

# Hemolytic Crisis due to Parvovirus B19 in Hereditary Spherocytosis in Two Siblings

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#### ABSTRACT

Hemolytic anemia due to erythrocyte membrane disorder has an important place among hereditary anemia. Hereditary spherocytosis (HS) is one of the most common of them. It is an anemia which is apparent with the spherocyte-shaped erythrocytes and is usually dominantly inherited. Erythrocytes are quickly disintegrated on the periphery because of the membrane defect. Hemolytic, aplastic and megaloblastic crises are its major complications. Human Parvovirus B19 is a virus that can lead to different clinical pictures. It may lead to erythema infection in healthy children and to the aplastic crisis and severe anemia in patients with hemolytic anemia such as hereditary spherocytosis. In this article, two siblings who were diagnosed with hereditary spherocytosis as a result of severe hemolysis induced by the Parvovirus B19 infection are presented. Two brothers, one of them was 4 years old and another one was 5 years old, were brought with jaundice and weakness complaints beginning 3 days after a febril infection period. They had marked pallor, tachycardia, and splenomegaly in the physical examination. The hemoglobin level of one of them was 4.9 gr/dL, and another one's was 2.9 gr/dL. There was a large number of spherocytes in the peripheral smear. Parvovirus B19 Ig M was positive, and their osmotic fragility was increased. It was learned from their history that their father had splenomegaly. The aplastic crisis triggered by the parvovirus B19 infection and anemia due to severe hemolysis may occur as the first symptom of the hematological diseases such as hereditary spherocytosis. Attention should be paid to family history in the early diagnosis for the appropriate follow-up of children with hereditary spherocytosis which is frequently observed in our country, and hereditary spherocytosis should also be considered in the differential diagnosis of jaundice and anemia especially in the neonatal period. In addition, we wanted to remind that parvovirus B19 may lead to serious complications in the presence of hemolytic

Keywords: Anemia, hereditary spherocytosis, parvovirus B19

## INTRODUCTION

Hereditary spherocytosis, one of the most frequently observed hemolytic anemias in the population, usually displays autosomal dominant transmission. The main defect is erythrocyte membrane disorder, and cells display surface loss. Therefore, erythrocytes are spherocyte-shaped (1, 2). In these patients, hemolytic, aplastic, and megaloblastic crises may occur due to viral infections suppressing the bone marrow. Aplastic crises due to bone marrow suppression are rare. However, very severe anemia and serious complications can sometimes occur. The most frequent agent that causes aplastic crises by suppressing the bone marrow in hereditary spherocytosis is parvovirus B19 (3). Parvovirus B19 is the causative agent of erythema infectiosum. Erythema infectiosum is an infection associated with arthritis and arthralgia, intrauterine infection, and hydrops fetalis in healthy individuals, with temporary aplastic crises in cases with hemolytic disease and with chronic anemia in immunodeficient cases (4). Hereditary spherocytosis sometimes presents with signs such as jaundice and anemia in the neonatal period and thus enables early diagnosis, but it can sometimes progress asymptomatically (1). It can cause severe hemolysis if it accompanies parvovirus B19 infection. Here we present the cases of two brothers, aged 4 and 5 years, who developed severe anemia due to infection triggered by parvovirus B19 and were diagnosed with hereditary spherocytosis.

## CASE REPORTS

### Case 1

The 4-year-old male patient was admitted to the emergency service because of weakness and jaundice following 3 days of elevated fever. He was pale and tachycardic, and splenomegaly was detected. Measurement results were as follows: hemoglobin level: 4.8 g/dL, white blood cell count: 11,860/mm<sup>3</sup>, thrombocyte count: 258,000/mm<sup>3</sup>, and CRP level: 0.69 mg/L. Because viral infection was suspected, viral serology was requested, and microspherocyte cells were observed in his peripheral smear. Measurement results were as follows: MCHC: 37.5 g/dL, direct Coombs test: (-), haptoglobin level: 7.56 mg/dL, LDH level: 568 U/L, total bilirubin level: 1.59 mg/dL, and direct bilirubin level: 0.18 mg/ dL. His general condition improved after transfusion. His hemoglobin level increased to 8.0 g/dL, and his tachycardia remitted. Glucose-6-phosphate dehydrogenase and pyruvate kinase levels were normal. Epstein-Barr virus, cytomegalovirus, hepatitis B and C viruses, Salmonella, and Brucella were negative in his serological test results. Parvovirus B19 IgM level was 35.3 U/mL (normal

values 9–11 U/mL) and was positive. An increase in the patient's osmotic fragility test was detected, and his diagnosis was considered to be compatible with that of hereditary spherocytosis.

## Case 2

Two days after admitting the first case, his 5-year-old brother was brought as well due to weakness and jaundice following elevated fever. The patient looked pale and tachycardic, and splenomegaly was detected. His laboratory findings were as follows: hemoglobin level: 2.89 g/dL, white blood cell count: 12,730/mm<sup>3</sup>, thrombocyte count: 398,000/mm<sup>3</sup>, CRP level: 0.73 mg/L, MCHC: 35.44 g/dL, direct Coombs test: (–), haptoglobin level: 6.5 mg/dL, LDH level: 558 U/L, total bilirubin level: 4.05 mg/dL, and direct bilirubin level: 0.49 mg/dL. Microspherocytes were observed in his peripheral smear. Viral serology was requested. His parvovirus B19 IgM level was 53.2 U/mL. An increase in osmotic fragility was observed. The patient had tachycardia, and transfusion was performed. Clinical findings remitted following the transfusion.

Splenomegaly was noticed in the father, and there was occasional yellowing in the eyes in the history of patients, who are still followed up. Furthermore, it was discovered that both brothers had neonatal jaundice and anemia, but that they were not followed up.

## DISCUSSION

Clinical findings of hereditary spherocytosis can occur at any period, starting from the neonatal period. Clinical findings vary from asymptomatic carrier to severe hemolysis. In mild cases, early diagnosis may not be established if anemia is compensated by the bone marrow. The cases are sometimes diagnosed at an advanced age while being examined because of aplastic crisis due to infection, hemolytic crisis, and gallstones. Hemolytic crises during viral infections are frequently observed in patients younger than 6 years of age.

Hemolytic crises display signs of jaundice, splenomegaly, anemia, and temporary mild increase in reticulocytosis. Some of these patients can be in the recovery period of aplastic crisis and may require no medical treatment. Severe hemolytic crises are rare. Anemia, jaundice, vomiting, stomachache, and splenomegaly are common findings. These patients must be admitted and must undergo erythrocyte transfusion (5). The most frequent agent that, by suppressing the bone marrow, causes very severe anemia and serious complications is parvovirus B19. This virus particularly infects erythropoietic precursor cells and suppresses their growth (3). Neutropenia, thrombocytopenia, and sometimes, pancytopenia can develop, and distinct decreases in hematocrit and reticulocyte levels occur.

An increase in microspherocyte rates and osmotic fragility are observed (3, 6). Our patients had a history of anemia and jaundice in the neonatal period, but it was learned that they were not followed up. Hereditary spherocytosis was diagnosed with a hemolytic crisis triggered by parvovirus B19 infection. An apparent aplastic anemia was not detected, and the other series were normal, but there was a severe hemolytic anemia picture. The patients had apparent tachycardias, and they dramatically improved following erythrocyte transfusion. Our patients were unable to be diagnosed until the ages of 4 and 5 years because of the absence of follow up, despite having anemia and jaundice in the neonatal period and a familial history of splenomegaly and jaundice. The literature also reports a 12-year-old case that was diagnosed via aplastic crisis due to parvovirus B19 infection (7).

## CONCLUSION

Hereditary spherocytosis is commonly observed in Turkey, and paying attention to family histories in early diagnoses of children with hereditary spherocytosis is crucial for a proper follow-up. In particular, we wanted to emphasize, with the help of these cases, that this disease must be considered in the differential diagnoses of jaundice and anemia in the neonatal period and that parvovirus must be borne in mind when anemia and infection coexist.

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