Aplastic Anemia and Pregnancy: Case Report

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Abstract

Background: The prevalence of aplastic anemia following pregnancy is rare. Pregnancy associated with aplastic anemia is fortunately more uncommon considering the significant morbidity and mortality for both mother and fetus. The risk to the mother is mainly in the form of hemorrhage and sepsis, while the fetus may suffer from growth restriction and even intrauterine death.

Case: We here present you a case of pregnancy complicated by aplastic anemia diagnosed at early gestational weeks.

Conclusion: While the relationship between pregnancy and aplastic anemia remains controversial, there is universal agreement that a pregnancy complicated by aplastic anemia is a serious condition.

Keywords: Aplastic anemia, pregnancy, treatment.

Introduction

Aplastic anemia was first recognized in a pregnant woman by Ehrlich in 1888. Since then, the pathogenesis of aplastic anemia has remained elusive. The prevalence of aplastic anemia following pregnancy is rare. Aplastic anemia is a subtype of anemia characterized by a decreased number of circulating erythrocytes, thrombocytes and neutrophils and a hypocellular bone marrow. This situation can be due to chemicals, drugs, infections, irradiation, leukemia and inherited disorders. The treatment involves immunosuppressive therapy with antithymocyte globulin and cyclosporine and bone marrow transplantation. The observation has been made that pregnancy results in an increase in the synthesis of placental lactogen, erythropoietin and estrogens. Placental lactogen and erythropoietin stimulate the hematopoiesis whereas estrogens suppress the marrow. Based upon these observations, Fleming suggested that the imbalance between
these three hormones might cause hypoplasia. While the relationship between pregnancy and aplastic anemia remains controversial there is universal agreement that a pregnancy complicated by aplastic anemia is a serious condition. The risk to the mother is mainly in the form of hemorrhage and sepsis, while the fetus may suffer from growth restriction and even intrauterine death. Hemorrhage and sepsis are responsible for more than 90% of maternal mortality. Most of the fetal complications are due to maternal anemia. Maternal anemia may end up with fetal intrauterine growth restriction and mortality in the fetuses of mothers with aplastic anemia. All along with these, maternal infections may lead to the development of chorioamnionitis and the resultant preterm labor and birth. In the literature, fetal thrombocytopenia, placentomegaly and severe oligohydramnios have been reported. An interesting case of gangrene of the fetal intestine was reported in one case, perhaps due to chronic anemia and ischemia. We here present you a case of pregnancy complicated by aplastic anemia diagnosed at the early gestational weeks.

Case

A 21 year-old woman was diagnosed to be pregnant at 6 weeks of gestation. When she had the symptoms of spontaneous bruising, drowsiness, epistaxis and bleeding from the gingiva, a complete blood count has been performed. The analysis revealed a hemoglobin (Hgb) level of 11 gr/dl, white blood cell count (WBC) of 2300 e3/uL and platelet count of 16000 e3/uL and reticulocyte 0.2. She did not have any past medical history and other laboratory values were normal. When she was referred to hematology department, a bone marrow biopsy was taken from the iliac crest. The bone marrow biopsy was suggesting aplastic anemia, due to severely decreased cellularity. When the test dose of anti-thymocyte globulin (ATG) (1 mg of ATG in 100 cc saline), which binds to the receptors on the cell surfaces of the circulating erythrocytes and which is used in the dose of 150mg/10kg every 12-18 hours for 5 days for the treatment of aplastic anemia, was given, an allergic reaction had occurred. Then, cyclosporin 5mg/kg/day (a total dose of 300mg) had been started. This dose was continued till birth. The control blood counting was performed for every 3 months. The values were about Hgb:11 gr/dl, WBC: 3200-3500 and platelet: 60000, and reticulocyte 0.4. And the symptoms were regressed. The maternal and fetal complications and risks related to aplastic anemia in pregnancy was explained to the patient and her family. And they preferred to continue the pregnancy. During the pregnancy the complete blood count was performed monthly. She had no symptoms of bruising, bleeding from gingiva or nose, drowsiness, feeling tired, any infection or obstetrical hemorrhage. She was admitted to the hospital at 36 weeks of gestation for the uterine contractions. There was no bleeding or amniotic fluid leakage and her vital signs and fetal monitoring were normal. There was irregular contractions. At the cervical examination, there was 1 cm of dilatation and 40% of effacement. After the initiation of tocolytic therapy, the uterine contractions regressed and the cervical examination remained the same. The blood count values were of Hgb: 8.4gr/dl WBC: 3000 and platelet: 32000 and reticulocyte 0.6. The coagulation screen, kidney and liver function tests were normal. Obstetric, anesthetic and haematology teams planned an elective cesarean section under general anaesthesia at the advanced gestational weeks. At 38 weeks and 5 days of gestation, elective cesarean section procedure had been done under general anesthesia, upon patient's desire at this time the blood count values were of Hb: 8.2 gr/dl, WBC: 2800, PLT: 40000, reticulocyte 0.7. No transfu-
sion were needed perioperatively. A healthy female baby of 2800 gr and 48 cm was delivered with apgar scores of 9/10. The immunosuppressive therapy with cyclosporin 5mg/kg/day was continued after the delivery.

Discussion

Aplastic anemia is a serious hematological disorder characterized by pancytopenia, bone marrow hypocellularity, and absence of underlying malignant or myeloproliferative disease. As Oosterkamp concluded from his work that some substance released during pregnancy had toxic affects on bone marrow, he suggested that termination of pregnancy should be considered for management of aplastic anemia during pregnancy. Aplastic anemia is known to increase the antenatal complications. In a literature review, the ratio of preterm birth was 12.1%, the ratio of intrauterine death was 16.7%, the ratio of stillbirth was 15.1% and the ratio of spontaneous miscarriage was 16.7% among pregnant women with the diagnosis of aplastic anemia. Although previously cited complications are commonly encountered in cases of aplastic anemia, no such complications accompanied our case. Hemorrhage at the time of delivery-abortion is another danger. Secondary hemorrhage due to platelet deficiency is fortunately uncommon in aplastic anemia as compared to clotting factor deficiencies. Postpartum hemorrhage is an important complication among patients with the diagnosis of aplastic anemia due to decreased platelet count and impaired function. One patient among 7 in the series of Deka and 2 patients among 10 in the series of Coudhry had postpartum hemorrhage which were appropriately handled by thrombocyte and erythrocyte transfusions. In our case, postpartum hemorrhage was within normal limits and no supportive treatment was needed. Fetal morbidity and mortality in terms of intrauterine growth restriction and even intrauterine death has also been reported owing to the impaired fetal oxygenation. Intrauterine growth retardation did not complicate our case. In this case, a cesarean section was performed at 38 gestational weeks and female baby of 2800 grams (10-50 percentile) with an apgar score of 9/10 was born. No postpartum complications with the baby occurred. Way of delivery in cases of aplastic anemia is obscure once the literature is reviewed. But, usually, vaginal birth is preferred and cesarean section is performed only for obstetric indications. In our case, cesarean section was performed electively, upon patient's desire. In general, treatment for aplastic anemia includes withdrawal from offending drugs, supportive care, and some form of definitive therapy. Bone marrow transplantation (BMT) has been reported to be the most effective treatment, with a 5-year survival of 56 to 89%. However, BMT is contraindicated during pregnancy because it requires high-doses of immunosuppressive agents or radiation therapy, which would be toxic to the fetus. Although case reports have suggested a promising result with antithymocyte immunoglobulin or cyclosporine therapy during pregnancy, there is currently little agreement on the universal use of these therapies. The role of androgens is not clear and androgen treatment may cause the virilization of female fetuses. The efficacy of corticosteroids or granulocyte colony-stimulating factor is also equivocal. Overall, current evidence does not favor the routine use of any drug therapy in the treatment of pregnancy-associated aplastic anemia. Earlier case reports have proposed pregnancy termination as an alternative approach. Based on their experience of 5 cases, Aitchison and colleagues proposed to consider early termination followed by BMT for women with severe aplastic anemia diagnosed in the first trimester of pregnancy. Cyclosporine has been found to have results comparable to ATG when
used as first line therapy in non-pregnant patients. Cyclosporine (300 mg/day) and granulocyte macrophage colony stimulating factor (450 mg intravenous weekly) are used in severe aplastic anemia after 20 weeks of pregnancy.\(^1\) Data regarding its use in pregnancy with aplastic anemia is limited. However, experience from pregnancy following organ transplant shows that cyclosporine is apparently not teratogenic. Though it is excreted in milk, fetal growth and development were found to be normal.\(^9\) Perhaps the most important part of treatment of aplastic anemia is supportive therapy. Supportive therapy in the form of blood and platelet transfusions was given in order to keep hemoglobin above 8 g/dL and platelet count above 20x10^10/\(_*_\) L. Repeated blood transfusions should ensure that maternal hemoglobin is maintained at more than 8 g/dL during pregnancy to achieve adequate fetal oxygenation.\(^10\) Similar tests and treatment modalities were employed in our case once the diagnosis was confirmed by bone marrow aspiration. As the patient had a positive anti-thymocyte globuline (ATG) test, cyclosporine treatment was initiated (5 mg/kg/day; a total dose of 300 mg). After regression of the symptoms, the patient was followed up till term with complete blood counts performed every 3 months. Aplastic anemia is a rare complication of pregnancy. Pregnancies complicated by intrauterine growth retardation, preterm labor, stillbirth and spontaneous abortion can be successfully followed till term if appropriate diagnostic tests and treatment modalities are employed. In our case, we had successful maternal and fetal outcomes by the immunosuppressive therapy with the help of anaesthesia and haematology teams.

References