Sri Lankan Journal of Anaesthesiology **17(2) :** 75 – 79 (2009)

CASE REPORTS

THE SUCCESSFUL MANAGEMENT OF A PREGNANT MOTHER WITH SEVERE APLASTIC ANAEMIA

***Dr. S. Varathan.*[1]*, *Dr. G. H. K. K. Gunawardena*[2], *Dr. D. Vithanawasam*[3]**

[1] Senior Lecturer, [3] Temporary Lecturer, Department of Anaesthesiology, Faculty of Medicine, University of Peradeniya, Sri Lanka. [2] Senior Consultant Obstetrician and Gynaecologist, Teaching Hospital, Peradeniya, Sri Lanka.

**Corresponding authorl: varathansr@yahoo.co.uk*

Key words: pancytopenia, aplastic anaemia, caesarean section

Aplastic anaemia is a rare haematological disease in pregnancy, which carries a major risk of materno-fetal morbidity and mortality. Though there is no information regarding the prevalence of this disease in pregnancy, it has been reported that the incidence is 0.6 – 6.1 per million population in the USA[1]. This disease is characterised by pancytopenia and hypocellular bone marrow with impaired morphology and maturation. In addition, the peripheral blood pictures demonstrate cytopaenias resulting from ineffective blood cell production. A few cases of severe disease form has been described in pregnancy and in a majority the outcome had been unsuccessful.

Pregnancy can be one of the causes of this disease and in some instances the severity spontaneously reduces after delivery. Causes of death due to this disease include haemorrhage and / or infection secondary to thrombocytopenia and neutropenia especially following surgery. Haemorrhage is the major complication in pregnant mothers after caesarian section, which may lead to death. Here, we report a successful caesarean section performed by the combined effort of Anaesthetists, obstetricians, and haematologists, on a pregnant mother with severe aplastic anaemia.

Case Report

A 28 year old mother in her second pregnancy was admitted to hospital at 26 weeks period of amenorrhoea (POA) for investigation of anaemia. Aplastic anaemia was suggested as the tentative diagnosis based on haematological investigations. Laboratory analysis revealed; leukocyte count 1.5 X 10^9/L, Haemoglobin(Hb) 6.9g/dl, haematocrit 21%, platelet count 29X10^9/L. In addition to the above mentioned haematological investigations, the blood picture showed pancytopenia and bone marrow biopsy was compatible with hypoplastic marrow.

Lower Segment Caesarean Section (LSCS) was scheduled at 34 week of gestation as the platelet counts did not improve with repeated transfusion of platelet concentrate. In the ward, the patient received 10 mg vit K intramuscularly, oral prednisolone 5mg, oral haematinics and oral cephalosporins daily. Cyclosporine 150mg was administered for 7 days as the platelet counts did not reach the desired level (i.e. above 50x10^9/L). A day prior to surgery, haematological investigations revealed that the Hb concentration of 8.8g/dl and platelet count of 12x10^9/L. She was transfused with 8 units of platelet concentrates on the day prior to surgery and 6 units on the following day morning before surgery.

Patient was kept fasting overnight on the day prior to surgery.

Elective LSCS and ligation and resection of tubes (LRT) were performed under general anaesthesia. Anaesthesia was induced with 300 mg of

thiopentone sodium and tracheal intubation was facilitated with 100mg of suxamethonium. Thereafter, anaesthesia was maintained with nitrous oxide-oxygen. A boy infant weighing 1995g was delivered with good Apgar scores.
10 units of platelets were transfused during surgery and the recovery period.

Following surgery, the patient was sent to the intensive care unit (ICU) for further management. She was paralyzed and ventilated for 24 hours in order to maintain the basic parameters as severe bleeding was expected. Early feeding was initiated via nasogastric tube which was inserted 6 hours after surgery. Naso gastric (NG) feeds were stopped as she was able to take oral feeds. Since the patient was continuing to have low platelet counts, 20 units of platelet concentrate were transfused. Prophylactic antibiotics were started with oral Co-amoxyclav 1.2g, 8 hourly and i.v. metranidazole 500mg 8 hourly. The daily fluid requirement was maintained at 110ml/hr with 0.45% normal saline and patient had a satisfactory urine output.

Six hours after surgery, the patient became restless and arterial pressure dropped significantly. Per-vaginal bleeding was confirmed on speculum examination. After rapid i.v. infusion of 1 pint normal saline and 1 unit packed cells, her arterial pressure reached previous values. Thereafter, the patient was transfused with 6 units of platelet concentrate. Patient was extubated after 24 hours and she was closely observed in the ICU for further bleeding while monitoring the basic parameters.

The patient was extubated on the second post operative day and patient was discharged from the ICU on the third post operative day. Cyclosporine 150 mg was started according to the instruction given by the haematologist as the platelet counts were still below 50 $x10^9$/L. Since the patient recovered with no further complications, she was discharged from the hospital on the 10^{th} post operative day. Her platelet counts had reached the desired levels on discharge. The patient was followed up in the obstetric clinic for a period of six months to ensure she had an adequate haematological profile after discharge from the hospital.

Table 1
Haematological profile at presentation and at time of delivery

	On Admission	Day Prior to Surgery	Day of Surgery
WBC	$3.7x10^9$	$3.2 x10^9$	$4 x10^9$
Hb(g/dl)	5.1	8.6	8.8
PCV	14%	27%	24%
Platelets	$29 x10^9$	$12 x10^9$	$65 x10^9$

Table 2
Haematological profile during the immediate post-partum period

	Day 1 ICU	Day 2 ICU	Day 3 ICU	Day 1 ward	Day 2 ward	Prior Discharge
WBC	$2.9 x10^9$	$3.8 x10^9$	$5 x10^9$	$6.6 x10^9$	$4.2 x10^9$	$4.1 x10^9$
Hb(g/dl)	8.5	8.4	7	8	8.6	9.7
PCV	23%	23%	21%	21%	24%	28%
Platelets	$9 x10^9$	$25 x10^9$	$18 x10^9$	$25 x10^9$	$32 x10^9$	**$52 x10^9$**

Table 3
Blood investigations during the perioperative period

	Day prior to Surgery	Day 1 ICU	Day 1 ward	Prior Discharge
Serum Creatinine			60	46
Blood Urea(mmol/L)	1.3	2.9	4.8	5
Serum Na (mmol/L)	134	130	146	139
Serum K (mmol/L)	5.7	4.1	5.1	4.6

Discussion
Aplastic anaemia is a serious haematological disorder which results from marrow failure due to defects in the microenvironment or damage to the stem cells. This disorder is characterised by pancytopenia and bone marrow hypocellularity with the absence of haematopoietic elements, showing largely fat cells[2, 3]. The immune mediation has been postulated as the most probable underlying factor for this disease[2]. The causes of this disease can be broadly divided as acquired and inherited; however, more than 80% of the cases are acquired. Pregnancy has been identified as one of the acquired causes and

responds to immunesuppressive therapy which is the treatment of choice in other acquired conditions as well. Though variable degrees of ineffective anaemia and thrombocytopenia is always present in the peripheral blood, the severe form of this disease is defined as pancytopenia with at least 2 of the following criteria which includes: an absolute neutrophil count of $<0.5x10^9$/L, a platelet count of $<20x10^9$/L and anaemia with reticulocytes <1%, in association with either a bone marrow cellularity of <25% or a bone marrow cellularity of <50% but with <30% haemopoietic cells[3]. According to the above criteria, our patient would fit into the severe form of this disease.

This disease appears unexpectedly in pregnancy, hence whether pregnancy is an aetiological factor for this disease or not remains controversial. Pregnancy appears to have a close link with this disease as many reports indicate improvement of blood counts with the termination of pregnancy. It has been proven that high doses of oestrogen can inhibit haematopeiesis and a similar pathogenesis has been put forward in pregnant mothers[4, 5]. In addition, hormonal mechanism causing this disease is supported by the fact that in a few patients, the termination of pregnancy caused haematological recovery whereas subsequent pregnancies precipitated relapse[6, 7]. However, there are reports to indicate that pre existing aplastic anaemia is also known to worsen during pregnancy.

A doubt exists whether aplastic anaemia is a consequence of pregnancy or not and the question of termination of pregnancy is yet to be justified. However, considering the above facts, termination of pregnancy in the severe form of disease can be recommended[6]. Since the maternal mortality has been reported to be 20-60%, the decision to terminate should be collectively taken by the obstetrician, anaesthetist and haematologist in order to save the patient from this grave illness[8]. Furthermore, it has also been suggested that the maternal survival rate was better in pregnant mothers who had pre- existing aplastic anaemia prior to conception when identified during the course of pregnancy[9]. The maternal and fetal outcome was predicted to be poor as this disease had been diagnosed during pregnancy and the intensity of the disease was severe according to the criteria. Therefore, termination was decided collectively by the obstetricians, anesthesiologist and haematologist to ensure a better outcome.

In the absence of obstetric complications, vaginal delivery would be the route of choice in these patients, as there would be no surgical incision if episiotomy was avoided with proper obstetric management. During vaginal delivery, incisional damage to many layers as in Caesarean section is avoided, minimizing the risk of bleeding. This also leaves the uterine myometrium intact ensuring physiological contraction after delivery and thus, reducing atonic and secondary post partum haemorrhage. In addition, as these patients are more prone to infections, the risk of sepsis would be minimal in vaginal delivery compared to caesarean section. However, a decision was taken for an elective caesarean section in our patient, as the previous baby had also been delivered by caesarean section due to obstructed labour. There was a strong possibility of an emergency caesarian section that could take place if the patient was allowed for a vaginal delivery. It could be rather difficult to optimize the patient, within a short time frame, if an emergency caesarean section was decided upon. Hence, a decision was made for an elective caesarean section with the consent of the patient.

Though bone marrow transplant is widely accepted in the treatment of aplastic anaemia, it is contraindicated in pregnancy as it provokes the use of high doses of immunosuppressive drugs in order to prevent graft-versus-marrow-reaction. Furthermore, the use of anti thymocyte (ATG) [10] or anti lymphocyte globulin was found to be safe only in a few previous reports. However, there is an associated risk of thrombocytopenia with these drugs; therefore, platelet transfusion should be administerd. Furthermore, the use of cyclosporine was found to have results comparable to ATG in pregnant mothers[11]. A few reports demonstrated the safe use of cyclosporine in pregnant mothers who underwent organ transplant[12]. Though it is excreted in milk, fetal growth and development was found to be normal[13]. Granulocyte – colony stimulating factor (G-CSF) was used in order to combat neutropenia

in a few patients, provided there are some residual progenitors. However, unwarranted effect was shown by the use of this drug in some studies[14]. Thus, cyclosporine was administered with the platelet transfusion throughout the pregnancy and during the postpartum period.

General anaesthesia was preferred over regional anaesthesia, as we could not achieve a steady platelet count of >100 $x10^9$/L. Furthermore, it is easier to manage severe blood loss when a patient is anaesthetized and well oxygenated. Though there is a risk of uterine bleeding with the use of inhalational agents, there has been no significant increase in bleeding with the use of deep anaesthesia (<0.5MAC) [15], in practice. Generally, it is accepted that all inhalational agents as well as nitrous oxide have immunosuppressive properties[16]. But there is no clinical evidence to suggest these agents should be avoided in a patient with aplastic anaemia or any other haematological disorder. For a major surgery, a platelet count of >$50x10^9$/L is optimal[17]. This optimal level of platelet count was achieved in our patient, by transfusing platelet concentrates prophylactically prior to the surgery.

It is imperative to provide adequate supportive therapy during the post operative period. Repeated blood transfusions to ensure adequate maternal Hb of >8g/dl and the platelet count of >$20x10^9$/L by performing repeated platelet transfusions is recommended[18]. However there is a risk of cross immunization associated with repeated platelet transfusions. Therefore, HLA matched platelets are preferred.

We maintained Hb of more than 8 g/dl and platelet count of more than 20 $x10^9$/L by performing repeated blood and platelet transfusions. Infection was prevented by the use of antibiotics and barrier nursing. The use of white blood cell transfusion was not needed since our patient did not develop severe infection.

Conclusion

Aplastic anaemia in pregnancy is a life threatening condition both to the mother and the fetus.The outcome of the pregnancy depends on supportive therapy aiming to achieve an adequate platelet count and heamoglobin concentration and taking precautions against infection. The mode of delivery of the fetus and the anaesthetic technique, if operative delivery is chosen, should be decided individually for each patient in order to ensure favorable maternal and fetal outcome. These aspects can be achieved by the collective decisions taken by the obstetricians, heamatologists and anaesthetists.

Acknowledgement

We acknowledge the patient and the staff attached to Departments of Haematology, Obstetrics and the ICU Teaching Hospital, Peradeniya, Sri Lanka.

References

1. Bakhshi S, Abella E. Aplastic Anaemia. emedicine 2008.Available at: http://emedicine.medscape.com/article/201722-followup
2. Young N S, Rodrigo T, Scheinberg C, Scheinberg P. Current concepts in the pathophysiology and treatment of aplastic anemia. Blood 2006; 108(8):2509-2519.
3. Camitta B M, Storb R, Thomas E D. Aplastic anaemia: Pathogenesis, diagnosis treatment and prognosis. N Eng J Med 1982; 306:645-652.
4. Oosterkamp H M, Brand A, Kluin- Nelemans J C, Vanderbrouke J P, Pregnancy and severe aplastic anaemia: Causal relation or coincidence? Br J Haematol 1998; 103:315-316.
5. Fleming A F. Hypoplastic anaemia in pregnancy.Clin Haematol 1973; 2:477-496.
6. Aitchison R G M ,March JCW,Hows JM,Russel NH,Gordon-Smith EC. Pregnancy associated aplastic anaemia:A report of five case and review of current management . Br J Haematol, 1989; 73:541-545.
7. Maaita M. and Telfah A. Successful outcome of pregnancy in a case of aplastic anaemia in Jordan. Eastern Mediterranean Health J2004; 10(3): 445 – 8
8. Bourantas K, Makrydymas G,Georgiou I, Repousis P, Lolis D. Aplastic anaemia .Report of a case with recurrent episodes in consecutive pregnancies . J Reprod Med, 1997; 42; 672-674.
9. Pavithran K, Thomas M. Pregnancy associated aplastic anaemia. J Assoc Physicians India 1996; 4:273.
10. Bacigalupo A, Howis J, Glukman E et al.Bone marrow transplantation (BMT) versus immunosuppression for the treatment of severe aplastic anaemia(SAA):A report of the EBMT SAA working party. Br J Haematol 1988; 70:177-182.

11. Gluckmann E, Espero-Bourdeau H, Baruchel A et al.Multicenter randomized study comparing cyclosporine A alone and antithymocyte globuline with prednilolone for treatment of severe aplastic anaemia.Blood 1992;79:2540-2546.
12. Bar-Oz B, Hackman R, Einarson T, Koren G, Pregnany outcome after cyclosporine therapy during pregnany:A meta-analysis. Transplantation 2001; 71:1051-1055.
13. Nyberg G. Haljamae U, Frisenette-Fich C, Wennergren M, Kjelimer l.Breast feeding during treatment with cyclosporine. Transplantation 1998; 65:253-255.
14. Ohba T, Yoshimura T, Araki M et al.Aplastic Anaemia in pregnancy :Treatment with cyclosporine and granulocyte –colony stimulating factor. Acta Obset Gynecol Scand 1999; 78:458-459.
15. Yildiz K, Dogru K, Dalgic H et al. Inhibitory effects of desflurane and sevoflurane on oxytocin-induced contractions of isolated pregnant human myometrium. Acta Anesthesiol Scand 2005; 49(9):1355-9.
16. Schneemilch C E, Hachenberg T, Ansorge S, et al. Effects of different anaesthetic agents on immune cell function in vitro. Eur J Anaesthesiol. 2005; 22(8):616-23.
17. Thiagarajan P. Platelet Disorders: Follow-up. emedicine 2006. Available at: http://emedicine.medscape.com/article/201722-followup.
18. Guideline: Guidelines for the use of platelet transfusion. Br J Haematol. 2003; 122: 10-23.

****

THE COLLEGE OF ANAESTHESIOLOGISTS OF SRI LANKA

FREE PAPERS :

The rules of the competition are:

1. Open to all medical practitioners in anaesthesia.
2. Duration of the presentation must be no longer than 15 minutes.
3. The work in whole or in part should not have been presented or published elsewhere.
4. An abstract of not more than 200 words should be submitted before the closing date.
5. The first right of publication of the entries submitted lies with the editor of the College of Aanesthesiologists of Sri Lanka.
6. The decision of the panel of judges in all matters relating to the competition including questions relating to eligibility shall be final.
7. The prize will not be awarded if the judges decide the presentation is not up to standard.

The closing date for the 2010 competition is **31st October 2009**. The abstract should reach the College before the closing date. 3 copies of the full text should be submitted on or before **31st October 2009** to the anaesthetic office.