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Neonatal Thrombocytopenia

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Abstract

Platelets are the clotting factors in the blood, produced by Tpo and Interleukin-ll stimulator in megakaryocytes during Megakaryopoiesis, in neonates thrombopoiesis occurs in is bone marrow, Liver and Placenta. Platelets formulation begin at 5 weeks of gestation and reach the adult count in 24 to 28 weeks. 0.5% neonates develop severe thrombocytopenia and 5% newborn can develop thrombocytopenia due to impaired Platelet production, increased Platelet destruction and sequestration. Increase platelet destruction can be immune mediated or non-immune, associated with other diseases and immune mediated thrombocytopenia occur due to Alloimmune thrombocytopenia (NAIT), Auto immune thrombocytopenia or due to maternal antiplatelet antibodies. Onset of neonatal thrombocytopenia occurs within 72 hours and late onset after 72 hours risk intraventricular heamorrhage. Thrombocytopenia risks factor for Intracranial Haemorrhage. The present article describes the causes, clinical findings and the management of the neonatal thrombocytopenia.

Keywords: neonatal thrombocytopenia, neonatal alloimmune thrombocytopenia, management of neonatal thrombocytopenia

Introduction

Meaning of neonatal thrombocytopenia

Thrombocytopenia is defined as platelet count less than 150,000/microL, classified as mild, moderate and severe. In neonate thrombocytopenia is classified as early when decrease platelet count occur in first 72 hours and late thrombocytopenia occur after 72 hours of delivery.[6]

Risk factor and etiology associated with the incidence of neonate thromobocytopenia

Maternal factors: maternal history of thrombocytopenic purpura, systemic lupus erthymatous, previous delivery with thrombocytopenia affected child, genetic and chromosopmal disorders like trisomies 21,18 and 13, congential infection through vertical transmission like cytomegalovirus, rubella.[2]

Neonatal etiology

1. Increases destruction
2. Neonatal alloimmune thromobocytopenia
3. Neonatal autoimmune thrombocytopenia
4. Disseminated intravascular coagulation
5. Thrombosis
6. Type2b von willebrand diseases
7. Decreases production
8. Preeclampsia
9. Genetic disorders-congenital platelet disorders, chromosome abnormalities
10. Infiltrative disorders
11. Infection
12. Asphyxia

13. Drug related thrombocytopenia
14. Dilution
15. Hemolytic-uremic syndrome
16. Thrombotic thrombocytopenic purpura
17. Kasabach-Merritt syndrome
18. Necrotizing enterocolitis
19. Cyanotic congenital heart disease
20. Bone marrow failure or infiltrate- Acute lymphoblastic leukemia and other
21. Acquired aplastic anemia
22. Fanconi pancytopenia
23. Nutritional deficiencies
24. Genetically impaired thrombopoiesis
25. Thrombocytopenia with absent radii syndrome
26. Congenital amegakaryocytic thrombocytopenia
27. Wiskott-Aldrich syndrome
28. X-linked thrombocytopenia with thalassemia
29. Giant platelet disorders
30. Bernard-Soulier syndrome
31. May-Hegglin/Fechtner/Epstein and Sebastian syndromes

Mechanisms of thrombocytopenia in neonate

Placental insufficiency or fetal hypoxia are complication may raise impaired platelet production, develop thrombocytopenia by 72 hours, preterm may develop intrauterine growth restriction. The neonates have impaired megakaryopoiesis the megakaryocytes and progenitor cells are considerably reduced at birth and thrombo-poietin (Tpo) levels are elevated, This form of thrombocytopenia is usually mild to moderate and restrict and control and resolve within 10 days. The affected neonates also have a number of additional associated haematological abnormalities like neutropenia, increased numbers of circulating nucleated red cells with or without associated polycythaemia, increased erythropoietin levels and evidence of hyposplenism (spherocytes, target cells and Howell-Jolly bodies) and congenital amegakayocytic thrombocytopenia, thrombocytopenia with absent radii syndrome (TAR), Fanconi' s anemia (FA), Infants with trisomies of chromosome 13, 18, 21, Turners syndrome, congenital neuroblastoma, congenital leukemia, and thrombocytopenia with radioulnar synostosis.[1,2]

Increased platelet destruction and sequestration – It occur due to transplacental passage of of maternal platelet auto and allo antibodies. Disseminated intravascular coagulation is responsible for another 15% of cases with very ill babies in association of severe birth asphyxia and infection.

Immune mediated thrombocytopenia is Neonatal Alloimmune Thrombocytopenia (NAIT) occur due to trans-placental passage of maternal alloantibody against foetal platelets with inherited paternal antigen.[3]

In this condition the mother is asymptomatic and the neonates are with features of depending on severity of thrombocytopenia.

Autoimmune Thrombocytopenia- neonates generate autoantibodies against its own platelet and it is usually associated with other immune disorder.

Non immune thrombocytopenia occurs mainly due to accelerated platelet destruction, bacterial or viral sepsis, infection with Human Immuno Virus, Herpes simplex, cytomegalovirus, rubella etc, protozoal infections (toxoplasma, congenital malaria), necrotising enterocolitis, haemangiomas (Kassabach merritt syndrome), Disseminated intravascular coagulation, birth asphyxia and meconium aspiration syndrome in term neonates indwelling umbilical catheter, and respiratory distress syndrome in preterms, polycythemia and PPHN (persistent pulmonary hypertension).[5]

Combined mechanism is observed in mother with history of pre-eclampsia, occurred fur to bacterial infection, and baby with intrauterine growth retardation results in necrotising enterocolitis leads to impaired platelet production.

In preterm and Intra uterine growth retardation babies the early thrombocytopenia is self limiting and resolves spontaneously in 10 days

Late onset thrombocytopenia, is caused by sepsis and necrotising enterocolitis.[4]

Approach to understand the thrombocytopenia in newborn

The following are the steps in managing the child with thrombocytopenia:

Step1- term of gestation: preterm or term baby?

Step2 – is the new-born look healthy or ill?

Step3 – is the illness associated with medical condition?

Step4 – presence of congenital disorders in new-born

Volume 5, Issue 3; May-June 2022; Page No 330-334

Step5 – the congenital anomaly and dysmorphism association?

History collection in diagnosing neonatal thrombocytopenia

The Maternal history is examined for immune thrombocytopenia, systemic lupus erythematosus, drug history, history of previously thrombocytopenic affected baby, still birth, Pregnancy Induced Hypertension, eclampsia, intrauterine growth retardation, congenital and perinatal infection and history of perinatal asphyxia increases the incidence of thrombocytopenia in the neonates. Clinical identification like Dysmorphic features and abnormal physical findings indicating syndromic babies, jaundice, hepatosplenomegaly and retinal findings may suspect congenital intrauterine infection.[6,7]

Family history – There may be a family history of bleeding disorders, or a previously affected infant (NAIT).

Complication arose during labour should be recorded and documented Histopathologic examination of the placenta performed for evidences of congenital infection (CMV, syphilis), vasculopathy (preeclampsia or other maternal vasculopathy), haemorrhage, infarcts, thrombi, and rarely, vascular malformations or malignancy.

Examination- infant should be examined for evidence and extent of bleeding. Bleeding into the skin is one of the most common findings are petechiae, non-palpable purpura, and ecchymoses, neonatal bleeding will be manifested by cephalohematoma, bleeding from the umbilical cord or puncture sites, hematemesis, melena, and blood-tinged secretions.[8]

Overall clinical status of child, healthy infants are more likely to have immune or genetic causes of thrombocytopenia, whereas ill-appearing infants (poor perfusion, lethargy, respiratory distress, and apnea).

Laboratory studies for neonatal thrombocytopenia

Complete blood count- The CBC, which demonstrates a low platelet count, should also be evaluated for anemia and/or neutropenia.

Peripheral smear- Examination of the peripheral smear determines the platelet size and morphology, which can help distinguish between a destructive or consumptive process (large platelet size) and a decrease in platelet production (normal or small platelet size). In addition, platelet size and morphology can also be helpful in detecting congenital platelet disorders, which may have varying platelet sizes.[9]

Coagulation studies to determine whether DIC is the underlying cause of severe neonatal thrombocytopenia (platelet count <50,000/microL), as this has implications regarding intervention. Studies include prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen concentration, and fibrin split products (d-dimer).

Blood cultures obtained, Prophylactic antibiotics should be administered while awaiting culture results.

Evaluation for Neonatal Alloimmune thrombocytopenia, If the mother has a normal platelet count and a previous history of Neonatal Alloimmune thrombocytopenia, an evaluation should also be performed in a well appearing term infant with severe thrombocytopenia and a mother with a normal platelet count. The assessment entails platelet antigen typing of the mother, father, and sometimes newborn and testing the mother's serum for antiplatelet alloantibody.

Karyotype- If there are obvious dysmorphic features or physical findings suggestive of an underlying genetic condition, karyotype testing is performed.

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Management of neonatal thrombocyopenia

Treatment includes platelet concentrate donated by mother and high dose intravenous immunoglobulin. All babies with Neonatal Alloimmune thrombocytopenia undergo cranial sonogram, neuroimaging.

Immune thrombocytopenia due to maternal antiplatelet antibodies, In maternal Immuno

Volume 5, Issue 3; May-June 2022; Page No 330-334

thrombocytopenic purpura and systemic lupus erythematosus, passive transplacental transfer of maternal antiplatelet antibodies to the fetus and neonate occurs resulting in thrombocytopenia. The diagnosis is established by maternal history and platelet count. The neonate remains healthy and the platelet count correlates with that of mother. Spontaneous resolution occur over a few months depending on the clearance of maternal antibodies. Platelet transfusion in severe thrombocytopenia with haemorrhage. Only transfusions are ineffective due to antiplatelet antibodies. In persistent cases a short course of prednisolone are administered.[10]

Prophylactic platelet transfusion is not required in the first week of life for a neonate of any gestational age until the platelet count falls below 30,000/µL except in unstable extremely preterm with previous Intraventricular haemorrhage, where platelet transfusion can be given with platelet count threshold at 50,000/ µL

In neonates with platelet counts > 50,000/ µL, the platelet transfusion is required in active major bleeding conditions like pulmonary hemorrhage, new or extending Intraventricular haemorrhage or gastric-intestinal bleeding.

Ideally HPA (human platelet antigen) compatible platelets is to be transfused. platelets should be ABO matched and leukocyte depleted. Irradiation is done to prevent transfusion related graft-versus-host disease in infants with immunodeficiency diseases. The transfusion will be started as soon as it is received from the blood bank. It should be transfused as quickly as possible between 30 min to 2 hours. All babies should undergo neurosonogram to detect Intraventricular haemorrhage.

In neonatal autoimmune thrombocytopenia, the platelet count reaches nadir at 3 to 4 days and becomes normal by 7 days in most of the cases. Prophylactic platelet transfusion is done to maintain platelet count above 30,000/ µL regardless of bleeding.

Conclusion

Thrombocytopenia should be suspected in any child presenting with a history of easy bruising or bleeding or petechiae, but it also may present as an incidental finding in an asymptomatic individual. Thrombocytopenia may be caused by either increased destruction or removal of platelets from the circulation or decreased production of platelets. Destructive mechanisms resulting thrombocytopenia include immune-mediated destruction, platelet activation and consumption, mechanical platelet destruction, and platelet Sequestration or trapping. Impaired platelet production may be due to bone marrow infiltration, suppression, or failure or defects in megakaryocyte development and differentiation.

A thorough history and physical examination and judicious use of laboratory testing can lead to the appropriate diagnosis in most patients who have thrombocytopenia. Childhood Immune thrombocytopenia generally presents with the sudden appearance of bruising, bleeding, or petechiae in an otherwise healthy child.

The diagnosis of Immune thrombocytopenia can be made using two criteria:

1) isolated thrombocytopenia with otherwise normal blood counts and peripheral blood smear 2) no clinically apparent associated conditions that may cause thrombocytopenia.

Further evaluation, including bone marrow assessment, should be considered in patients who have atypical clinical or laboratory features at presentation; thrombocytopenia lasting more than 6 months; or a subsequent clinical course that is inconsistent with the natural history of Immune thrombocytopenia, including failure to respond to usually effective therapies.

Management of thrombocytopenia should be guided by an understanding of its cause and clinical course, with the principal goal in all patients being to maintain a safe platelet count to prevent significant bleeding.

For childhood Immune thrombocytopenia, pharmacologic intervention, including corticosteroids, IGIV, and anti-Rho(D) immune globulin, has been shown to raise the platelet count more quickly than no therapy and is recommended for children who have or at risk for severe or life-threatening bleeding, based on strong evidence.

Immune thrombocytopenia in children usually is short-lived, with at least two thirds of patients making a full and sustained recovery within 6 months of presentation, with or without treatment.

Volume 5, Issue 3; May-June 2022; Page No 330-334

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Volume 5, Issue 3; May-June 2022; Page No 330-334