Anesthesiologic Management of Cesarean Section at 35-weeks Pregnancy with Acute Myeloid Leukemia and Profound Thrombocytopenia Refractory to Platelet Transfusion: A Case Report

Abstract
Leukemia is a very rare condition in pregnancy. The pathology itself poses a great challenge to the anesthesiologist due to the inherent risks such as blast crisis, tumor lysis syndrome, anemia, and thrombocytopenia. The authors present the case of a 30-year-old G3p2002, complicated by profound thrombocytopenia refractory to platelet transfusion who underwent general anesthesia for cesarean section.

Keywords: Acute Myeloid Leukemia, anesthesiologic management, cesarean section, profound thrombocytopenia

Introduction
Leukemia is a very rare condition in pregnancy accounting for an annual incidence of 1 in 100,000 pregnancies, with acute myeloid leukemia (AML) accounting for more than two thirds of such cases. Management remains a great challenge due to therapy-attributable risks for mother and fetus and the low survival rates (~30%).

The anesthesiologist has to deal with the associated complications of the disease such as anemia, thrombocytopenia, blast crisis, and tumor lysis syndromes. Thrombocytopenia, especially when profound, has limited therapeutic options and can lead to significant bleeding and death. Profound consumptive thrombocytopenia complicating anesthesiologic management of cesarean section for acute myeloid leukemia in pregnancy is a very rare pathology. Our literature search has resulted in no such case reports. We thus present and discuss the anesthesiologic management of cesarean section in a 35-week pregnant lady presenting with acute myeloid leukemia complicated by profound consumptive thrombocytopenia refractory to treatment by platelet transfusion.

Case History
A 30-year-old G3p2002, of African origin, 71.7 kg and 1.62 m tall was admitted in the obstetric ward for management of a lymphoproliferative disorder at 33 weeks, 5 days gestation. Onset of ill health dated 1 month prior to presentation, with history of asthenia, bleeding gums, and hematuria which motivated consultation in a local health facility. The initial work up revealed hyperleucocytosis (45700/m3) with lymphocyte predominance (53.5%, n = 24450/m3), moderate normochromic normocytic anemia Hb8.4 g/dl, and profound thrombocytopenia (27000/m3) on a full blood count. A blood smear requested revealed predominant hyperleucocytosis (lymphocytosis with some plasmocytes, many pro-lymphocytes, and rare atypical lymphocytes), moderate hypochromic anemia with poikilocytosis, and profound thrombocytopenia with some giant platelets. A diagnosis of a chronic lymphoblastic syndrome was concluded upon, with lymphoma as a differential. Immunophenotyping was prescribed and the patient was referred to our hospital for better management.

In our hospital, an obstetric ultrasound was done revealing an oblique lie of the fetus. Immunophenotyping results revealed acute myeloid leukemia. After multidisciplinary concertation, urgent delivery by cesarean section was decided as the safest method of delivery so as to permit the mother begin chemotherapy, while sparing the fetus. Fetal
lungs [10-12] with dexamethasone 6 mg/twice daily IV for 2 days was initiated and the patient was referred for anesthesiologic management.

A per-operative work up revealed hyperleucocytosis (52000/m3) with profound thrombocytopenia (15000/m3). The coagulation profile revealed a prothrombin time of 80%, INR 1.13, activated cephaline time of 30 seconds, and a raised LDH of 675 g/L. The patient was thus classed American Society of Anesthesiology (ASA) class 3.

A preoperative preparation aimed at reducing the bleeding risk by administration of platelet concentrates with a target of 70000/m3 platelets for cesarean section was conducted. Initially, 2 units of platelets were transfused and a control platelet count done revealed 15000/m3, a further 4 units was transfused with control results revealing 27000/m3, another 4 units of platelets transfused over 2 days revealed a poor response in platelet count. Even after 4 days of treatment with platelet transfusion, the platelet count was only 15000/m3. A conclusion on consumptive thrombocytopenia was made. To manage this problem, a collegial decision was taken to transfuse 5 units of platelets in the theater, just prior to induction of anesthesia and 4 pints per-operatively, after incision to minimize bleeding. Other strategies to minimize bleeding risks included intravenous administration of tranexamic acid (4 grams loading dose 30 minutes prior to incision, and 1g for every hour per operatively), 2g of calcium gluconate, and 250 mg of ethamsylate. The intervention was successfully carried out under general anesthesia and endotracheal intubation. Standard monitoring with a scope and non-invasive blood pressure monitoring were used. Prior to induction, the patient received preoxygenation for 3 minutes with 100% oxygen. Propofol at 2 mg/kg and suxamethonium at 1 mg/kg were administered intravenously and the patient was then intubated with a size 6 cuffed endotracheal tube and assisted under manual ventilation. Midline lower abdominal incision was performed and a live female baby, APGAR 6/10 in first minute and 10/10 at five minutes weighing 2600g was extracted. After cord clamping, 10 IU of oxytocin was administered IV, and 30IU in 500ml of 5% glucose solution was set to flow at a rate of 20 drops/min. Antibioprohylaxis with 2g of amoxicillin clavulonic acid was also administered. Anesthesia was simultaneously reinforced with fentanyl at a dose of 2 mg/kg. Maintenance of anesthesia was with halothane at 0.8%. Pharmacologic measures to control bleeding as previously described was continued. Also, 4 units of platelets were administered following incision (5 units having been administered before induction).

Per-operative complications encountered were uterine atonia managed by the administration of misoprostol 800 micrograms intrarectally, IV oxytocin drip, and uterine massage. Also, anesthetic gases were further reduced. Per-operative bleeding was estimated at 1300 ml and managed by transfusion of 2 pints of cross-matched red blood cell concentrates. The surgery lasted 1 hr 20 minutes. The neonate was later transferred to the neonatal unit for prematurity. Immediate postoperative complications were bleeding from the abdominal wall at the site of incision. This was managed with compressive wound dressing over incision site. Also, further pressure was applied over the abdominal wall with a load of sand. When stabilized, the mother was transferred to the surgical intensive care unit for further management. The postoperative platelet count was 18000/m3. A further 5 units of platelets was administered to prevent bleeding and the control platelet count revealed 43000/m3. Other postoperative complications were malaria managed with IV 170 mg artesunate as per protocol, for 3 days with oral relay. The patient was transferred to the hematological unit after 4 days of hospitalization in the surgical ICU for further management.

Discussion

Leukemia in pregnancy is a very rare and challenging medical condition with an annual incidence of approximately 1:100,000 pregnancies.[9,10] Thrombocytopenia may complicate disease when advanced and is often a poor prognostic factor.[7] Etiologies may be bone marrow failure, gene polymorphism, mutation transcription factors, and adverse effects of treatment.[9] Grade 1B evidence suggest that women diagnosed with AML in pregnancy should be treated without delay.[10-12] In the first trimester, a therapeutic abortion should be considered and treatment started.[10-12] In the second and third trimesters, fetal risks linked to treatment are to be considered and where possible early delivery should be implemented before the commencement of treatment.[10-12] When applicable, corticosteroids, for fetal lung maturation should be administered if delivery is anticipated between 24 and 35 weeks gestation, over a 48h period during the week prior to delivery.[11,13] In the case where cesarean section is considered as the means of delivery, anesthesiologic management becomes challenging due to problems posed by the pregnant patient, disease, and choice of technique of anesthesia. In our patient, problems linked to pregnancy were those of pre-term pregnancy. Those linked to the pathology included impaired immunity with increased risk of infections, chronic anemia, and profound thrombocytopenia with high risk of hemorrhage.[14] Other problems of the disease were hyperleukocytosis with associated complications of leukostasis and tumor lysis syndrome. Profound thrombocytopenia posed a major problem in particular in the management of our patient due to the significant associated risk of mortality from bleeding complications. Platelet transfusion remains the mainstay of therapy for this complication.[7,8] Pharmacologic agents such as Oprelvekin (recombinant human interleukin [IL]-11), IL-3, IL-6, thrombopoitin and recombinant activated factor VII have been shown to improve platelet count.[7]
However, none of these are without significant side effects. Where platelet transfusion is not working, rFVIIa has been shown to have promising activity in controlling bleeding in patients not responding to platelet transfusions.[7] This, however, was not available in our context. In the case of our patient, platelet transfusion was used as the means to manage thrombocytopenia. However, our patient proved to be refractory to platelet transfusion posing a major therapeutic challenge. We, therefore, resorted to massive platelet transfusion, transfusing 5 units of platelets immediately prior to induction (so as to bypass consumptive mechanisms) and 4 units during the intervention after incision to help control bleeding. IV calcium gluconate was administered to prevent hypocalcemia and promote blood clotting. To reduce the risk of allogetic reactions, only male donors were accepted to donate blood for apheresis for our patient. Other mechanisms to prevent bleeding involved the administration of a high doses of tranexamic acid (TXA) and ethamsylate as described. Tranexamic acid inhibits conversion of plasminogen, thereby inhibiting fibrin cleavage, with reduction in risk of hemorrhage.[15] At high doses, TXA also inhibits plasmin activity directly[15] and was thus used in our patient to maximize its benefits in controlling bleeding. Ethamsylate is known to improve platelet adhesiveness and restore capillary resistance,[16] reason for its use in managing our patient.

A problem of choice of anesthetic technique was posed in this patient. We did not practice regional anesthesia (RA), spinal and/or epidural due to increased bleeding tendency as a result of profound thrombocytopenia contraindicating regional techniques.[17] Also, RA in patients with leukemia has been shown to be associated with central nervous system (CNS) contamination by circulating blast cells when spinal or epidural approach is traumatic.[17,18] This could further worsen our patient’s prognosis and so was avoided. Also, regional techniques can be associated with infiltration of malignant cells in surrounding ligaments and other tissues.[19] General anesthesia with endotracheal intubation was, therefore, the technique of choice in our patient. This was done with a small-sized endotracheal tube to minimize risk of bleeding.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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