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# Case report

# Peripheral stem cell transplantation in a child with amegakaryocytic thrombocytopenia

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**Summary:**

**Congenital amegakaryocytic thrombocytopenia (CAMT) is an unusual cause of thrombocytopenia without radial or other congenital anomalies in the newborn. Generalized bone marrow dysfunction developing later in life has been reported. We present a 13-month-old girl who was diagnosed as having congenital amegakaryocytic thrombocytopenia and was successfully treated with allogeneic peripheral stem cell transplantation (PSCT) from her fully matched sibling donor. The neutrophil engraftment was on post transplant day 12 and platelet engraftment was on day 14. Her last hemogram revealed platelets of $168 \times 10^9$/l 20 months post transplant.** *Bone Marrow Transplantation* (2000) **26,** 571–572.
**Keywords:** congenital amegakaryocytic thrombocytopenia; peripheral stem cell transplantation; childhood

Congenital amegakaryocytic thrombocytopenia (CAMT) is an extremely rare cause of hypoproductive neonatal thrombocytopenia. The syndrome appears to have an autosomal recessive inheritance pattern. The patients do not have any evidence of skeletal abnormalities. Diagnosis depends on excluding other possible etiologies. Most of the patients will progress to complete aplasia, and many infants die because of infection or hemorrhage. Conventional therapy is usually not beneficial. Allogeneic stem cell transplantation offers the only possibility for cure.[1]

We report a girl with CAMT, but no associated physical abnormalities who showed a progressive mild marrow failure and was treated with peripheral stem cell transplantation.

## Case report

This 13-month-old girl was referred to us because of recurrent petechia and ecchymoses on her body for a month. Her sister had died in infancy with similar findings. There was first degree consanguinity between parents. Physical examination was normal except widespread petechia and ecchymoses. Her Hb was 13.2 g/dl, WBC $5.3 \times 10^9$/l, platelets $8.0 \times 10^9$/l, MCV 103 fl, HbF 4.2%. No mature or immature megakaryocytes could be seen in bone marrow aspiration smears, but myeloid and erythroid cells and bone marrow cellularity were normal. Antiplatelet antibody was negative and CD41 and CD61 levels were zero. Serum TPO level was 339 pg/mm$^3$ (normal 150–200 pg/mm$^3$). BM cytogenetic analysis revealed a normal karyotype and showed no chromosomal breakage. The blood count results of the parents and two siblings were normal. The dead sibling's count is not available.

She did not respond to corticosteroid and androgen therapy. Five months later, her hemogram revealed a decrease in hemoglobin and WBC levels (Hb 6.8 g/dl, WBC $3.38 \times 10^9$/l, platelets $1.43 \times 10^9$/l), and her bone marrow smears showed hypocellularity. Hyposegmentation and hypogranulation were noticed in a few white blood cells in BM. She needed regular packed red cell and platelet transfusions. At the age of 20 months, she underwent allogeneic PSCT from her fully matched and MLC nonreactive sibling. She received cyclophosphamide 50 mg/kg for 4 successive days between day −5 and day −2 (total 200 mg/kg) and ATG for conditioning regimen.

We used G-CSF 5 $\mu$g/kg/day, subcutaneously, for 5 consecutive days for donor stem cell mobilization. The donor's blood count was Hb 12.8 g/dl, WBC $4.82 \times 10^9$/ l, platelets $190 \times 10^9$/l and Hb 13.0 g/dl, WBC $22.5 \times 10^9$/l, platelets $177 \times 10^9$/l before G-CSF and on the day of apheresis, respectively. She was 11 years old and her weight was 32 kg. A temporary dual-lumen catheter was inserted for venous access. Fresenius AS104 was used for peripheral blood stem cell collection. After a single apheresis, $10.2 \times 10^8$/kg mononuclear cells were given without T cell depletion or CD34 enrichment. CsA and MTX were used for GVHD prophylaxis. CsA was initiated at 3 mg/kg on day −1 and than adjusted according to blood levels. MTX on days +1, +3, +6 after stem cell infusion was combined with CsA. The neutrophil engraftment was on post-transplant day 12 and the platelet engraftment was on day 14. Now she is well with Hb 12.1 g/dl, WBC $6.0 \times 10^9$/l, platelets $168 \times 10^9$/l 20 months post PSCT without any bleeding symptoms or complications.

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## Discussion

Congenital amegakaryocytic thrombocytopenia is a rare and fatal disorder characterized by isolated severe thrombocytopenia. It differs from thrombocytopenia absent radii (TAR) syndrome, by the absence of physical anomalies. Bone marrow aspirates and biopsies reveal no megakaryocytes or a few bizarre megakaryocytes. In early childhood, hematological findings progress to marrow failure in most patients.[1] The defect in thrombopoiesis is not well understood. It is well known that thrombopoietin (TPO) plays a key role in the regulation of megakaryopoiesis. After cloning of TPO, the ligand for the c-mpl receptor, the c-mpl gene was considered as one of the genes responsible for this disorder. Muraoka *et al*[2] reported that the pathophysiology in CAMT may be a defective response to TPO in hematopoietic cells through impaired expression of c-mpl mRNA. Ihara *et al*[3] also suggested that a certain type of CAMT is caused by the c-mpl mutation, which disrupts the function of the thrombopoietin receptor.

In our patient, it was not difficult to diagnose CAMT because of her typical clinical and laboratory findings which are mentioned in the case report section. She had a normal karyotype and no skeletal or morphological abnormalities.

Conventional treatment modalities, like corticosteroids, androgens, immunosuppressive drugs or splenectomy, have been ineffective. *In vitro* studies revealed that thrombocytopenia in CAMT can not be corrected by administration of TPO.[2] The high TPO serum level of our patient is consistent with the literature. Bone marrow transplantation (BMT) offers the only possibility of cure for these patients. There are few reports of BMT in CAMT patients but, some of them showed difficulty in achieving engraftment and a more aggressive preparative regimen or an increased stem cell dose was suggested to be necessary to achieve engraftment.[4–6] The results of allogeneic BMT are better in untransfused children so it is recommended to be done prior to the development of aplastic anemia.[4,7]

Recent studies have shown that peripheral blood stem cell transplantation (PSCT) results in rapid hematological and immunological recovery without excessive acute GVHD compared with BMT. This contributes to less transfusion before hematological recovery, early discharge and lower transplantation costs.

After diagnosis, our patient showed no response to corticosteroid and androgen therapy. When she was 20 months of age, alloPSCT was performed from her fully matched sibling. After PSCT, she showed rapid hematological recovery. Twenty months post transplant she is well with normal hematological parameters. We think that this is the first CAMT patient in the literature who has been cured with PSCT.

We conclude that allogeneic PSCT offers a chance for cure in a congenital amegakaryocytic thrombocytopenia patient.

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