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JOURNAL OF Gynecological Research and Obstetrics OPEN ACCESS JOURNAL

ISSN: 2581-5288 DOI: https://dx.doi.org/10.17352/jgro

Case Report

Immune thrombocytopenia secondary to Cytomegalovirus infection during pregnancy: A case report and review of the literature

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Received: 25 October, 2022
Accepted: 03 November, 2022
Published: 04 November, 2022

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Keywords: Pregnancy; Thrombocytopenia; Cytomegalovirus; Immune thrombocytopenic purpura; Neonatal thrombocytopenia; Congenital cytomegalovirus infection

Abstract

Background: Cytomegalovirus (CMV) is a rare cause of Immune Thrombocytopenic Purpura (ITP) and even rarer during pregnancy.

Case: A 27-year-old pregnant woman presented with severe thrombocytopenia in the latent phase of labor. She was treated with dexamethasone and platelet transfusions and underwent a successful vaginal delivery. The neonate had severe thrombocytopenia as well. Serology assays of the mother revealed CMV seroconversion with a negative Polymerase Chain Reaction (PCR). The neonate had a positive PCR and was treated with Intravenous Immunoglobulin (IVIG), steroids, platelets and Valganciclovir with a good response. The mother's platelet count normalized three months later.

Conclusions: CMV infection should be considered as a potential cause for severe thrombocytopenia during pregnancy and can lead to early detection and treatment for Congenital CMV.

Introduction

Thrombocytopenia, defined as a platelet count of less than 150 K/uL, is common and occurs in 7% - 12% of pregnancies at the time of delivery [1]. The most common etiology is Pregnancy-Associated Thrombocytopenia (PAT), which accounts for 65% to 80% of the cases [2]. The most common non-pregnancy-related cause is Immune thrombocytopenic purpura (ITP). Nonetheless, the incidence of ITP with a platelet count below 50 K/uL is rare and occurs in only 0.85 per 100,000 pregnancies [3].

Viral infections such as rubella, varicella, mumps, Cytomegalovirus (CMV) and Epstein-Barr virus have all been linked to ITP. In children, ITP has been estimated to be post-infectious in approximately two-thirds of the cases. It is hypothesized that "molecular mimicry" leads to the production of anti-platelet antibodies that cause immune dysregulation and platelet destruction [4].

Herein we present a case of immune-mediated thrombocytopenia secondary to CMV during pregnancy. To date, this is the second case in the literature.

Case presentation

A 27-year-old, 39+0 weeks pregnant woman presented to the obstetric emergency department because of uterine contractions. Her pregnancy up until that point was uneventful,

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except for one episode of petechia on her limbs at 27 weeks. She was asked by her primary obstetrician to perform a complete blood count but failed to do so. She also mentioned an episode of epistaxis during pregnancy, without any gingival bleeding, which resolved spontaneously. Her prenatal follow-up was sparse. She did not do any prenatal genetic or biochemical screening, diabetes screening, or organ scans during her pregnancy.

She was normally healthy, without any previous surgeries, had no known drug allergies, and did not take any medications. Her obstetric history included one vacuum delivery at term (birth weight 2800 g) and no spontaneous miscarriages. She had no known personal or family history of venous thromboembolism or clotting abnormalities. Her social history was negative for smoking, drugs, or alcohol consumption. She denied any toxemia-related symptoms, or recent febrile illness, but mentioned that her 2-year-old son had a fever that lasted one day, a week and a half prior to admission and that her two nephews were recently "unwell". Serology tests that were performed 4.5 months earlier included: CMV IgG negative/IgM negative, HBsAg negative, HCV negative, Rubella IgG positive and Treponema Pallidum negative.

On physical examination: the patient had normal vital signs without any fever. She had a mild rash on her face (cheeks), which was described as "flushing". According to the patient the rash had been present for 6-7 years and was treated with minocycline in the past with partial improvement. The rest of her skin was without any rash, petechiae, purpura, or without edema. No mucosal bleeding was present. Her abdomen was soft and non-tender, and her heart and lungs were without any abnormalities. Fetal monitoring and sonogram were reassuring and on vaginal examination, the cervix was 1.5 cm dilated. Her laboratory results showed isolated thrombocytopenia of 35 K/uL platelets, No anemia or leukopenia, normal liver and kidney functions, normal electrolytes, and normal Clotting function. A blood smear showed megakaryocytes without fragmented cells or blast cells. A previous complete blood count performed 4.5 months earlier was normal: 178 K/uL platelets. The urine dipstick was normal.

The patient was admitted to the fetal-maternal unit with a working diagnosis of ITP and was treated with IV dexamethasone and 6 platelet transfusions with an improvement in her platelet count to 149 K/uL. She delivered vaginally 36 hours after admission, a 3,150 g male, with an Apgar score of 9/10. On initial exam, the neonate was noted to have widespread petechiae, and a complete blood count showed a platelet count of only 8 K/uL. The neonate was given multiple doses of platelets, IVIG and steroids.

The mother had one episode of fever after delivery and she was treated with antibiotics (amoxicillin and clavulanic acid) until blood cultures came back negative. Abdominal ultrasound postpartum showed homogenous splenomegaly of 14.1 cm. Serology for HIV and Coxiella Burnetii were negative, but a repeat serology for CMV came back positive for CMV IgG and IgM antibodies. CMV IgG AVIDITY 0.64 implying infection was not recent and had most probably been in the second trimester.

Due to the suspicion of maternal CMV, the neonate was tested and found to have a PCR positive for CMV in the saliva and urine, and was treated with Valganciclovir with good response, and suffered no significant bleeding.

The mother was treated with steroids and was discharged for ambulatory follow-up with a platelet level of 78 K/uL. One month after delivery, the patient's platelets were still low (40 K/uL platelets) despite steroidal treatment, and she was admitted for further evaluation.

CMV PCR was taken and the patient started treatment with IV Ganciclovir while awaiting the results. There was a mild improvement in her platelet count to 59 K/uL. She was also evaluated for connective tissue diseases: antinuclear antibody (ANA), Anti-neutrophil cytoplasmic antibodies (ANCAs), anti-double-stranded DNA (anti-dsDNA) and anti-phospholipid antibodies all returned negative. C3, C4 and Rheumatoid Factor (RF) were normal.

She continued treatment with oral Valganciclovir until the result of the negative CMV PCR. Following this, all medication was stopped. Platelets returned to normal without any further treatment by three months post-delivery (Figure 1).

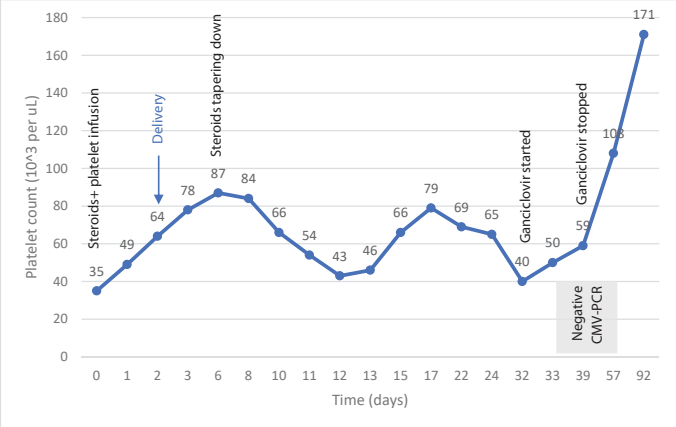

Figure 1: Change in the patient's platelet count over time.

Discussion

In this case, we presented a pregnant patient with severe isolated thrombocytopenia that was first discovered when the patient was already in the latent phase of labor. An accurate diagnosis had to be made as quickly as possible, to give her the most appropriate treatment.

The differential diagnosis of thrombocytopenia during pregnancy is wide, but usually pregnancy related. Nonetheless, when the platelet count is below 100 K/uL, an underlying medical condition should be considered such as autoimmune diseases (systemic lupus erythematosus and antiphospholipid antibody syndrome), infections (particularly Human Immunodeficiency Virus, Hepatitis C and CMV), drug-induced thrombocytopenia, systemic disorders (such as disseminated intravascular coagulation or thrombotic thrombocytopenic

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purpura), splenic sequestration, hereditary thrombocytopenia, and primary bone marrow disorders (such as myelodysplastic syndrome and acute leukemia). In this case, even though the woman had a negative serology a few months earlier, and was without any signs of infection, the fact that we widened our differential diagnosis enabled us to reach a more rapid neonatal diagnosis and start earlier treatment for Congenital CMV infection.

Several cases of CMV-induced thrombocytopenia, in immunocompetent adults, have been reported in the literature [5-7]. In some cases, especially with active CMV infection, the thrombocytopenia persists despite standard steroid therapy and even worsens with corticosteroids [6]. DiMaggio, et al. showed an improvement in the platelet counts after starting gancyclovir and Cytogam with steroid taper [6].

There is limited literature on ITP secondary to CMV during pregnancy. We found only one case report of an immunocompetent pregnant female diagnosed with CMV-associated ITP [4]. Shimanovsky, et al. presented a pregnant woman with refractory ITP that started in the first trimester. After a successful delivery, the newborn was thrombocytopenic with congenital CMV. One week after delivery, the patient's platelet count began to improve and was normalized ten months after delivery without treatment. The researchers hypothesized that the placenta was a reservoir for CMV, thus causing persistent ITP that was refractory to standard therapy, resolving only after delivery. In our case, the mother also had a spontaneous recovery after birth with steroid tapering, and she returned to normal platelet count three months after delivery.

This case depicts an exceedingly rare cause of ITP in pregnancy (the second case in the literature). Despite its rarity, the correct diagnosis was made, which led to early detection and treatment for Congenital CMV. It emphasizes the importance of a wide differential diagnosis when addressing thrombocytopenia during pregnancy.

This figure shows the change in the patient's platelet count over time. We can see that the patient platelet count improved spontaneously after birth, returning to the normal range three months post-partum.

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