Successful Pregnancy and Delivery in a Woman with Gray Platelet Syndrome

Osnat Jarchowsky Dolberg MD[1] and Martin Ellis MD[2,3]

[1]Department of Medicine A and [2]Hematology Unit, Meir Medical Center, Kfar Saba, Israel
[3]Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

KEY WORDS: gray platelet syndrome, thrombocytopenia, pregnancy, delivery

IMAJ 2011; 13: 117–118

Gray platelet syndrome or α-granule platelet syndrome is a rare inherited platelet disorder that was first described in 1971. It is characterized by moderate to severe thrombocytopenia and large dysfunctional platelets with a specific absence of α-granules, resulting in the platelets' gray appearance on a Wright-stained peripheral blood smear. The α-granules contain proteins that are essential for hemostasis, thus patients with gray platelet syndrome exhibit bruising and mucocutaneous bleeding out of proportion to their mild to moderate thrombocytopenia [1]. Although the molecular basis of the disease is unknown, evidence suggests that α-granules fail to mature during megakaryocyte differentiation. Transmission of gray platelet syndrome is autosomal-dominant in some cases but recessive in others, suggesting heterogeneity in the origin of the defect [2].

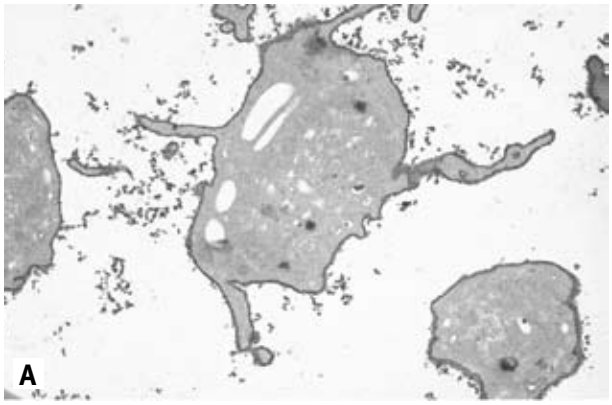
Thrombocytopenia in pregnancy is not rare. It is observed in 6% to 15% of pregnant women at the end of pregnancy and is usually moderate. Gestational thrombocytopenia is the most common cause of thrombocytopenia during pregnancy, occurring in approximately 7% of women. It is thought to be caused by estrogen-mediated suppression of megakaryocytopoiesis [3]. The potential effect of pregnancy on the platelet count in gray platelet syndrome has not been described and the outcome of such pregnancies is unknown. In this report, we describe the course of a pregnancy and delivery in a patient with gray platelet syndrome.

PATIENT DESCRIPTION

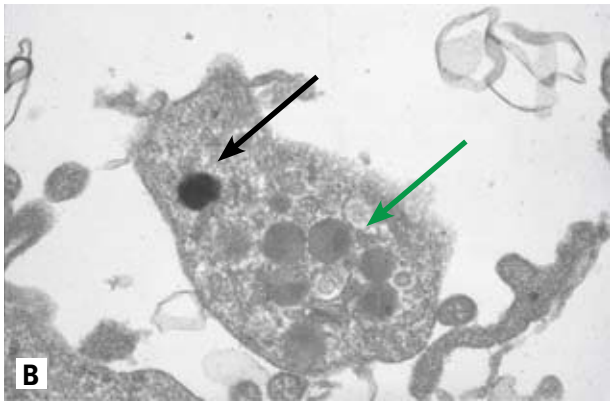
The patient is a woman with a history of thrombocytopenia since age 11 years. Gray platelet syndrome was diagnosed on the basis of the characteristic findings of a chronic stable thrombocytopenia with a platelet count of approximately 40,000/μl, mild splenomegaly, reticulin and collagen deposition on bone marrow biopsy, and typical electron microscopy findings showing platelets devoid of α-granules [Figure]. She had no history of mucocutaneous or deep tissue bleeding. The patient became pregnant for the first time at age 35. When seen in the first trimester of pregnancy for routine follow-up, physical examination was unremarkable apart from a palpable spleen extending 2 cm below the left costal margin. Complete blood count revealed a platelet count of 37,000/μl. Obstetric evaluation including fetal ultrasound was normal.

As the pregnancy progressed, the patient developed progressive thrombocytopenia without any bleeding or bruising. At 34 weeks gestation however, she presented with numerous petechiae on her legs and her platelet count was

[A] Electron microscope image (x 10,000) of the patient's platelets showing absence of α-granules. A few dense granules are seen.



[B] Electron microscope image (x 10,000) of a normal platelet showing the presence of dense (black arrow) and α-granules (green arrow)



17,000/μl. She received a single unit of leuko-reduced apheresis platelets and the 1-hour post-transfusion platelet count was 47,000/μl. She was examined over the following month and underwent weekly platelet counts. Her platelet count declined gradually to 30,000/μl, and induction of labor was planned with the obstetric team.

At 40-weeks gestation, labor was induced using an oxytocin infusion. The platelet count was 16,000/μl. A total of three leuko-reduced apheresis platelet units were transfused during the 24 hours she was in labor in order to maintain the platelet count at a predefined target of 50,000/μl. Immediately before delivery the platelet count was 36,000/μl. She had an uncomplicated vaginal delivery and the infant's platelet count was normal. There was no postpartum hemorrhage and she was discharged 2 days later with hemoglobin 9.8 g/dl and a platelet count of 35,000/μl.

COMMENT

The most common causes of thrombocytopenia in pregnancy are gestational thrombocytopenia (74%), preeclampsia and HELLP syndrome (21%), and immune thrombocytopenia purpura (4%). The former is a benign condition occurring in 7% of pregnancies and by definition does not confer a risk for maternal or fetal hemorrhage. Immune thrombocytopenia purpura occurs in 0.4% of pregnancies and occasionally causes significant maternal bleeding, and is a very rare cause of fetal or neonatal hemorrhage [4]. The incidence of congenital thrombocytopenia in pregnant women is unknown, but it may be presumed to be exceedingly low as these forms of thrombocytopenia are very rarely encountered. For example, the incidence of X-linked thrombocytopenia and the Wiskott-Aldrich syndrome, the most common congenital platelet deficiency syndrome, is 4 cases per 250,000 live male births among Caucasians. The incidence of gray platelet syndrome is very rare, with anecdotal case reports only.

The course of pregnancy and delivery in women with congenital thrombocytopenia has not been well described, and no clear guidelines exist for managing these patients. The issues confronted during our patient's pregnancy were the use of platelet transfusions and the potential for fetal thrombocytopenia and thus the risk of fetal hemorrhage, particularly during delivery. We planned to use therapeutic platelet transfusions in the event of clinically significant bleeding during pregnancy and prophylactic platelet transfusions prior to delivery, which would be induced in order to maximize control of any potential hemorrhage. This approach was derived from platelet transfusion guidelines that apply to other clinical situations, such as chemotherapy-induced thrombocytopenia [5]. Single-donor, apheresis platelet units were preferred to minimize donor exposure and reduce the risk of transfusion-transmitted infection and platelet alloimmunization. During pregnancy the patient required a single unit of apheresis platelets and during labor, which was prolonged, she required a further three units of apheresis platelets. These prophylactic transfusions were successful in preventing clinically significant bleeding even though her predelivery platelet count was only 36,000/μl – lower than the 50,000/μl that is considered the minimum platelet count for invasive surgical procedures [5].

Monitoring the fetal platelet count by percutaneous umbilical blood sampling is considered the standard of care in pregnancies potentially affected by neonatal alloimmune thrombocytopenia. However, PUBS is a specialized procedure that requires technical expertise and is associated with a risk of cord hematoma and fetal death. Since gray platelet syndrome is an autosomal-dominant trait, we recommended PUBS monitoring to our patient, but she declined this procedure. Therefore, we considered various options to minimize the risk of fetal hemorrhage during delivery, the period of highest risk for this complication. Delivery by cesarean section was considered, but since the fetus was not large and the patient's pelvic structure was "favorable," it was decided to allow a trial of normal vaginal delivery after induction of labor, and cesarean section if labor did not progress. Active labor and delivery were uncomplicated and neither clinical nor ultrasonographic hemorrhage was detected. Subsequently, the baby was found to be unaffected by gray platelet syndrome, having a normal platelet count.

In conclusion, this case demonstrates that women with gray platelet syndrome may experience a safe pregnancy and delivery. We recommend that a multidisciplinary management team be responsible for the obstetric and hematologic aspects of the care of the mother and fetus, and if necessary, the neonate. Judicious use of platelet transfusions and active management of labor and delivery should be considered.

PUBS = percutaneous umbilical blood sampling

Corresponding author:
Dr. M. Ellis
Hematology Unit, Meir Medical Center, Kfar Saba 44281, Israel
Phone: (972-9) 747-1045
Fax: (972-9) 747-1295
email: martinel@clalit.org.il

References

1. Levy-Toledano S, Caen JP, BretonGorius J, et al. Gray platelet syndrome: α-granule deficiency. *J Lab Clin Med* 1981; 98: 831-48.
2. Nurden AT, Nurden P. The gray platelet syndrome: clinical spectrum of the disease. *Blood Rev* 2007; 1: 21-36.
3. Schwartz KA. Gestational thrombocytopenia and immune thrombocytopenia in pregnancy. *Hematol Oncol Clin North Am* 2000; 14 (5): 1101–6.
4. Sukenik R, Ellis MH, Feijgen M. Management of immune thrombocytopenic purpura in pregnancy. *Obstet Surv* 2008; 63: 182-8.
5. Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood* 2010; 115 (2): 168-86. Epub 2009 Oct 21. PMID: 19846889.