CLINICAL VIGNETTE

Immune Thrombocytopenic Purpura in a Pregnant Patient

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Case Report

A 25-year-old Hispanic female with no significant past medical history was referred to our institution for evaluation of thrombocytopenia in the setting of pregnancy. She initially presented to an outside facility complaining of "abdominal movement" and was found to have a 19-week intrauterine pregnancy. She reported gum bleeding brushing her teeth, as well as occasional blood clots from her nose after sneezing for the last two weeks. She denied any personal or family history of bleeding disorders and was taking no medications other than prenatal vitamins.

On physical exam, the patient had normal vital signs. There was neither gum bleeding nor petechiae on exam. Her pulmonary and cardiovascular examination was unremarkable and her abdominal examination was consistent with a 19-week pregnancy.

Laboratory evaluation revealed WBC of 7.8 x 10^9/L, hemoglobin of 11.7 g/dL, and platelets of 23 x 10^9/L. Liver function tests were within normal limits. Hepatitis panel, HIV, RPR and ANA were negative. The peripheral smear showed markedly decreased number of platelets with occasional large platelets.

The patient was treated as immune thrombocytopenic purpura (ITP) and initiated on oral prednisone at a dose of 1 mg/kg/day. She was monitored as an inpatient for 3 days and at the time of discharge, her platelet count had improved to 51 x 10^9/L. Two days later, her platelet count had increased to 145 x 10^9/L.

Discussion

Thrombocytopenia is defined as a platelet count of less than 150 x 10^9/L and is a common laboratory finding during pregnancy. As many as 10% of pregnant patients are thrombocytopenic at some point during pregnancy. The majority occurs during the third trimester as gestational thrombocytopenia. Most of these patients do not have a prior history of thrombocytopenia and present with low platelet counts for the first time during pregnancy. Patients are usually asymptomatic and have mild thrombocytopenia, with platelet counts generally above 50 x 10^9/L. However, when patients present with very low platelet counts and/or signs of bleeding, therapy is typically initiated.

The diagnostic workup of thrombocytopenia during pregnancy is very similar to that in a non-pregnant patient. A complete history and physical examination is important, with particular attention to any medication that may suggest an etiology of the low platelet count. The presence of symptoms may determine the aggressiveness of potential therapy. A complete blood count should be obtained and followed frequently, especially if thrombocytopenia is severe and/or causes symptoms. A peripheral blood smear is also indicated to corroborate the machine count and evaluate other morphologic abnormalities, such as schistocytes. Comprehensive metabolic panel, PT, PTT, hepatitis serologies, HIV and ANA titer are helpful to determine whether the low platelet count is associated with any particular syndrome and to rule out other causes of thrombocytopenia.

The differential diagnosis of thrombocytopenia in a pregnant patient is broad and includes immune thrombocytopenic purpura (ITP), gestational thrombocytopenia, preeclampsia, HELLP syndrome, thrombotic thrombocytopenic purpura (TTP), disseminated intravascular coagulation (DIC), systemic lupus erythematosus (SLE), viral infection, and medication use. The diagnoses of preeclampsia, HELLP syndrome, TTP, DIC, SLE can generally be established with the combination of physical examination findings, evaluation of peripheral blood smear, and a review of laboratory results such as liver function tests and antinuclear antibodies. Gestational thrombocytopenia is a mild incidental form of thrombocytopenia (typically a platelet count above 70 x 10^9/L) associated with pregnancy. Its etiology is not entirely clear, although it is thought to be related to relative hemodilution during pregnancy and accelerated clearance of platelets.
In contrast, ITP is a diagnosis of exclusion and describes the action of anti-platelet antibodies on platelet glycoproteins, resulting in a decrease in platelet count. The clinical presentation of patients with ITP ranges from absence of symptoms to symptoms such as petechiae, epistaxis, or gum bleeding. ITP may be clinically indistinguishable from gestational thrombocytopenia. In general, the onset of thrombocytopenia prior to 28 weeks gestation and a platelet count below 50 x 10^9 /L strongly suggest ITP. Extensive laboratory testing to distinguish gestational thrombocytopenia from ITP is unnecessary since treatment for presumed ITP is typically initiated based on platelet count and symptoms. Bone marrow biopsy and anti-platelet immunoglobulin measurements are not recommended.

The management of ITP in pregnancy is similar to that in other adult patient populations. However, the potential risks of the treatment in the developing fetus must be considered. As with other patients, the treatment for ITP involves corticosteroids, intravenous immunoglobulin (IVIg), and splenectomy. IV anti-D has also been shown to be effective. TPO-receptor agonists and cytotoxic agents such as cyclophosphamide and vinca alkaloids are contra-indicated during pregnancy given the potential teratogenic risks. The use of rituximab and azathioprine for ITP during pregnancy has not been evaluated and is generally avoided. The method of delivery of the fetus should be based on obstetric indications. There are currently no randomized studies to determine the optimal platelet thresholds for delivery.

**Corticosteroids**

As in non-pregnant patients, the administration of corticosteroids is considered to be first-line treatment for ITP during pregnancy. Short-term corticosteroids are generally safe to use during pregnancy, though hypertension, gestational diabetes mellitus and post-partum psychiatric disorders may be exacerbated. A starting dose of 1mg/kg/day (based on pre-pregnancy weight) is typically used, although some have advocated starting at a lower dose (10-20 mg/day). The initial dose is then slowly tapered to the minimum dose that can maintain an adequate platelet count. Tapering should not be too rapid in the last few weeks just before delivery in order to avoid potential bleeding complications.

**IVIg**

IVIg may be used if corticosteroids therapy is ineffective or causes significant side effects. In addition, some experts suggest high-dose IVIg (2 gm/kg) as a potential first-line therapy. No randomized trials have compared IVIg to corticosteroid therapy for ITP during pregnancy, although response rates are noted to be similar to those in the non-pregnant population. IVIg provides a rapid rise in the platelet count and may be considered for significant bleeding or during delivery. However, multiple courses of IVIg may have to be administered since responses are typically transient.

**Splenectomy**

If a patient fails first-line therapy, splenectomy is an option. However, the procedure may lead to preterm labor if performed in the first trimester and may be technically difficult in the third trimester given the increased size of the uterus. Data on the magnitude of splenectomy risks and on laparoscopic splenectomy are lacking. If the procedure must be performed, appropriate vaccination during or after pregnancy should be administered.

**Refractory ITP**

Patients who fail to respond to the above conventional therapies may respond to higher doses of corticosteroids and IVIg (methylprednisolone 1 gram, IVIg 1-2 gm/kg) in combination. IV anti-D at 50-75 µg/kg has been used in non-splectomized Rh(D)-positive patients and shown to be effective. Rituximab and azathioprine have been used during pregnancy for indications other than ITP without significant toxicity. Clinicians should carefully weigh the potential risks and benefits of cytotoxic agents during pregnancy.

**Conclusion**

Thrombocytopenia is not an uncommon finding in pregnancy. When it occurs, it is important to evaluate the patient thoroughly and determine what intervention, if any, is appropriate after weighing the risks and benefits of each potential treatment. In this case, our patient was diagnosed with probable immune thrombocytopenia purpura. Given the platelet count was quite low at 23 x 10^9 /L and the patient was symptomatic, oral prednisone at 1 mg/kg/day was initiated. The patient's platelet count...
responded appropriately, and corticosteroid therapy was eventually tapered.

REFERENCES


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