Neonatal thrombocytopenia associated with placental insufficiency: A case report

Laksmi Handini[1]

[1]Faculty of Medicine Universitas Pembangunan Nasional Veteran Jawa Timur

Corresponding Author:

Laksmi Suci Handini

Faculty of Medicine Universitas Pembangunan Nasional Veteran Jawa Timur

Rungkut Madya Street Number 191, Rungkut Kidul, Rungkut District, Surabaya, Jawa Timur 60293

Tel/Fax: +6287880020082

Email: laksmi.suci.fk@upnjatim.ac.id

Abstract

Thrombocytopenia commonly found in neonatal, especially in ill-appearing infant. However, it may happened in well-appearing infant. This following case showed infant could have thrombocytopenia right after delivery process. This thrombocytopenia phenomenon assumed due to plasental insufficiency in mother with preeclampsia. Placental insufficiency is a condition where the placenta, which is responsible for providing nutrients and oxygen to the developing fetus, is not functioning adequately. Finding the correct etiology made early interventions given in this patients.

Keywords. Neonatal, thrombocytopenia, preeclampsia, plasental insufficiency

Introduction

Thrombocytopenia, defined as a platelet count below 100 x 10^9/L, is a very common finding in the neonatal period, especially in critically ill infants and preterm newborns. Its causes are multiple: it may be due both to pediatric conditions and to other factors involved in the fetal-placental-maternal interface. This case report discusses early onset thrombocytopenia in well appearing infant of maternal pre-eclampsia. Understanding the underlying causes, diagnostic pathways, and tailored interventions for neonatal thrombocytopenia due to placental insufficiency is crucial for optimizing neonatal outcomes and long-term health.

Case Illustration

A well-appearing male infant was born at 38 weeks gestational age by Caesarean Section with indication maternal pre-eclampsia. At 28 weeks gestation, maternal blood pressure was beginning to increase and at 32 weeks gestation there were swollen legs and proteinuria. The infant had good Apgar score at birth with 3570-gram birth weight and 50 centimeters length. The infant had normal facies without syndromic features and normal head circumference. He had no hepatosplenomegaly or other notable physical findings. The baby began got routine neonatal care with vitamin k injection and eye ointment. Early skin to skin and breastfeeding was done well in the first two hours of birth. At the age 3 hours there were petechiae noticed at baby's facial skin and the observation showed that it spread to the trunk and extremities of baby within 5 hours. Routine blood examination showed severe thrombocytopenia at the age 8 hours with platelet count was 22 $x10^9$/L, Hemoglobin count was 16 g/dL, white blood count was 19,8 with 49,8 in hematocrit. Head ultrasound was not performed for intracranial hemorrhage but there were no signs of it. The infant suffered slight difficulty of breathing with sign of nostril breathing so nasal oxygenation was given with flow 0,5 liter/minute.

The infant was transferred to the neonatal intensive care unit (NICU) and received a transfusion of apheresis donor platelets (blood type AB Rhesus positive), with increase in platelet count to 330 × 10^9/L. Infant's condition increase rapidly and discharge at day 3 with negative antibody IgM Cytomegalovirus. The following routine blood examination showed platelet count above 300 $x10^9$/L at outpatient clinic visit and the infant grows well.

Discussion

Platelets are highly organized nuclear cellular fragments involved in primary hemostasis. Megakaryocyte progenitor cells develop under the stimulus of thrombopoietin to produce platelets. Mature megakaryocytes then generate and release platelets into the bloodstream, where they have a half-life of 7 to 10 days.[1]

Neonatal thrombocytopenia refers to a condition in which a newborn baby has a low platelet count in the blood. Platelets are crucial for blood clotting, and a decreased platelet count can lead to an increased risk of bleeding or bruising.[2] Neonatal immune thrombocytopenia represent less than 5% of cases of early thrombocytopenia (early-onset <72 hours post-delivery). As in adults, thrombocytopenia in neonates is defined as a platelet count less than 100 x 10^9/L. They are either auto- or alloimmune. The major complication of severe thrombocytopenia is bleeding and particularly intracranial hemorrhage and neurologic

sequalae following.[3] A prospective study of 807 hospitalized NBIs found severe thrombocytopenia in 20 % of subjects.[3] A similar study reported that thrombocytopenia was much more common among preterm (18.2 %) than term infants (0.8 %).[4] Newborns in particular may be predisposed to bleeding events as a result of recent trauma associated with the birthing process. The most feared bleeding complication in the newborn population is intracranial hemorrhage (ICH), due to risk of death and adverse neurologic outcomes.

Etiologies are divided into two broad categories according to the time of onset of thrombocytopenia (less or more than 72 hours).[2] Early thrombocytopenia (less than 72 hours) is mainly due to chronic fetal hypoxia (placental vascular pathologies, intrauterine growth retardation), viral (CMV, HIV, etc) and bacterial (*Streptococcus*) infections and disseminated intravascular coagulation. Neonatal immune thrombocytopenia accounts for less than 5% of early thrombocytopenia, with maternal-fetal platelet alloimmunization and thrombocytopenia of autoimmune origin, mainly due to idiopathic thrombocytopenic purpura or maternal systemic lupus erythematosus.[3]

The differential diagnosis for thrombocytopenia is classically divided into disorders of decreased platelet production versus those of increased platelet consumption. However, when assessing the infant with thrombocytopenia, it is more useful to consider the overall clinical picture of the patient, as the common causes of thrombocytopenia in the “sick” infant tend to be distinct from the most likely causes in well-appearing infants.[1]

Table 1. Cause of Neonatal Thrombocytopenia

	Ill-Appearing, premature		Well-Appearing, full term	
Type	Early onset (< 24 h)	Late onset (> 72 h)	Early onset (< 24 h)	Late onset (> 72 h)
Common	Sepsis TORCH infection Birth asphyxia DIC NEC	Sepsis Thrombosis DIC NEC Drug-induced	Plasental insufficiency Autoimmune Alloimmune (NAIT) Occult infection	Occult infection Anemia
Rare	Chromosomal disorders. • Trisomy 13 • Trisomy 18 • Trisomy 21 • Turner syndrome	Inborn error of metabolism Fanconi anemia	Inherited syndromes • Bernard-Soulier • Wiskott-Aldrich • Thrombocytopenua absent radii • Others vascular tumors	Inborn error of metabolism Fanconi anemia

			• Kasabach-Merritt	

In healthy-appearing infant, thrombocytopenia is most likely secondary to placental insufficiency or an immune-mediated process, either autoimmune or alloimmune, in which maternal antibodies passed to the newborn in-utero lead to destruction of the baby's platelets. Of these, neonatal alloimmune thrombocytopenia (NAIT) produces the most pronounced thrombocytopenia, with platelets typically below 50 × 103 /mcL.[3] NAIT occurs when the fetus inherits a paternal platelet antigen not carried by the mother; this antigen then becomes a target for maternal antibodies. Maternal platelets are not targeted and are thus within normal range. NAIT affects an estimated 1 in 800 to 1,000 children of live births.[6] Unlike Rh-incompatibility, NAIT frequently causes disease in a woman's first pregnancy. The severe thrombocytopenia caused by NAIT carries a significant risk of potential morbidity and mortality. Approximately 10% to 30% of newborns with NAIT will develop ICH, with about half occurring in-utero; neurological sequelae and death will occur in 20% and 10% of affected neonates, respectively.[7]

In contrast, placental insufficiency usually produces only mild to moderate thrombocytopenia (50 × 103 to 150 × 103 /mcL) that resolves spontaneously within 7 to 10 days after birth. Clinical features supportive of this diagnosis include an infant who is small for gestational age, a history of intrauterine growth restriction, or maternal hypertension, diabetes, or preeclampsia.[1] Autoimmune thrombocytopenia typically causes a similarly mild to moderate thrombocytopenia and results from maternal autoantibodies targeting both maternal and fetal platelets. Maternal platelet counts are expected to be low; however, the severity of maternal thrombocytopenia does not correlate well with the degree of thrombocytopenia in the infant.[1] As a result, a newborn whose mother is known to have idiopathic thrombocytopenic purpura, systemic lupus erythematosus, or other autoimmune disease should be screened for thrombocytopenia at birth, regardless of maternal platelet count at delivery. Platelet levels eventually normalize at age 10 to 60 days as maternal autoantibodies are cleared from the baby's circulation.

Placental insufficiency is a condition where the placenta, which is responsible for providing nutrients and oxygen to the developing fetus, is not functioning adequately. This insufficiency can result in various complications for the fetus, including thrombocytopenia. The etiology of neonatal thrombocytopenia can be associated with placental insufficiency, as follows:

1. Platelet formation in fetal liver. Platelets are produced in the fetal liver. Placental insufficiency can lead to inadequate oxygen and nutrient supply to the fetus, affecting the development and function of organs, including the liver. Impaired liver function may contribute to lower platelet production.
2. Immune-mediated destruction. Placental insufficiency can lead to intrauterine growth restriction (IUGR), where the fetus does not grow adequately. In IUGR, the fetal immune system may be activated, leading to the destruction of platelets, a condition known as immune-mediated thrombocytopenia.
3. Hematopoietic stem cell development. Placental insufficiency can disrupt the normal development of hematopoietic stem cells in the fetus, affecting the production of various blood cells, including platelets.
4. Hypoxia-induced thrombocytopenia. Insufficient oxygen supply to the developing fetus (hypoxia) due to placental insufficiency can affect the maturation and function of platelets, leading to thrombocytopenia.
5. Inflammatory responses. Placental insufficiency may trigger inflammatory responses in the fetal circulation, affecting platelet function and survival.

Diagnosing and managing neonatal thrombocytopenia due to placental insufficiency involves close monitoring of the baby's platelet count, identifying the underlying cause, and providing appropriate medical interventions. Treatment may include supportive care, addressing the underlying cause, and in severe cases, transfusions of platelets.

The treatment approach for neonatal thrombocytopenia primarily depends on the severity and cause of the condition. In cases attributed to placental insufficiency, supportive care and management of complications are crucial.

Platelet transfusion is recognized as a vital therapy, particularly in hematological malignancies. Although controversies have emerged in recent years, it remains necessary to save the lives of patients every day. Transfusing platelets may be considered in severe cases to prevent bleeding complications. (**Figure 1**)

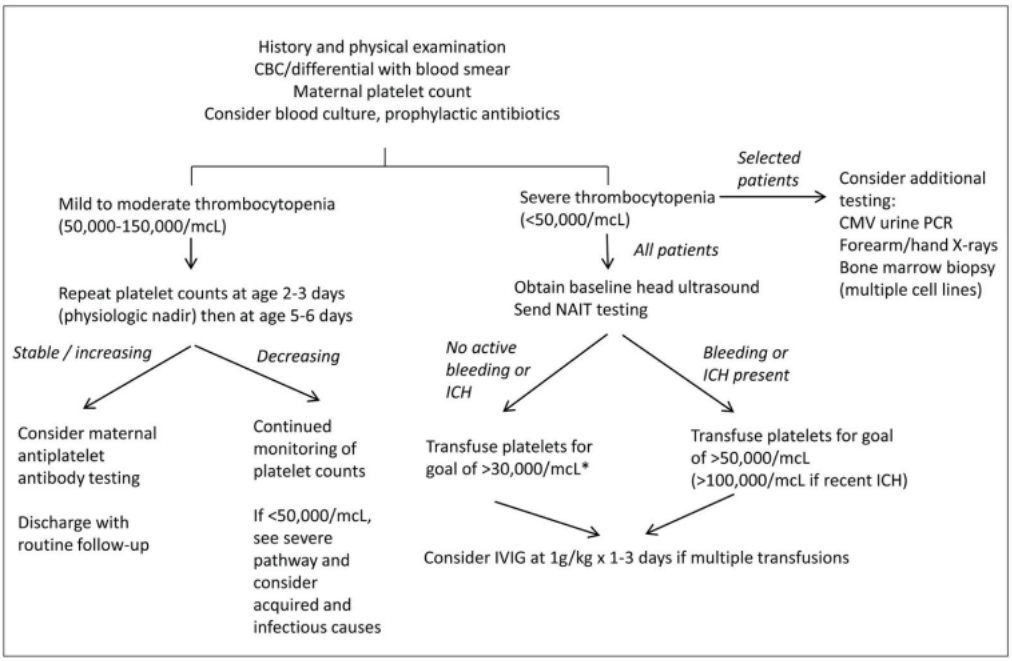

Figure 1. Approach to the well-appearing newborn with platelets <150,000/mcL. CBC, complete blood count; CMV, cytomegalovirus; ICH, intracranial haemorrhage; IVIG, intravenous immunoglobulin; NAIT, neonatal alloimmune thrombocytopenia; PCR, polymerase chain reaction.

There are currently differing opinions on when exactly is the correct time to transfuse without bleeding, but many centers follow these guidelines. If available, washed maternal platelets are preferred due to high suspicion of NAIT in an otherwise well-appearing term infant with severe thrombocytopenia. Random donor platelets can be used if washed maternal platelets are unavailable. If diagnosis of NAIT is not established, some institutions will transfuse random donor platelets initially to look for a subsequent sustained increase in platelet counts, which suggests against NAIT.[1]

Severe neonatal thrombocytopenia due to placental insufficiency can lead to intracranial hemorrhage, neurodevelopmental issues, and long-term health concerns. Long-term monitoring and potential intervention may be required to address developmental delays and associated complications. It's essential for healthcare professionals to closely monitor newborns at risk for neonatal thrombocytopenia and address any associated complications promptly. Management decisions will depend on the specific circumstances of each case.

Conclusion

In conclusion, understanding the underlying causes, diagnostic pathways, and tailored interventions for neonatal thrombocytopenia due to placental insufficiency is crucial for optimizing neonatal outcomes and long-term health.

References

1. Sillers L, Slambrouck CV, Lapping-Carr G. Neonatal thrombocytopenia: etiology and diagnosis. Pediatr Ann. 2015 July;44(7):e175–e180.
2. Donato Hugo. Neonatal thrombocytopenia: A review. I. Definitions, differential diagnosis, causes, immune thrombocytopenia. Arch Argent Pediatr. 2021 Jun;119(3):e202-e214.
3. Petermann R. Platelet transfusion role in neonatal immune thrombocytopenia. Transfus Clin Biol. 2016 Nov;23(4):217-221.
4. Castle V, Andrew M, Kelton J, Giron D, et al. Frequency and mechanism of neonatal thrombocytopenia. J Pediatr. 1986; 108(5 Pt 1):749-55. 7.
5. Oren H, Irken G, Oren B, Olgun N, et al. Assessment of clinical impact and predisposing factors for neonatal thrombocytopenia. Indian J Pediatr. 1994; 61(5):551-8.
6. Kamphuis MM, Paridaans NP, Porcelijn L, Lopriore E, Oepkes D. Incidence and consequences of neonatal alloimmune thrombocytopenia: a systemic review. Pediatrics. 2014; 133(4):715–721.
7. Kaplan C. Immune thrombocytopenia in the fetus and the newborn: diagnosis and therapy. Transfus Clin Biol. 2001; 8:311–314.