Pregnancy Complicated by Aplastic Anemia

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A case of a 27-year-old Bahraini female, pregnant for the first time and was not known to have any medical illness presented with pancytopenia. She had an uneventful pregnancy up to 17 weeks when she was referred from local health center with an incidental finding of pancytopenia. She received a total of 32 units of platelets and 3 units of packed red blood cells. Bone marrow biopsy revealed severe hypoplastic bone marrow without infiltrates, and a diagnosis of severe aplastic anemia was confirmed.

The pregnancy was terminated by cesarean section at 29 weeks of gestation. The patient remained stable during surgery and postoperatively while the preterm newborn was transferred to the neonatal intensive care unit for optimal care. The pancytopenia persisted post-partum, and the patient is currently being followed up.

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Aplastic anemia is peripheral blood pancytopenia (anemia, leukopenia and thrombocytopenia) associated with unexplained hypocellularity of the bone marrow and deficiency of hematopoietic stem cells[1]. Numerous case reports of pregnancy associated with aplastic anemia have been reported. The management along with the prognosis of such cases remains controversial[1,2]. The disease has an estimated incidence of 2-4 per million with a higher incidence in Asia 4-6 per million. It could be either congenital or, much more often, acquired. The most common congenital cause is Fanconi anemia while idiopathic aplastic anemia is the most common form of acquired aplastic anemia.

The major causes of morbidity and mortality from aplastic anemia include sepsis and bleeding, particularly intracranial hemorrhage[1]. Aplastic anemia has occasionally occurred in pregnancy; the first case of aplastic anemia described in literature occurred in a pregnant woman in 1888[2]. However, it is uncertain whether or not pregnancy is causally related to the development of aplastic anemia and the management along with the prognosis of such cases remains controversial[1,2].

The aim of this presentation is to report a case of a young female whose pregnancy was complicated by Aplastic anemia.

THE CASE

A primigravida 27-year-old Bahraini female was not known to have any medical illness. She had right breast fibroadenoma which was excised in 2008. She was using folic acid and multivitamin supplements during pregnancy. No significant family history was revealed.

At 17 weeks of gestation, she had an incidental finding of pancytopenia during the regular check-up (WBC $1.38x10^9$/L, Neutrophils $0.07x10^9$/L, Hematocrit 19%, Hemoglobin 6.7g/dl, Mean Cell Volume 84.4 fl; Reticulocyte count 0.33%, Platelets count $8x10^9$/L). She had a one-month history of fatigability, dyspnea on exertion, palpitations, dizziness, as well as the positive history of self-remitting mild fever with a sore throat. Clinical examination was unremarkable, and there were no signs of lymphadenopathy, hepatosplenomegaly or hemorrhagic manifestations. Coagulation profile, liver function test (LFT) and renal function test (RFT) were within normal range. The patient was transfused with 12 units of platelets and 1 unit of packed red blood cells (PRBCs).

In addition, the patient received 32 units of platelets and 3 units of PRBCs to maintain the platelet counts at $>10x10^9$/L if there was no bleeding, $>20x10^9$/L if accompanied with fever, $>50x10^9$/L if there was active bleeding and Hemoglobin was to be maintained at >10g/dl. Bone marrow biopsy revealed severe hypoplastic bone marrow without infiltrates and a diagnosis of severe aplastic anemia was affirmed. Obstetric ultrasounds were normal, confirming a single alive fetus.

Cyclosporine and prednisolone were given. At more than 27 weeks of gestation, the patient was admitted complaining of fever and sore throat while her platelet count was 11x10^9/L and WBC 1.6x 10^9/L. The patient was started on intravenous antibiotics and transfused 6 units of platelets, upon which, her condition improved. In view of the persistent pancytopenia, the frequent platelet and packed red blood cell transfusions and the reported cases that there could be a possible remission following termination of pregnancy, a decision was made in agreement with a neonatologist to terminate the pregnancy by elective cesarean section at 29 weeks of gestation.

The patient was transfused 6 units of platelets the night before surgery, 6 units the morning of surgery and 6 units post-surgery with two units of packed red blood cells. Lower Segment

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Cesarean Section under general anesthesia was performed on 7 September 2014. The estimated blood loss was 900ml. A single alive female neonate of 1.370kg birth weight with Apgar score of 3, 6 and 9 was delivered. The preterm was transfered to NICU. The patient was discharged seven days postoperatively with no resolution of pancytopenia (WBC 2.3x10^9/L, Hb 9.9 g/dl, platelet count 13x10^9/L). The patient received a course of intravenous antithymocyte globulin (ATG) on 15 March 2015. The patient was advised to avoid subsequent pregnancy by using appropriate contraception methods until complete remission is achieved.

The newborn was discharged from hospital on 20 October 2014 at 43 days of age, in good health. Latest growth parameters are in line with normal age percentiles; the newborn's weight was 7 kg, length was 61cm and head circumference was 42 cm at 7 months of age.

DISCUSSION

Management of aplastic anemia complicating pregnancy remains controversial with no clear guidelines. While some authors have recommended termination in early pregnancy, others believe there is no difference in the prognosis between those undergoing early termination and those continuing the pregnancy[3,4]. In addition, in previous case reports, some patients experienced spontaneous resolution after delivery while others had persistent pancytopenia and died of complications during pregnancy or post-partum[3-6].

Our patient had very severe aplastic anemia according to the criteria of the International Aplastic Anemia Study Group, with platelet count <20x10^9/L, anemia with reticulocyte count <1% and absolute neutrophil count <0.2x10^9/L[3,7]. According to Shin et al, platelet count should serve as the main risk factor in evaluation of the severity of aplastic anemia in pregnancy; our patient had persistently low platelet counts despite continuous supportive measures and platelet transfusions[4].

For severe aplastic anemia, bone marrow transplantation from HLA matched donor is the treatment of choice in patients aged ≤60 years, with survival rates of 70% to 90%[2,4]. However, during pregnancy, bone marrow transplantation is contraindicated because of potential embryo toxicity. Supportive measures in the form of platelet and packed red blood cells transfusion is needed with prednisolone and cyclosporine[2,4,5]. Based on recent case reports and as suggested by Shin et al, continuation of the pregnancy, rather than early termination, is recommended[2,4-7]. However, our patient had large number of transfusions by 27 weeks of gestation and since bone marrow transplant (BMT) is the recommended treatment post-delivery, having more transfusions would run the risk of BMT failure, due to the risk of transfusion refractoriness and developing HLA antibodies[2,4,5]. Although pregnancy in women after bone marrow transplantation is less likely in comparison to patients who only received immunosuppressive treatment, multiple successful pregnancies have been reported following bone marrow transplantation. A report by the Center for International Blood and Marrow Transplant Research revealed 178 pregnancies of patients transplanted between 2002 and 2007, 85% of these pregnancies ended in live birth with most pregnancies occurring 5-10 years post-transplant. Patients should be counseled prior to transplant regarding strategies to preserve fertility[3,8-11].

The patient was advised to avoid subsequent pregnancy until complete remission is achieved. It is agreed that females whose disease is in remission before conception with normal platelet counts are more likely than those with persistent cytopenias to have an uneventful pregnancy[3,4,8].

CONCLUSION

We report a case of pregnancy complicated by aplastic anemia which was successfully managed with supportive care and immunosuppressive therapy up to delivery by elective caesarean section at 29 weeks of gestation. Aplastic anemia is potentially life-threatening disease and poses great challenge to the team of treating obstetricians and hematologists. Recently, it has been made possible to manage a patient with severe aplastic anemia and severe thrombocytopenia through pregnancy up to delivery.

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