Obstetric Forum

Anaesthetic management of Caesarean section in a patient with Myelodysplastic Syndrome

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Purpose: This case report describes the anaesthetic management for Caesarean section in a patient with myelodysplastic syndrome.

Clinical features: A woman with myelodysplastic syndrome underwent Caesarean section on two occasions. The first Caesarean section was performed at age 20 yr using general anaesthesia with nitrous oxide-oxygen and fentanyl. In her second pregnancy at 25 yr, there was severe pancytopenia at 28-wk gestation with a leukocyte count $3.6 \times 10^9 \text{ L}^{-1}$, erythrocyte count $1.2 \times 10^{12} \text{ L}^{-1}$, haemoglobin 50 g L^{-1} , haematocrit 14.7% and platelet count $51 \times 10^9 \text{ L}^{-1}$. Following leukocyte poor red cells and platelet transfusion, general anaesthesia was maintained with nitrous oxide-oxygen-sevoflurane and fentanyl. Both operations were uneventful and healthy infants were delivered.

Conclusion: It is important to have a team approach (anaesthetist, obstetrician and haematologist) for the peri-anaesthetic management of patients with myelodysplastic syndrome. An exact assessment of the haematological condition, the need for prophylactic treatment and anaesthetic management should be determined for each individual patient.

Objectif : Rapporter la prise en charge anesthésique pour césarienne d'une patiente présentant un syndrome myélodysplasique.

Éléments cliniques : Une patiente présentant un syndrome myélodysplasique a subi deux césariennes. La première, à l'âge de 20 ans, fut réalisée sous anesthésie générale avec N_2O - oxygène et fentanyl. La seconde grossesse, à l'âge de 25 ans, s'est compliquée d'une pancytopenie sévère à 28 semaines de gestation : les leucocytes étaient à $3,6 \times 10^9 \text{ L}^{-1}$, les érythrocytes à $1,2 \times 10^{12} \text{ L}^{-1}$, le taux d'hémoglobine à 50 g L^{-1} , l'hématocrite à 14,7% et les plaquettes à $51 \times 10^9 \text{ L}^{-1}$. Suite à des transfusions d'érythrocytes déleucocytés et de plaquettes, une césarienne fut réalisée sous anesthésie générale avec N_2O - oxygène, sevoflurane et fentanyl. Les deux interventions se sont déroulées sans problème et des nouveaux-nés en bonne santé sont nés.

Conclusion : Il est important d'avoir une approche d'équipe multidisciplinaire (anesthésiste, obstétricien, hématologiste) pour la prise en charge périanesthésique de patients avec syndrome myélodysplasique. Une évaluation précise de la condition hématologique, la nécessité de traitements prophylactiques et le choix de la technique anesthésique doivent être adaptés à chaque patient.

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Accepted for publication November 9, 1997.

MYELODYSPLASTIC syndrome (MDS) is a haematological disorder, characterised by cytopenia in the peripheral blood and normo- or hypercellularity in the bone marrow with morphological dysplastic change.¹ Causes of death in these patients are haemorrhage and/or infection secondary to thrombocytopenia and leukopenia.² When these patients require surgery, haemorrhage and infection are critical risks which determine their postoperative outcome. The anaesthetic management, including preoperative care, is important in preventing or minimising these complications. Haemorrhage is also a major complication of Caesarean section, very occasionally causing death.³ There have been few reports of anaesthesia for patients undergoing Caesarean section, since MDS is a rare disease in young people.^{1,4} We describe a case of MDS in which general anaesthesia was successfully employed for Caesarean section on two separate occasions without severe haemorrhage. No haematological exacerbation was noted following either procedure.

Case report

The patient developed mild anaemia at age 16 yr and was admitted to hospital for evaluation. Haemolytic anaemia was suggested as a tentative diagnosis based on a decreased haptoglobin concentration, increased serum LDH, and an increased number of reticulocytes. However, the diagnosis was not confirmed at that time as she refused further testing and treatment for the anaemia. When the patient became pregnant at age 20, the cytopenia was exacerbated. Laboratory studies at 18-wk gestation revealed a leukocyte count of $2.8 \times 10^9 \cdot L^{-1}$, erythrocyte count $1.74 \times 10^{12} \cdot L^{-1}$, haemoglobin 71 g·L⁻¹, haematocrit 21.2%, platelet count $71 \times 10^9 \cdot L^{-1}$. The diagnosis of myelodysplastic syndrome was made based on cytopenia in the peripheral blood, hypercellular bone marrow, and chromosomal abnormality. Caesarean section was scheduled at 38-wk gestation. Preoperative haematological investigations included leukocyte count $6.2 \times 10^9 \cdot L^{-1}$, erythrocyte count $2.17 \times 10^{12} \cdot L^{-1}$, haemoglobin 80 g·L⁻¹, haemat-

ocrit 24.7%, platelet count $81 \times 10^9 \cdot L^{-1}$. Atropine sulphate 0.5 mg was administered one hour preoperatively. Anaesthesia was induced with 200 mg thiamylal and tracheal intubation was facilitated with 70 mg succinylcholine. Anaesthesia was maintained with nitrous oxide-oxygen. A female infant, weighing 2534 g was delivered with an Apgar score of 9. Intravenous fentanyl was administered after delivery. The duration of surgery was 45 min, and there was no unusual bleeding. The estimated blood loss (including amniotic fluid) was 510 ml and blood transfusion was not required during the perioperative period. On the seventh postoperative day, her leukocyte count was $3.2 \times 10^9 \cdot L^{-1}$, erythrocyte count $2.13 \times 10^{12} \cdot L^{-1}$, haemoglobin 80 g·L⁻¹, haematocrit 24.6%, platelet count $99 \times 10^9 \cdot L^{-1}$. The patient recovered without complication and was discharged on the 11th postoperative day.

In her second pregnancy at age 25 the pancytopenia was more severe. At 28-wk gestation she was admitted complaining of massive vaginal bleeding. Laboratory studies showed a leukocyte count of $3.6 \times 10^9 \cdot L^{-1}$, erythrocyte count $1.2 \times 10^{12} \cdot L^{-1}$, haemoglobin 50 g·L⁻¹, haematocrit 14.7%, platelet count $51 \times 10^9 \cdot L^{-1}$. Cervical bleeding was confirmed by speculum examination. It stopped with direct compression and she was transfused with 800 ml leukocyte poor red blood cells. She was discharged 11 days later and a Caesarean section was scheduled at 38-wk gestation. Preoperatively her haemoglobin was 66 g·L⁻¹ and platelet count $40 \times 10^9 \cdot L^{-1}$, and she was transfused with 800 ml leukocyte poor red cells and 10 units of platelets. Anaesthesia was induced with 200 mg thiamylal and tracheal intubation was facilitated with 60 mg succinylcholine. Anaesthesia was maintained with nitrous oxide-oxygen until a normal female infant was delivered, weight 2556 g, Apgar 9 and then sevoflurane 0.5% and intravenous fentanyl were administered. The duration of surgery was 70 min and the intraoperative blood loss 1520 ml (including amniotic fluid). Ten units of platelets were given intraoperatively, and 400 ml leukocyte poor red cells postoperatively (see Table below). The patient recovered uneventfully and was discharged 14 days postpartum.

TABLE Blood cell counts and blood transfusions which were performed during the perioperative period for the 2nd Caesarean section

Pre-anaesthesia		Anaesthesia induction		POD ₀	POD ₁	POD ₂
WBC $\times 10^9 \cdot L^{-1}$	3.8	4.2		5.1	3.4	4100
RBC $\times 10^{12} \cdot L^{-1}$	1.6	2.48	caesarean section	2.16	2.33	2.53
Haemoglobin g·L ⁻¹	66	95	blood loss 1520 ml	81	79	91
Haematocrit (%)	19.1	27.2	PC 10 units	23.7	24.1	26.8
Platelets $\times 10^9 \cdot L^{-1}$	40	63		70	61	59

WBC: white blood cell, RBC: red blood cell, LRPC: leukocyte poor red cells, PC: platelet concentrate, POD: postoperative day

Discussion

Myelodysplastic syndrome refers to a heterogeneous group of primary haematological disorders, which result from neoplastic transformation at the level of the pluripotent stem cell. This produces a variable degree of ineffective haematopoiesis and cytopenia (anaemia, thrombocytopenia) is always present in the peripheral blood. The outcome of patients with MDS is dependent on the underlying haematological condition. Some patients remain symptom-free for many years and have prolonged survival, whereas others develop leukaemia or die as a result of infection and/or haemorrhage.^{1,2}

In non-MDS women, haemorrhage is a potential complication of Caesarean section and a leading cause of death.³ In pregnant women with MDS it is an even greater risk and haemostasis is important as they often have a bleeding tendency, secondary to thrombocytopenia. In fact, intracranial or pulmonary haemorrhage has been reported in non-surgical cases.^{1,2} Case reports of MDS in pregnancy are few. There is a report in which severe pancytopenia occurred during pregnancy but improved post partum.⁵ In another report, MDS presented during pregnancy and there was a poor prognosis.⁶ These reports suggest a possible adverse relationship between pregnancy and MDS. As severe haemorrhage may decrease platelets, further exaggerating haemorrhage, it is important to prevent bleeding in these patients and to optimise their condition preoperatively through prophylactic transfusion and preparation of sufficient blood products. If haemorrhage occurs, blood transfusion and measures to promote haemostasis must be performed promptly. In previous reports, vaginal delivery was chosen for patients with a normal platelet count and Caesarean section with transfusion for those patients with a low platelet count.^{5,6} In our case, the obstetrician, haematologist and anaesthetist discussed her management before surgery and decided on Caesarean section. If bleeding occurs during vaginal delivery it may be massive and difficult to control with an immediate need for blood products. In contrast, with elective Caesarean section it is possible to control the preoperative condition and to have sufficient blood products available.

In surgical patients with thrombocytopenia, platelet transfusion is indicated when the platelet count is below $50 \times 10^9 \text{ L}^{-1}$ and may be recommended when the platelet count is between $50 \times 10^9 \text{ L}^{-1}$ and $100 \times 10^9 \text{ L}^{-1}$.⁷ Abnormal platelet function may contribute to exaggerated haemorrhage in MDS and leukaemia⁸ and this should be considered when deciding on the need for platelet transfusion. However, transfusion of blood products, especially platelets, has adverse effects including the risk of viral infection, immunosuppression and

production of antibody which would decrease the efficacy of platelet transfusion.⁹ Therefore, transfusion of platelets should be determined strictly on the basis of the balance between its benefit and risk. Our patient did not receive a platelet transfusion in the first operation despite a platelet count of $80 \times 10^9 \text{ L}^{-1}$. However, platelets were administered prophylactically to prevent haemorrhage during her second Caesarean section because we assessed that a platelet count of $40 \times 10^9 \text{ L}^{-1}$ was critical and could produce haematological deterioration. The second operation was uneventful with no complications from immune interference although the intraoperative blood loss was larger than that during the first operation. When platelet transfusion is necessary, the use of single donor platelets is recommended to prevent antibody production and infection. HLA matched single donor platelets are preferred in patients who require platelets repeatedly or in those who have been sensitised and leukocyte poor red cells are recommended to prevent antibody production. It is preferable to avoid sensitisation by transfusion since these patients may undergo bone marrow transplantation in the future. Moreover, blood products should be irradiated to prevent graft versus host disease. The use of specific filters to remove leukocytes is also helpful to prevent the leukocyte reactions, including sensitisation.

Anaesthetic techniques for these patients are also restricted due to their haematological condition. Regional anaesthesia is relatively contraindicated because of a risk of epidural haematoma secondary to thrombocytopenia. Therefore, although epidural anaesthesia has advantages including postoperative pain relief, it was avoided. There are reports that nitrous oxide may inhibit the activity of methionine synthetase, resulting in megaloblastic anaemia,^{10,11} but we chose to use it for both operations since it is a precisely controllable anaesthetic with rapid onset and recovery. For short periods nitrous oxide may not affect bone marrow biochemical function and megaloblastic haematopoiesis,¹² supporting its short term use for Caesarean section. In the second operation, sevoflurane was added to avoid intraoperative maternal awareness. Because of the small blood and tissue solubilities and high potency, sevoflurane provides easy control of anaesthetic depth and rapid recovery. Potent inhalational anaesthetics, such as sevoflurane, may theoretically increase blood loss secondary to uterine relaxation during Caesarean section but there is no clinical evidence to show that operative blood loss is increased. When spinal and general anaesthesia with approximately 0.5 MAC isoflurane or sevoflurane were compared, there were no differences in neonatal outcome.^{13,14} Both operations in this patient were uneventful and healthy infants were delivered.

For a patient with MDS, there should be an exact assessment of their haematological condition and the mode of anaesthesia should be determined for the individual patient. Therefore, a team approach by the obstetrician, haematologist and anaesthetist is essential. Prophylactic treatment may be necessary to ensure safe perianaesthetic management without major complications, especially massive haemorrhage due to thrombocytopenia.

Commentary

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We cannot predict the future. Therefore, decision-making is difficult when patients with MDS present for operative delivery as they may develop frank leukaemia or aplastic anaemia in the future and need bone marrow transplantation to save life. Patients with low haemoglobin and platelet counts are often given replacement therapy before surgery. Every cell and platelet transfusion given may sensitise the patient and make rejection of a future transplant more likely. One must, therefore, balance the need for immediate therapy with the chance that future life-saving treatment may be jeopardised.

We have changed the way that we treat anaemic and thrombocytopenic pregnant women before surgery. Fifteen years ago we did not anaesthetise people with a haemoglobin $<100 \text{ g}\cdot\text{L}^{-1}$ and the lower limit of platelets for safe epidural anaesthesia was considered to be $100 \times 10^9\cdot\text{L}^{-1}$. We also routinely transfused people whose haemoglobin decreased after surgery or delivery. Over the last decade, the catastrophic events that can befall transfusion recipients have become evident, and there are now much clearer, and more restricted policies regarding transfusion practices.¹⁵ We now deliberately haemodilute non gravid patients and allow their haemoglobin to decrease to 60 or 70 $\text{g}\cdot\text{L}^{-1}$ before transfusing red cells, provided cardiovascular variables are stable. As well, normal pregnant women may have thrombocytopenia of pregnancy (periparturient thrombocytopenia) without any symptoms or bleeding tendencies.¹⁶ Obstetrical anaesthetists will insert epidural catheters for pain relief in labour in such patients after careful explanation of risks and benefits. There is no magic lower limit of platelet count. Each patient is evaluated carefully, her haematological status assessed, and epidurals are used judiciously. Many will insert an epidural in a patient who has a haematological disorder with a platelet count between 50 and $70 \times 10^9\cdot\text{L}^{-1}$ providing the platelet count is stable, and they are otherwise perfectly normal.

We have changed the way we assess the need for platelet transfusion for surgery as well. Patients now go to the operating room with a platelet count of $30 \times 10^9\cdot\text{L}^{-1}$ and below without platelet replacement. The key to successful outcome is haematological consultation, immediate availability of blood products and judicious anaesthetic management.

The current paper describes the treatment of a woman with MDS who underwent two Caesarean sections. The authors recommend transfusion with leucocyte poor red cells and platelets before the second Caesarean section as the haemoglobin concentration and platelet count were $66 \text{ g}\cdot\text{L}^{-1}$ and $40 \times 10^9\cdot\text{L}^{-1}$ respectively.

We have just treated two pregnant women with this condition. The first patient was treated in hospital with prednisone and she delivered vaginally. Her platelet count was $10 \times 10^9\cdot\text{L}^{-1}$ with a normal INR and PTT and Hb of $110 \text{ g}\cdot\text{L}^{-1}$ before delivery. Intravenous morphine was used for analgesia in labour. Blood loss was "normal." The platelet count was $11 \times 10^9\cdot\text{L}^{-1}$ and the Hb $94 \text{ g}\cdot\text{L}^{-1}$ the day after delivery. She did not receive any blood product transfusions in the peripartum period.

The second patient presented for an elective third Caesarean section, having had a previous still birth. The platelet count was $12 \times 10^9\cdot\text{L}^{-1}$ with a Hb of $84 \text{ g}\cdot\text{L}^{-1}$ preoperatively. I elected to give a transfusion of platelets immediately before surgery. The haematologist disagreed. In retrospect, I probably now would wait to see if bleeding developed before giving platelets. The blood loss was $<1000 \text{ ml}$. On the second postpartum day, the patient's Hb was $59 \text{ g}\cdot\text{L}^{-1}$, and she received two units of leukocyte poor red cells as she was symptomatic.

The anaesthetic management of the case described was straight forward. In such cases, it is prudent and wise to avoid regional anaesthesia for operative delivery and for pain relief in labour. Uncontrolled bleeding into a confined epidural space can be catastrophic and there are options available for labour pain management. General anaesthesia for Caesarean section in a prepared patient with a normal airway is safe. It is easier to manage severe blood loss should it arise, when the patient is anaesthetised and the airway controlled. The theoretical risk of increased uterine bleeding from the use of inhalational agents is just that: theoretical. In practice, there is no evidence that 0.5 MAC of an inhalational anaesthetic agent increases bleeding or causes severe uterine hypotonia.¹⁷ One would avoid deep anaesthesia with these agents in any patient who is bleeding, or indeed in any patient undergoing Caesarean section. All inhalational agents,

as well as nitrous oxide, have immunosuppressive properties. This is not of clinical importance, and is not a reason to avoid the agents in a patient with MDS or any other haematological disorder.¹⁸

We should get away from fixed numbers when it comes to transfusion. Red cells and platelets should be available and be used, if needed. We should rethink the need for prophylactic transfusion. Platelet transfusion in patients with MDS is best given after excess bleeding happens. The advantage is that for many patients, in fact, platelet transfusions can be withheld. We should bear in mind that platelet transfusions are not sterilised and are the single most dangerous blood product we use. Multiple units are required, and platelet transfusions carry lymphocytes which may contain viruses.

I agree with the authors that a multidisciplinary approach to patients with haematological disorders is key to successful management. Close consultation among the haematologist, anaesthetist and obstetrician, and a clear management plan that the patient understands and agrees to, will simplify care and prevent confusion and immediate as well as long term complications.

Commentary

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This case brings forward a number of issues which relate to the haematologic management of patients with primary lesions of the marrow. Such lesions include the myelodysplastic states, aplastic anaemia, chemotherapy induced marrow hypoplasia and, more unusually, the syndrome of paroxysmal haemoglobinuria which can present as a hypoplastic process, as well as a haemolytic state.

In patients with a primary lesion which results in insufficient and/or ineffective haematopoiesis, it is common for the peripheral cytopenias to worsen during the pregnancy, and to improve, often returning to the pre-pregnant levels, post partum. This is the result, primarily, of plasma volume expansion in pregnancy and an inability of the marrow to respond with increased erythropoiesis and thrombocytopoiesis. With normalisation of the plasma volume post partum, the counts return to the baseline level. This is consistent with the history of the first pregnancy and the trend in the pregnancy described in this case report.

The management of these pregnancies can really be separated into the antepartum and peripartum periods. Considerable anaemia can be tolerated during pregnancy by both mother and fetus and, in general,

the indication for transfusion is triggered by the development of symptoms in the mother or evidence that the baby is not flourishing. Haemostasis is also important although much less of a concern antepartum when the platelet count can drift down into the 20 to $30 \times 10^9 \cdot L^{-1}$ range with no discernable clinical problem. Spontaneous vaginal bleeding during pregnancy related to a low platelet count is very rare and usually an obstetric cause will explain the haemorrhage. In this patient, vaginal bleeding at a platelet count of $51 \times 10^9 \cdot L^{-1}$ responded to pressure on the cervical lesion which precipitated it. A platelet transfusion was unnecessary.

When trying to assess when to intervene with platelet transfusion in a primary marrow lesion, the rules are similar for any other situation. Control of the local lesion is essential. Platelets should be transfused when there is evidence that the level of the count is contributing to ongoing bleeding. Prophylactic transfusion in anticipation of surgery or intervention such as amniocentesis may be necessary, depending on the platelet count. The patient's history with regard to bleeding history related to specific platelet counts as well as the clinical findings are very important in making these decisions. In general, the work of Harker and Slichter¹⁹ in the 1970s established the relationship between the platelet count and bleeding in patients with *hypoplastic thrombocytopenia*. Our subsequent experience, based on their work, has resulted in the following rules of thumb: for major surgery or any blind manoeuvre such as a deep block, epidural, a platelet count $>75 \times 10^9 \cdot L^{-1}$ is optimal. For minor procedures (lumbar puncture, skin biopsy), a count of $50 \times 10^9 \cdot L^{-1}$ is acceptable, and for prophylaxis against spontaneous haemorrhage, 10 to $20 \times 10^9 \cdot L^{-1}$ is the trigger. These guidelines for hypoplastic marrow states must be distinguished from the situation of thrombocytopenia associated with ITP or pre-eclampsia where platelet function at equivalent platelet counts is usually far superior than in patients with primary marrow disorders. In this patient's care, at the time of delivery, it is noted that 10 units of platelets were given intraoperatively. From her preoperative platelet count of $40 \times 10^9 \cdot L^{-1}$, it is appropriate that she received platelets, however, perhaps not the number given. In general, it is optimal to transfuse prophylactically prior to surgery and establish that the target platelet count has been reached. In this situation, in the absence of any consumptive process, a transfusion of four to six units would most likely have raised the platelet count over $75 \times 10^9 \cdot L^{-1}$ which would be adequate for her surgery. Transfusing in this way has two advantages: it allows assurance that the patient has had an adequate response to the transfusion, and it allows

thoughtful approximation of the volume needed so as to avoid unnecessary units.

Pregnant women have a 20 to 30% HLA immunisation rate even if they have not received a transfusion. It is important that the additional risk of alloimmunisation to platelets, conferred by transfusion, is minimised in these patients. Normally, it would be our practice to check for platelet and HLA antibodies before delivery to ensure an optimal response to transfusion. If antibodies are present, arrangements for an HLA compatible donor for plateletpheresis might be necessary.

Transfusion of patients with primary marrow disorders also requires consideration of future treatment regimens which dictate the need to use manipulated products. Thus, prevention of CMV infection as well as HLA alloimmunisation, both of which can be achieved with leukocyte-depleted blood products, is important in a patient with MDS for which the only curative therapy would be a bone marrow transplant.

I would argue with the authors with regard to their decision to deliver the patient by Caesarean section in order to minimise the risk of haemorrhage. In fact, vaginal delivery, in the absence of complicating obstetric factors, would be the route of choice in this situation. There is a good chance that there would be no surgical incision, if episiotomy is avoided, and with good obstetric management and prophylactic platelet transfusion (for a vaginal delivery we would be happy with a platelet count of 50 to $75 \times 10^9 \cdot L^{-1}$) the uterus will contract down and there will be minimal bleeding. Vaginal delivery avoids the many layers of incision with a Caesarean delivery and also leaves the uterine myometrium intact ensuring physiological contraction after delivery.

The authors make the observation that platelet dysfunction may contribute to exaggerated haemorrhage in MDS. This is true and can usually be ascertained by careful history, review of records and clinical observation. In the situation of platelet dysfunction, the usual guidelines for the platelet count threshold for transfusion as noted above must be modified to reflect the intrinsic dysfunction of the autologous platelets. There are two clues in this patient's history that there was no dysfunction. During the first pregnancy, the patient underwent Caesarean section with a platelet count of $81 \times 10^9 \cdot L^{-1}$ (non-transfused) without problem. Then, in the second pregnancy, the bleeding from the cervical erosion was controlled by pressure alone at a platelet count of $51 \times 10^9 \cdot L^{-1}$. This suggests normal platelet function.

Finally, it is always important to remind house staff and nurses that the platelet count in these patients will

decrease in the first one to three days post partum as the lifespan of the transfused platelets is reached. During the postpartum period, in any patient with thrombocytopenia, intramuscular injections, aspirin and NSAIDs should all be avoided. The latter are potent platelet inhibitors and will increase considerably the risk of bleeding in a patient with hypoplastic thrombocytopenia. In our institution, a careful review of standard postpartum orders is always necessary as a both NSAIDs and intramuscular medications are commonly ordered routinely.

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