

# Aplastic Anemia Associated with Pregnancy

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Aplastic anemia is not an uncommon disorder. Estimated frequency is 3-6 per million populations per year<sup>1,2</sup>. Occurrence of aplastic anemia however, concurrently with pregnancy in a previously healthy woman is a rare phenomenon. Since 1888 when it was first described not more than a handful of cases have been reported in literature<sup>3</sup>. Pregnancy associated with marrow aplasia poses great problems for the hematologist as well as the obstetrician as the management of such a case challenges the skill of both in deciding the best option for the patient. We report a case of a young woman whose pregnancy was complicated by Aplastic anemia.

## Case Report

A 21-year-old, 16 weeks pregnant primigravida presented in February, 1992, with a few weeks history of bleeding gums, epistaxis, easy fatigability and low-grade fever. We did not know of her pre-pregnant state of health or blood counts but the patient claimed herself to be symptom less. Patient had already received three units of packed cells and one unit of platelet concentrates when first seen. There was no history of intake of any medicines or exposure to either toxins or chemicals. Pertinent physical findings included generalized pallor, severe anemia and petechiae of lower limbs. Her preliminary routine lab tests were as follows: Hemoglobin: 4.8 g/dl, red cell count:  $1.45 \times 10^{12}/l$ , hematocrit: 5.4%, MCV 106.2 fl, MCH:33.1 pg, MCHC: 31.2g/dl, reticulocyte count was 0.8%, platelet count:  $23 \times 10^9/l$ , total leukocyte count was  $1.0 \times 10^9/l$ , differential of white cell count was not possible. Erythrocyte sedimentation rate was 147 mm 1st hour. Serum B12 and folate were 299.3 pg/ml and 1.8 ng/ml respectively. Serum iron was 149 ug/ml and total iron binding capacity 629 ng/ml. Liver function tests, serum electrolytes, stool and urine examination had no abnormal findings. There were no red cells in urine or occult blood loss in stool.

Bone marrow aspirated from sternum was very hypocellular with general depression of erythroid and myeloid cells. No megakaryocytes were seen. A bone marrow trephine was not performed as the patient refused permission for the procedure.

Clinical and laboratory data supported the diagnosis of aplastic anemia. The case was fully discussed with her obstetrician considering the various possibilities for managing this patient. The patient and her husband were also informed of the disease, its severity and options for treatment and their consequences.

The final decision was the continuation of her pregnancy with maintenance of her hemoglobin above 10 gm/dl with packed red cells transfusion and treatment of infection or bleeding episode if any such occurred. More intensive treatment of the aplastic anemia was the only option left if her condition deteriorated. This was fully explained to the patient and her spouse. However, the patient did well on supportive therapy and such a need did not arise.

Her more persistent complaints were mild gingival bleeding and epistaxis. Only twice did she have more severe episodes of epistaxis and hemoptysis, which were promptly controlled with tranexamic acid. The only infections encountered during pregnancy were vaginal candidiasis effectively treated with Clotrimazole pessaries and giardial diarrhea, treated with oral Metronidazole.

She received a total of 6 units of packed cells at variable interval during her antenatal period to maintain the target hemoglobin.

At 37 week of gestation, she went into spontaneous labor. She received 3 units of packed cells and 6 units of platelets during her delivery. Postpartum bleeding was about 200 ml. Her labor was completed within five hours. She gave birth to a live male infant weighing 2.5 kg with apgar score of 8 and 9. Immediately after delivery her hemoglobin was 10.6 gm/dl, platelets  $60 \times 10^9/l$ , total leukocyte count  $4.0 \times 10^9/l$  and absolute neutrophil count of  $1.2 \times 10^9/l$ . Further 2 units of platelets were transfused on each three successive days following delivery. During seven days of her hospital stay, her prothrombin time and activated partial thromboplastin time were within normal limits and her blood counts remained satisfactory. She had an essentially uneventful postpartum course. New born was normal physically and his blood counts were within neonatal limits.

The patient was followed up closely after delivery. Her marrow examination, five months later, showed islands of cells comprising normoblasts and granulocytes with occasional megakaryocytes, while plasma cells were marginally elevated thus heralding recovery of aplastic anemia.

This patient has now been followed for a period of over six years. She is clinically well with normal blood counts. A bone marrow trephine done recently showed normocellular marrow with normal hemopoetic cells.

## Discussion

Paul Ehrlich first described aplastic anemia as a clinical entity in 1888<sup>3</sup>. Incidentally his patient was a young pregnant woman, aged 21, who died within a month of diagnosis due to intra uterine hemorrhage. Many of the cases reported around this time are difficult to evaluate because of the paucity of investigations and diagnostic criteria. Hence the number of such proven cases is very low.

The relation between the two conditions is still unclear. Some of the earlier workers found no conclusive evidence to suggest the pregnancy as a cause of aplastic anemia<sup>3,4</sup>. The fact has been revised recently in a study of 35 pregnant patients with newly diagnosed aplastic anemia, which showed no strong correlation between the two-conditions<sup>5</sup>. However, others had jointly supported the idea of pregnancy being somehow involved in genesis of disease<sup>6,7</sup>. The two conditions seem to be interlinked as the disorder begins and ends with pregnancy. Moreover, if the disease pre-exists then it worsens during pregnancy<sup>8,9</sup> and relapses are seen in subsequent pregnancies<sup>10,11</sup>. It could be interpreted that association between pregnancy and aplastic anemia is more than coincidental. It is very likely that an occasional and susceptible patient reacts abnormally to a physiological phenomenon and develops marrow aplasia.

To further support the association between the bone marrow aplasia and pregnancy, it has been observed that in none of the patients described so far, aplasia resolved during pregnancy. Many confirmed the fact that remission of aplastic anemia was related to evacuation of uterus<sup>6,7,11</sup>. However, cases reported in earlier part of the century showed no such favourable effect with termination of gestation and patients subsequently died without evidence of recovery<sup>12</sup>. This was perhaps related to the absence of proper management.

The guidelines for treating the condition have not been established due to the rarity of the problem. However, an attempt for doing so was done repeatedly in the past and would be done in future too. Aitchison et al in 1989 considered termination of pregnancy for patients with severe aplastic anemia if they present in first trimester and suggested the same for patients who have non-severe but deteriorating aplastic anemia<sup>13</sup>.

The improved survival seen in last few years with the termination of pregnancy is related to availability of better blood transfusion services, more effective antibiotics as well as HLA typed platelets and granulocytes that have added greatly to optimize treatment of these patients.

Anti lymphocyte globulin were used in only three of the patients described by Aitchison et al in 1989<sup>13</sup>;

two of whom received it after delivery and remission was seen in only one. The third patient received it during pregnancy and died few months later without recovery. On the basis of limited experience, the therapy should be cautiously used if at all.

Bone marrow transplantation though highly successful in treatment of aplastic anemia<sup>14</sup>, cannot be performed during pregnancy, as pre-transplant immunosuppressive therapy would be too toxic for the developing fetus.

The use of steroids and intravenous immunoglobulins has been described in very few pregnant patients with aplasia but their result seem to be promising<sup>15,16</sup>. Immunosuppressive agents like cyclosporine cannot be used in pregnant patients because of their teratogenic effects.

The hemopoetic growth factors like granulocyte macrophage colony stimulating factors (GM-CSF) and interleukin (IL-3) have been tried in patients with aplastic anemia having some residual bone marrow function<sup>17,18</sup>. Some transient rise in leukocyte count was observed. However, till more reports on their use, effectiveness and adverse effects are available, growth factors cannot be recommended to treat aplastic anemia during pregnancy.

From the evidence available today, it appears that pregnancy does play a role in causing aplastic anemia in an occasional otherwise susceptible patient. Termination of pregnancy produces favorable effect in terms of remission and survival, which should be the option of choice in early gestation with severe aplasia. The patient with less cumbersome disease can be managed with supportive care alone till term. Immunosuppressive therapy and bone marrow transplantation is not advisable till patient has delivered. The hemopoetic growth factors cannot be recommended unless more reports on its use in non-pregnant patients become available.

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