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STEROID RESISTENT IMMUNE THROMBOCYTOPENIC PURPURA IN PREGNANCY : A CHALLENGE TO MANAGE

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ABSTRACT Immune thrombocytopenic purpura is a common acquired autoimmune disorder defined by a low platelet count secondary to accelerated platelet destruction or impaired thrombopoesis by anti-platelet antibodies. The most common condition confused with ITP is gestational thrombocytopenia, which occurs in 4-8% of the pregnancies. A 21 year old G3A2 with 28 weeks of gestation case of steroid resistent Immune thrombocytopenic purpura managed by intravenous immunoglobulins with good maternal and fetal outcome .

KEYWORDS : autoimmune , Immune thrombocytopenic purpura , Intravenous immunoglobulins

INTRODUCTION

Immune thrombocytopenic purpura is an acquired autoimmune disorder characterized by a low platelet count secondary to accelerated platelet destruction and impaired thrombopoiesis as a result of circulating antiplatelet antibodies directed against platelet glycoproteins.[1] Immune thrombocytopenia (ITP) has been estimated to affect approximately 1 in 10,000 in the general population; about half of them are children. The incidence of ITP during pregnancy is reported to be 1-2 per 1,000 deliveries.[2] ITP is responsible for 4-5% pregnancy-associated thrombocytopenias.[3] The most important fetal or neonatal complication of ITP in pregnancy is "fetal or neonatal alloimmune thrombocytopenia."[4]

The approach to treatment of ITP during pregnancy is different from that in nonpregnant women because the potential side effects of drugs may complicate fetal development and the course of pregnancy. Glucocorticoids are considered for initial therapy if there are no life-threatening bleeding symptoms. Other treatment options include intravenous immunoglobulin (IVIgG), which is safe for the fetus but often associated with maternal side effects and high costs. Experience with anti-Rh(D) therapy in pregnant women is limited.[4]

CASE REPORT

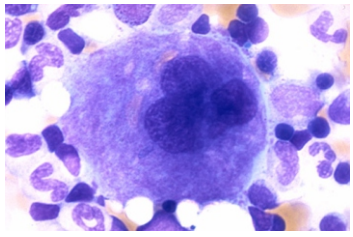
A 21 year old G3A2 with 28 weeks of gestation admitted i/v/o thrombocytopenia . She was given platelet transfusions eight times in the current pregnancy before she was admitted to our hospital .No complaint of bleeding from any site of body ,petechial rashes on admission. On examination, She had no pallor,icterus or lymphadenopathy. The blood pressure was 110/80 mm Hg. Cardiovascular and chest examinations were unremarkable. Abdominal examination revealed no hepatosplenomegaly. Uterus was 22 weeks enlarged.

Her investigations revealed haemoglobin to be 11.2 gm/dl, total leucocytic count to be 11,900 /µl (differential: 74% neutrophils, 17% lymphocytes, 3% monocytes, and 1.2% eosinophils). The platelet count was 10,000 /µl. PBS- normocytic normochromic ,leucocytosis with giant platelets with markedly reduced platelets ,no parasite detected. Urine examination was unremarkable. Kidney and liver function tests were within normal limits.

Antinuclear antibody, beta 2 microglobulin, lupus anticoagulant, anticardiolipin antibodies were negative. Dengue antigen,antibody negative.Usg abdomen no hepatosplenomegaly detected .Bleedi ng time prolonged(9min),clotting time normal ,aptt normal(30s).USG obstetrics -normal with normal doppler study. **Bone marrow** aspirate showed normal maturation of myeloid and erythroid series. Megakaryocytes were seen.

After advice from haematologist patient was started on tab.pred nisolone 40 mg daily, (platelet count -8000 /µl).simulta niously 4 platelet transfusion also given.After 2 weeks of treatment,platetet count did not improve so, prednisolone was increased to 50 mg daily ,added with tab daspsone 100 mg daily and tab azathioprine 75mg daily started .after 3 weeks of treatment platelet count increased to 50, 000 /µl. Regular monitoring of platetlet count was continued .At 37 weeks of gestation platelet count again droped progressively to 9000 /µl, even after regular drug intake platelet count was not improving and patient developed purpuric rashes on face and abdomen.Again 4 point platelet transfusion was given .Decision for INTRA VENOUS IMMUNOGLOBULIN was taken and at patient was given 45gm of IVIG 2 doses. The platelet count increased to 1,50,000 cells per cu mm on the 3rd day.

At 38 weeks of gestation, she delivered an active male baby weighing 3 kg with LSCS i/v/o fetal distress . As platelet count was 1,45000 /µl , no platelet transfusion was given at time of delivery . The postpartum and peripartum periods were uneventful. On investigation of baby did not have neonatal thrombocytopenia .after 1 month post delivery platelet count again dropped to 20,000 /µl but no purpuric rashes nor any active bleeding from any site .and patient was advised to continue oral steroids and immunospr essents,regular follow up. As due to financial reasons repeated intravenous immunoglobulin was not possible .



BONE MARROW WITH MEGAKARYOBLAST IN IMMUNE THROMBOCYTOPENIC PURPURA

Discussion

ITP is caused by antiplatelet antibodies called platelet-associated immunoglobulin (PAIg), which binds to glycoprotein (GP) IIb/IIIa complex or GP1b/IX complex or other glycoprotein complexes. This antibody-coated platelets are destroyed by tissue macrophages located primarily in the spleen.[6,7] A marked reduction in platelet production was also observed in acute and chronic ITP since autoantibodies against this platelet glycoprotein interfere with megakaryocytic maturation.[8,9]

The most common condition confused with ITP is gestational

thrombocytopenia, which occurs in 4-8% of the pregnancies. Gestational thrombocytopenia is likely when an otherwise healthy woman with a previously documented normal platelet count develops mild thrombocytopenia with platelet count between 70,000/µl and 100,000/µl in the third trimester of an uncomplicated pregnancy. ITP generally causes moderate to severe throm bocytopenia in the first trimester. ITP may exacerbate during pregnancy but generally the platelet count returns to the prepregnancy level after delivery.[10]

While treating ITP during pregnancy, the potential side effects of the drugs have to be considered as they affect the course of the pregnancy and the development of the fetus. A multidisciplinary approach should be adopted to manage the mother and fetus with the help of a hematologist, an obstetrician, and a neonatologist.

Glucocorticoids are considered for initial therapy if there is no life-threatening bleeding. Glucocorticoids are not teratogenic but they can induce gestational diabetes or hypertension. Cytotoxic drugs, such as vinca alkaloids, azathioprine, and cyclophosphamide, are potentially teratogenic. In our patient, azathioprine was started during the second trimester. The rigors of splenectomy may induce preterm labor and so it was not considered for our patient. IVIg should be considered if patients fail to respond to glucocorticoids and if there is life-threatening bleeding, IVIg is safe for the fetus but is often associated with maternal side effects, its effect is transient, and it is not cost-effective. Experience with anti-(Rh)D therapy in pregnant women is limited.[4]

Some studies showed that eradication of H. pylori with antibiotics resulted in a marked increase in the platelet count in patients with ITP.[11]

Platelet count and bleeding symptoms are important for the management of these patients. A platelet count above 30,000/µl with no bleeding symptom requires only observation. Platelet transfusions are required if a pregnant woman has a platelet count of less than 10 × 109/L in any trimester, a platelet count of 10 to 30 × 109/L in the third trimester, or if there is any sign of bleeding.

Platelet requirement -vaginal delivery(20,000 /µl),caesarean delivery(50,000 /µl),regional anesthesia(75,000 /µl).

Intravenous immunoglobulin (IVIG) preparations comprise pooled IgG antibodies from the serum of thousands of donors and were initially used as an IgG replacement therapy in immunoco mpromised patients. Since the discovery, more than 30 years ago, that IVIG therapy can ameliorate immune thrombocytopenia, the use of IVIG preparations has been extended to a wide range of autoimmune and inflammatory diseases. Despite the broad efficacy of IVIG therapy, its modes of action remain unclear. In this Review, we cover the recent insights into the molecular and cellular pathways that are involved in IVIG-mediated immunosuppression, with a particular focus on IVIG as a therapy for IgG-dependent autoimmune diseases The rapid rise in platelet count after immunogl obulin treatment in acute and chronic forms of idiopathic thrombocytopenic purpura (ITP) is well documented. It is suggested that the rise in platelet count is due to competitive inhibition of the macrophage binding of platelets by preferential sequestration of immunoglobulin-coated red blood cells. Inspite of all benefits it is not regularly used as not cost effective .

Conclusion

Intravenous immunoglobuline can be considered as a treatment option in transfusion-dependent pregnant patients with ITP who failed to respond to steroids and immunosuppressant. We can also reduce the risks associated with repeated platelet transfusions.

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