

ADVANCES IN HEMATOLOGY

Current Developments in the Management of Hematologic Disorders

Section Editor: Craig M. Kessler, MD

Thrombocytopenia in Pregnancy

Ronit Yerushalmi, MD
Sheba Medical Center
Tel Hashomer, Ramat Gan
Israel

H&O What is the definition of thrombocytopenia in pregnancy?

RY As in the general population, thrombocytopenia in pregnancy is defined as a platelet count below 150,000 platelets/mL. Counts between 150,000 and 100,000 are considered mild, between 100,000 and 50,000 moderate, and below 50,000 severe. Women can give birth relatively safely with platelet counts of 30,000–50,000. A safe cesarean section is possible with counts between 50,000 to 70,000, with physicians in the United States generally using 70,000 as the cut-off level for deeming the procedure to be safe.

H&O Is cesarean section recommended if a pregnant woman is thrombocytopenic?

RY When pregnant women are thrombocytopenic, natural birth is always considered safer. In the past, when physicians were concerned about possible bleeding, cesarean section was used. It has been found, however, that natural birth is still safer despite these fears. Cesarean section should be performed if there is an obstetric indication, not because of thrombocytopenia itself. For birth, physicians generally prefer the patient's platelet count to be above 50,000 platelets/mL, and higher if the patient requires epidural anesthesia.

H&O How is thrombocytopenia diagnosed?

RY Hematologists are called by obstetric/gynecologic clinicians if a pregnant woman is found to be thrombocytopenic using standard tests of platelet counts. It is important to assess the patient history, including previ-

ous blood counts. It is necessary to know, if possible, whether the thrombocytopenia is new or if it had been present before the pregnancy. Additionally, it is useful to know if the woman was thrombocytopenic in a previous pregnancy or afterward, and during which trimester the thrombocytopenia appeared. Hematologists must look at the peripheral blood smear, blood counts, liver function test, and clotting test. It is important to rule out pseudothrombocytopenia (platelets clumping due to ethylenediaminetetraacetic acid in the laboratory tube).

H&O What are the causes of thrombocytopenia?

RY Thrombocytopenia is diagnosed in about 10–15% of pregnant women. Most of these women (60–80%) have gestational thrombocytopenia (GT), 10–15% have immune thrombocytopenic purpura (ITP), 20% have eclampsia or HELLP (hemolytic anemia, elevated liver enzymes, and low platelet count) syndrome, and very low percentages have other rare causes, such as thrombotic thrombocytopenic purpura (TTP), disseminated intravascular coagulation (DIC), antiphospholipid antibody syndrome, acute fatty liver of pregnancy, and others.

In most thrombocytopenic pregnant women, approximately 80%, the cause is GT, defined as mild to moderate thrombocytopenia according to platelet counts, which rarely fall below 70,000 platelets/mL. The causes of gestational thrombocytopenia are not understood but may be due to hemodilution or accelerated clearance of platelets. This condition generally appears in the third trimester, and it is necessary to follow the patient to be certain the platelet counts do not continue to fall (as in ITP). GT does not progress and poses no danger to the mother or the fetus. GT usually resolves within 12 weeks after delivery, but it may present in subsequent pregnancies, which is why it is important to know a patient's history.

The second most common cause of thrombocytopenia in pregnant women is ITP, which is quite common in children and young women. With this condition, platelets are destroyed by the reticuloendothelial system due to autoantibodies against membrane glycoprotein complexes. In this case, it is necessary to assess whether the patient's platelet count was low prior to pregnancy. The condition can be diagnosed in all trimesters, and it

is necessary to follow the patient closely because platelet counts may fall significantly.

The third most common cause of thrombocytopenia is related directly to pregnancy: eclampsia and HELLP syndrome. Eclampsia is diagnosed when a pregnant woman has hypertension and proteinuria, whereas HELLP syndrome comprises hemolytic anemia, elevated liver enzymes, and a low platelet count. It is seen more in young nulliparus or elderly women with risk factors such as hypertension or obesity and appears mostly after 20 weeks of gestation. In both syndromes, maternal and fetal morbidity are high and require immediate treatment. It is necessary to stabilize the patient and advance delivery if possible because the best treatment is evacuating the uterus. The condition resolves within 5 days after delivery.

Other, rare causes of thrombocytopenia in pregnancy include DIC, acute fatty liver of pregnancy, and TTP. DIC can be caused by sepsis, placental abruption, placenta previa, missed abortion, retained fetus syndrome, or amniotic fluid embolism. These syndromes are associated with significant morbidity and mortality. In these cases, the thrombocytopenia is not isolated and is usually severe.

H&O What are the methods of treatment of these underlying conditions?

RY As mentioned, GT resolves when the woman gives birth, generally within 12 weeks. It is generally not necessary to treat the woman or the infant; one needs only to follow the platelet counts. The two most commonly used treatment modalities for patients with ITP are steroids and intravenous immunoglobulins, which are safe and generally produce a good response. In the normal population with ITP, a platelet count below 20,000 platelets/mL warrants treatment, whereas in pregnant women, it is advised to treat if the platelet count is below 30,000 platelets/mL. Bleeding also requires treatment in pregnant women with ITP. The antibody that causes the destruction of platelets does cross the placenta, as it is an immunoglobulin G, so it is important to consider the welfare of the fetus when ITP is diagnosed. Nevertheless, only approximately 5% of babies are born with severe thrombocytopenia, and bleeding complications are seen in less than 25% of them, with intracranial bleeding being rare. Treating the mother, however, does not decrease the incidence of thrombocytopenia in the fetus. The best tool to predict thrombocytopenia of the neonate is a history of thrombocytopenia in older siblings. With HELLP syndrome, the treatment is termination of the pregnancy. The patient must be stabilized and the clinician must ensure that she has a platelet count above 50,000 platelets/mL, if possible. There may be some exacerbation of the condition within 48 hours of evacuation of the uterus, but the condition

will end within a few days. In TTP, the treatment is complicated and involves plasmapheresis and avoiding platelet transfusions. With DIC, usually the treatment is aimed at the main cause and resolution follows evacuation of the uterus. Support with blood products is used as needed.

H&O What is the prognosis associated with these underlying conditions?

RY GT has a very good prognosis. The same is true for ITP when treated. The percentage of patients with ITP requiring blood or with fetal morbidity is low. Still, these patients must be followed closely during pregnancy. The prognosis for HELLP syndrome is comparably poorer. There is a significant percentage of severe morbidity and some risk of mortality. With HELLP syndrome and eclampsia, more stillbirths, bleeding events, and intrauterine growth restrictions are seen. The follow-up of these patients, as well as those with acute fatty liver of pregnancy, is complicated.

H&O Does the prognosis differ when the pregnancy is twins or triplets?

RY Generally speaking, twin and triplet pregnancies are more complicated than single-fetus pregnancies. The more complicated the pregnancy, the higher the risk of hypertension, diabetes, eclampsia, and HELLP syndrome. Research by Morikawa and colleagues published in 2005 showed that triplet pregnancies were associated with higher rates of HELLP syndrome and eclampsia. Twice as many triplet pregnancies were associated with these conditions as compared to single-fetus pregnancies.

H&O Where do you see research into thrombocytopenia in pregnancy headed in the future?

RY It would be useful to have better ways of diagnosing ITP and differentiating it from the other causes of thrombocytopenia. For patients with ITP who do not respond to steroids or intravenous immunoglobulin G, there are no other safe drugs. Some novel agents for the treatment of ITP exist for the general population, but none is approved for use during pregnancy.

Suggested Readings

- Sainio S, Kekomaki R, Riikonen S, Teramo K. Maternal thrombocytopenia at term: a population-based study. *Acta Obstet Gynecol Scand.* 2000;79:744-749
- Win N, Rowley M, Pollard C, et al. Severe gestational (incidental) thrombocytopenia: to treat or not to treat. *Hematology.* 2005;10:69-72
- Morikawa M, Yamada T, Kataoka S, et al. Changes in antithrombin activity and platelet counts in the late stage of twin and triplet pregnancies. *Semin Thromb Hemost.* 2005;31:290-296.
- Weintraub AY, Sheiner E, Levy A, Yerushalmi R, Mazor M. Pregnancy complications in women with inherited thrombophilia. *Arch Gynecol Obstet.* 2006;274:125-129.