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Congenital Amegakaryocytic Thrombocytopenia (Camt) -An Updated Review

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Abstract

Congenital Amegakaryocytic thrombocytopenia is genetic disorder caused due to autosomal recessive gene disorder cause decreased platelet count, presents as anemia, thrombocytopenia, leukemia. The pathological is due to mutation in TPO and Mpl receptor gene which lead to low platelet count and decreased megakaryocytes present as purpura, bleeding early identified in newborn on day of birth can progress to worse in months to years. Diagnosed by complete blood picture, bone marrow biopsy, genetic testing. The CAMT is treated with help of supportive therapy where in the platelets are transfused in multiple sittings, gene therapy used and prevented by genetic counseling. The present article describes the cause, diagnosis and management of CAMT.

KEY WORDS- Congenital Amegakaryocytic thrombocytopenia, bleeding disorder, Myeloproliferative (Mpl) gene

Introduction

Congenital Amegakaryocytic Thrombocytopenia (CAMT) is autosomal recessive disorder presents thrombocytopenia and amegakaryocytes. CAMT is a bone marrow failure syndrome present with severe thrombocytopenia, aplastic anemia and leukemia. In CAMT the bone marrow loss the function to produce platelets which lead to thrombocytopenia, leads to bleeding disorder.[1-5] The bleeding disorder is identified on first day of birth until one month. And progress to worst over period of time, manifested with low platelet count, pancytopenia managed by multiple platelet transfusion.

Epidemiology

The incidence of the CAMT is not estimated accurately as the disease presentation is confused and diagnosis inconsistency. However few reviews identify prevalence as less than hundred cases in a given time.[6,7,8]

The CAMT condition is seen in infants with or without any physical anomalies.

Types of CAMT

The CAMT disorder is condition similar to neonatal alloimmune thrombocytopenia, the differential diagnosis is confirmed by bone marrow diagnostic test.

With the outcome of the disease, the CAMT is classified as:

1. TYPE I CAMT, in this type of CAMT the platelets are below 21millions/ L, the functionality of c-Mpl is lost, the onset causes severe pancytopenia, decreased bone marrow function and low platelets.
2. TYPE II CAMT, the platelet count is between 35million/L to 132million/L, in this condition the platelets increase from mild to near normal in first year of life of newborn, the bonemarrow failure begins late in 3 to 6years.
3. TYPE III CAMT, c-Mpl gene shows no defect yet the ineffective megakaryopoeisis.[12,15,17]

Causes for CAMT

The thrombopoietin TPO and c-Mpl receptors are genetically mutated lead to decreased thrombocytes, impairment in megakaryocytes.[9,11,13]

In type I CAMT the Mpl receptor get mutated leads to complete loss of TPO receptors.

In type II CAMT the extracellular TPO receptor domain gets affected by missense mutation of Mpl gene.

This mutation in the gene leads to thrombocytopenia, anemia and leukemia.[14,16,10]

Pathology of CAMT

The Myeloproliferative (Mpl) gene is play vital role in megakaryopoeiesis this is regulated by thrombopoietin (TPO) receptor. Any mutation in the TPO receptor results in high level of TPO.[18,19]

The high level of TPO bindings stimulate the megakaryopoiesis, results in increase number and size of megakaryocytes which promotes the expression of platelet specific markers.

TPO is essential to number of hematopoietic stem cells any mutation leads to thrombocytopenia and pancytopenia.

The Mpl is a cytokine receptor functions to hematopoietic tissues and cell of bone marrow, liver, spleen of fetus. Stimulation of these leads to bone marrow failure causing CAMT in newborn.

On the other hand, an abnormality in the central nervous system, cerebrum, cerebellum cause TPO and Mlp deficiency leads to reduction in megakaryocytic precursor cells and decrease in erythroid and myeloid progenitors.[20,22]

The TPO and Mlp needed for growth of megakaryocytes, the deficit of TPO and Mlp causes the bone marrow failure results in platelet disorder, amegakaryocytic thrombocytopenia, aplastic anemia, pancytopenia.

Clinical presentation of CAMT

- The newborn shows megakaryocytopenia, thrombocytopenia.
- Bleeding percutaneous, gastro intestinal, pulmonary and intracranial hemorrhage.

The risk factors for CAMT can be assessed by

- Assessing the history of thrombocytopenia in family.[21,23,25]
- Assess newborn for the symptoms of bruising, bleeding in mouth and nose, patecheiae, purpura.
- CAMT is identified in infants, short after birth, with no specific birth defects.
- In Type-I CAMT presents persistent low platelet count.
- In Type-II CAMT milder to near normal platelet count.
- Central nervous system manifest as cerebral and cerbellar hypoplasia, retardation of psychomotor development.

Diagnosis of CAMT

The diagnosis of CAMT is skill full and requires identifying the differential diagnosis.

- A routine blood investigation indicates the low platelets count.[24,26]
- Bone marrow biopsy test gives information on megakaryocytes.
- Genetic testing to trace and rule our Mpl, C-MPL gene it nature and mutation.
- In colony formation absence of thrombopoietin, megakaryocytes.
- Clonal culture shows decreased number of erythroid and myelocytic progenitors.
- The genetic testing for lack of Mpl mRNA in bone marrow monocellular cells.
- Blood picture shows elevated serum levels of TPO, decreased white blood cells and red blood cells.

Treatment of CAMT

Preliminary treatment aim to prevent bleeding and stopping, supportive treatment by multiple platelet transfusion.

The management of the CAMT include platelet transfusion.[27]

Bone marrow transplantation and stem cell transplantation effective in genetic disease.

The gene therapy for malfunction of TPO and c-Mpl receptor.

CAMT managed by curative therapy through stem cell transplantation.

Prognosis of CAMT

Prognosis is poor, supportive treatment, in first year life bone marrow failure occur, without hemotopoietic stem cell transplantation nearly 30% of newborn with CAMT and with heamotopoietic stem cell transplantation 20% newborn die with CAMT.[29]

Prevention of CAMT

Antenatal diagnosis of the possible cause of the CAMT,

Genetic counseling to individuals at risk of developing CAMT disorder and family history of thrombocytopenia.[30]

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