***Case Report* / Olgu Sunumu**

Pregnancy-associated Aplastic Anemia: Case Report

Gebelikle İlişkili Bir Aplastik Anemi Olgusu

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Aplastic anemia in pregnancy is a rare condition with high maternal morbidity and mortality rates. Intensive hematological support during antenatal course remains the mainstay of the therapy. A successful obstetric outcome can be best accomplished with the clinical collaboration of the obstetrician and the hematologist. We present a patient with moderately severe aplastic anemia who was managed with intensive hematological support given repeatedly once in a month during pregnancy. She delivered a healthy infant by cesarean section.

Key words: Aplastic anemia; pregnancy.

Gebelikte aplastik anemi yüksek mortalite ve morbidite oranlarına sahip ender bir durumdur. Tedavinin temelini gebelik süresi boyunca uygulanan yoğun hematolojik destek oluşturmaktadır. Başarılı bir obstetrik sonuç en iyi şekilde obstetrisyen ve hematoloğun klinik işbirliği ile gerçekleştirilebilir. Bu yazıda orta ciddi aplastik anemisi olup, gebeliği süresince ayda bir kez tekrarlanan yoğun hematolojik destekle tedavi edilen bir hasta sunulmaktadır. Hasta sezaryen ile sağlıklı bir çocuk doğurmuştur.

Anahtar sözcükler: Aplastik anemi; gebelik.

Aplastic anemia (AA) is a serious, rare hematological disorder seen during the course of a normal pregnancy.[1] It is characterized by diminished numbers of hematopoietic precursor cells in the bone marrow. Stem cell failure can be either congenital or acquired. Pregnancy, as a possible cause of aplasia, has been suggested on the basis that an imbalance between levels of erythropoietin and placental lactogen can lead to suppression of hematopoiesis.[2] Despite its rarity, it is important to know how to recognize and treat this condition. The mother can have life-threatening episodes of bleeding and infections. The fetus is at risk because maternal anemia can lead to intrauterine growth retardation and intrauterine abortions or death. Also, an infection in the mother can cause chorioamnionitis leading to preterm delivery. The mortality in AA associated with pregnancy is more than 20% and fetal complications are up to 60% of cases.[3,4] The pregnancy is continued with intensive hematological support given repeatedly during pregnancy. Androgens, glucocorticoids, antilymphocytic or antithymocyte globulin and cyclosporin are the other treatment options available to restore hematopoiesis.[5-8]

Here, we present a patient with moderately severe aplastic anemia who was managed with intensive hematological support given repeatedly once in a month during pregnancy. She delivered a healthy infant by cesarean section.

CASE REPORT

A 31-year-old woman, with a 21-week period of gestation, was referred to our outpatient clinics for antenatal care. Her last menstrual period had occurred about six months before. She had gravida 4, para 3 with one living

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sibling. On obstetrics history, we learned that she was diagnosed as AA about five years before during her first pregnancy. Urine hemosiderin was negative and serum bilirubin, LDH, and ALT were normal. Both parvovirus B19 IgG and IgM were negative. Her bone marrow aspiration was hypocellular, consistent with aplastic anemia. She was treated with glucocorticoids, antilymphocytic and antithymocyte globulin. She showed regression after vaginal delivery at 27 weeks of the first pregnancy, a premature male baby was delivered following spontaneous onset of labor. After two years, the patient delivered vaginally at 31 weeks. She developed postpartum hemorrhage, severe anemia (Hb 5.5 g/ dl), and received two units of blood. The neonate expired on the tenth day due to prematurity.

During this pregnancy, her follow-ups were normal, regarding blood pressure examinations, maternal weight gain and repeated ultrasonographic evaluation of fetal growth. Severe pallor was observed with no lymphadenopathy or organomegaly. First visit investigations showed Hb 5.6 g/dl, total leukocyte count (TLC) $4.2x10^9$/l and platelet count was $54x10^9$/l, and reticulocyte count was 0.7%. Bone marrow aspiration was performed in which the cellularity was <25% with depression of all cell lineages. Supportive therapy in the form of packed red blood cells (pRBC) and random donor platelets (RDP) were given to keep Hb above 8 g/dl and platelet counts above $100x10^9$/l. She received five units of pRBC, 18 units of RDP during her antenatal period. Amniocentesis was performed for bad obstetrics history and demonstrated a male fetus with normal karyotype.

The patient was admitted to our clinics because of premature rupture of the membranes in her 32nd week of gestation. Her laboratory investigations revealed a urinary tract infection which was tought to induce preterm labor. Appropriate antibiotherapy was started. Fetal heart monitoring showed a variable deceleration that cesarean section was performed immediately. A male infant weighing 1870 g was born, with Apgar scores of 6 at 1 min. and 8 at 5 min. Cord blood gases, which is a routine procedure done to confirm the newborn's wellbeing, were normal. The premature newborn was admitted to the neonatal intensive care unit because of his age and weight. Apart from a transient event of hypoglycaemia, which was effectively treated with i.v. glucose, and phototherapy due to indirect hyperbilirubinemia, the newborn was otherwise healthy with normal platelet counts and with no congenital malformation.

During labor and in the postpartum period, she received two units of pRBC and two units of RDP transfusion. She had no fever or infection. Hematological recovery was seen four weeks after delivery.

DISCUSSION

Aplastic anemia is a life-threatening hematological disorder characterized by absent or markedly diminished hematopoietic precursors in the bone marrow resulting in the deficiency of circulating erythrocytes, granulocytes and platelets. Pregnancy-associated aplastic anemia is known to be a serous disorder, with a reported maternal mortality of 20% to 60% which is mainly due to hemorrhage and sepsis.[2]

The occurrence of aplastic anemia in pregnancy has been long recognized but its rarity has made it difficult to establish the relationship between the two conditions and the optimal management.[4] Pre-existing AA associated with pregnancy has a better prognosis as compared to when it occurs during pregnancy.[9] There is no conclusive evidence to implicate pregnancy as an etiological factor for AA. Pregnancy, as a possible cause of aplasia, has been suggested on the basis that an imbalance between levels of erythropoietin and placental lactogen can lead to suppression of hematopoiesis. Some authors feel that it is the pre-existing AA that worsens and becomes overt due to the stress of pregnancy. Others have supported the association of pregnancy with aplastic anemia by the fact that it can relapse in subsequent pregnancies and it resolves with pregnancy termination.[2] However, whatever may be the etiological factor, pregnancy seems to have a detrimental effect on the disease process as it either worsens or becomes overt during pregnancy, as it happened with our patient reported here. Termination of pregnancy is usually advised in severe aplastic anemia. Moreover, only in one third of patients, aplastic anemia resolves following abortion or delivery.[9]

Pregnancy outcome has also been reported to be unsatisfactory. A summary of the published reports showed a preterm birth rate of 12.1%, an intrauterine death rate of 16.7%, a stillbirth rate of 15.1%, and a spontaneous abortion rate of 16.7%; while only 39.4% of patients had uncomplicated pregnancies.[9]

In general, treatment for aplastic anemia includes withdrawal from offending drugs, supportive care, and some form of definitive therapy as bone marrow transplantation has been reported to be the most effective treatment. In our case, the pregnancy was continued with intensive hematological support given repeatedly during pregnancy. New antibiotic agents and advances in transfusion medicine have led to improvements in supportive management for this disease. Androgens, glucocorticoids, antilymphocytic or antithymocyte globulin and cyclosporin are the other treatment options available to restore hematopoiesis.[2] Infection is a major complication in aplastic anemia and our patient had a urinary tract infection which was tought to induce preterm labor. Appropriate antibiotherapy was started immediately. Besides, caesarean section posed a major risk for infection. In retrospect, antibiotic prophylaxis could have been instituted at the onset of labor in view of neutropenia in aplastic anemia. The risk of infection continues to increase in puerperium.[1] Our patient also received antibiotics in the postoperative period.

Although these recent results are in favor of supportive management, large studies are needed to determine the best prenatal strategy.

As shown in the obstetrics history of our patient, the fetus is at risk because maternal anemia can lead to intrauterine growth retardation and intrauterine abortions or death. On the other hand, infection in the mother can cause chorioamnionitis leading to preterm delivery.

Human parvovirus B19 causes several symptoms, including erythema infectiosum, chronic arthritis in adults, aplastic crisis in patients with hemolytic anemia, fetal death and chronic anemia and neutropenia in immunosuppressed patients.[10] Without known exposure, about 1% to 3% of susceptible pregnant women will develop serologic evidence of infection in pregnancy. Pregnant women exposed to, or who develop symptoms of, parvovirus B19 infection should be assessed to determine if they are susceptible to infection (nonimmune) or if they have a current infection, by determining their parvovirus B19 IgG and IgM status. [11,12] If both parvovirus B19 IgG and IgM are negative (and the incubation period has passed), the woman is not immune and has not developed the infection.

In conclusion, pregnant women with aplastic anemia are at high risk. The severity of the disease and choice of the patient have to be considered before treatment. Gestational age and severity of the disease are the key factors in deciding the management protocol in a patient with AA associated with pregnancy. Termination is advised if the patient comes early in pregnancy. For patients who come late or are unwilling for termination, intensive supportive treatment is the mainstay of the treatment.[9] Multidisciplinary effort of obstetricians and hematologists can lead to successful pregnancy outcome in selected patients as presented in our case.

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