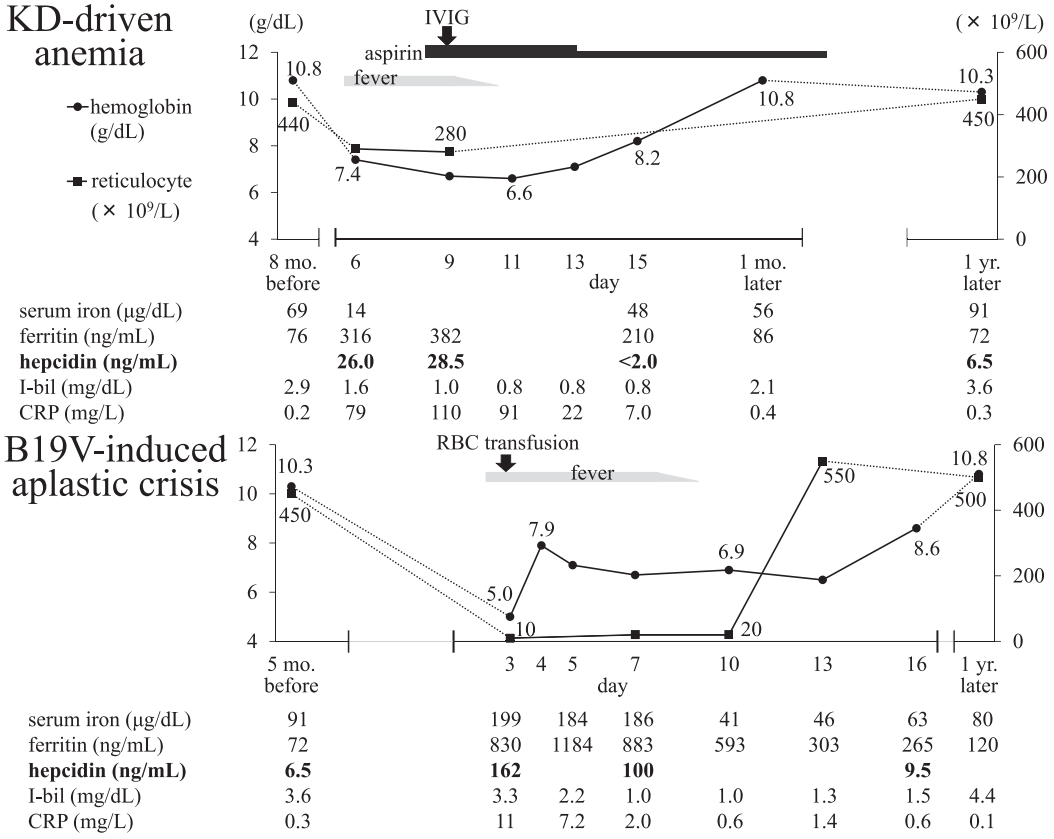

Figure 1 Clinical course and laboratory data during Kawasaki disease (KD) compared with that during an aplastic crisis (AC). Intravenous immunoglobulin (IVIG) at a dose of 2 g/kg and an initial dose of aspirin at 30 mg/kg/day were administered on day 9 of KD. The aspirin dose was reduced to 5 mg/kg/day from day 13 and stopped on day 50. The RBC transfusion was performed on day 3 of AC. The laboratory data was collected at the same time point 1 year after KD and 5 months before AC.
B19V, human parvovirus B19; CRP, C-reactive protein; I-bil, indirect bilirubin; IVIG, intravenous immunoglobulin; mo, month; RBC, red blood cell; yr, year.

Declaration of competing interest

The authors declare no conflicts of interest relevant to this article.

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