

## **Case Report**

### **Congenital Leukemia In Down's Syndrome- A Rare Case Report**

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#### **Abstract:**

Congenital leukemia is a rare disorder presenting in the immediate neonatal period & diagnosed at or within few days of birth.<sup>1</sup> Because of the doubling time of leukemic cells, the disease becomes clinically evident after birth or shortly thereafter.<sup>2</sup> Neonates with Down's syndrome have an increased risk for congenital leukemia particularly acute megakaryoblastic leukemia (FAB M7).<sup>3</sup> The incidence of acute megakaryoblastic leukemia in Down's syndrome is estimated to be 400 times than in normal children.<sup>4</sup> We present a case of congenital leukemia in a 22 day old female child with Down's syndrome who had cyanosis and skin rashes for 2 days. Diagnosis was established on the basis of hematological investigations and cytochemistry of the cells.

**Key Words:** Congenital leukemia; Down's syndrome

#### **Introduction:**

Congenital leukemia (CL) is defined as leukemia that develops in utero. It is an extremely rare malignancy associated with very grim prognosis and a poorly understood natural history.<sup>5</sup> Incidence is reported to be 1 per 5 million.<sup>6</sup> Neonates with Down's syndrome have an increased risk of CL, a 20 fold increased risk of developing acute leukemia is seen.<sup>7</sup> A large proportion of these CLs are of myeloid lineage in contrast to pediatric leukemias which are primarily lymphoid in origin. A characteristic hematopoietic manifestation of Down's syndrome is the occurrence of a transient leukemia like process in the newborn which has a spontaneous clinical and hematological recovery in a week or month's time of diagnosis.<sup>8,9,10</sup> Whereas congenital leukemia is a very aggressive and has poor prognosis.<sup>11</sup> Hence, it is important to differentiate CL from transient myeloproliferative disorder (TMD) associated with Down's syndrome. All cytogenetic types of Down's syndrome predispose to leukemia.

#### **Case Report**

A 22 day old female child with Down's syndrome presented in pediatrics OPD with blueness of skin along with rashes for two days. Child had phenotypic stigmata of Down's syndrome (low set ears, pro-

truded tongue, flattened nasal bridge, mongoloid slant of eyes). Chromosomal analysis revealed a 47 XX+21 karyotype, confirming the diagnosis of Down's syndrome.

On examination, there was cyanosis, bilateral cataract, bilateral crepts, hepatosplenomegaly, bounding pulse and systolic murmur. Tests done to rule out congenital infections such as TORCH, WR and VDRL were within normal limits. Urine culture and sensitivity was normal. The hematological testing revealed a hemoglobin of 16.7g/dl and total leukocytes count of 1,24,000/mm<sup>3</sup>. Platelets were 80,000/mm<sup>3</sup>. The peripheral blood smear showed normocytic normochromic blood picture with marked leucocytosis; shift to left, and 43% blasts. The blasts were large in size with fine nuclear chromatin, two to three nucleoli and variable amount of cytoplasm with evidence of cytoplasmic budding. Cytochemistry was done and it was positive for Sudan Black. The results of chest X-ray were normal. After confirmation of acute myeloid leukemia, combination chemotherapy was started, child improved symptomatically and remission was achieved.

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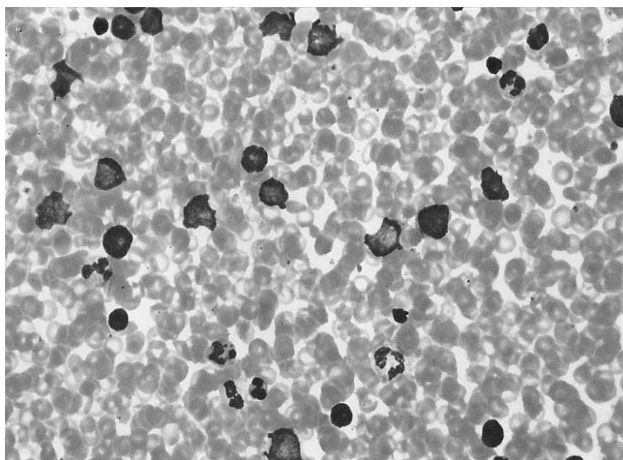
**Discussion:**

Congenital leukemia is a rare disorder which is diagnosed at, or within few days of birth.<sup>12</sup> Patients with chromosomal anomalies such as Down's and Turner's syndrome. Have higher incidence of CL. There is a 15-20 times increased risk congenital leukemia in patients with Down's syndrome. 80% of the cases are myeloid phenotype<sup>13</sup>. Majority of cases of acute myeloid leukemia (AML) are diagnosed on morphology alone. It has recently been known that acute megakaryoblastic leukemia.(AML M7) is more common in children with Down's syndrome.<sup>8</sup> In the present case, the increased percentage of blasts in the peripheral blood & bone marrow indicated a leukemic process. There was no evidence of secondary disorders which could mimic leukemia. Karyotyping confirmed the diagnosis of congenital leukemia in Down's syndrome.

One of the most important manifestations of CL is chloromas, which manifest as nodular infiltration of the skin. They are solid collections of myeloblasts and their most favoured location is in the skin where they are termed as leukemia cutis. The diagnosis is confirmed on biopsy of the involved skin. Most of these patients usually present with petechiae, purpura, hepatosplenomegaly, lethargy, fever and pallor.<sup>14</sup> In the present case although skin biopsy could not be performed, cutaneous lesions and hepatosplenomegaly were indicators of extramedullary infiltrates.

Characteristic haematopoietic manifestation of Down's Syndrome is the occurrence of a transient leukemia known as TMD.<sup>8,9,10</sup> TMD is reported in about 10% cases of Down's syndrome and is distinguished from congenital AML primarily by spontaneous remission within the first three months of

life.<sup>11</sup> The essential diagnostic criteria are: proliferation of immature leukemic cells, organ infiltration,



no evidence of underlying infective pathology/hemolysis, and the absence of Down's syndrome or cytogenetic abnormality of 21<sup>st</sup> chromosome.<sup>5,10</sup> There is lower blast percentage in marrow than in peripheral smears in TMD. Clonal, cytogenetic abnormality in AML is not seen in TMD. Differentiation is possible only on follow up. Continued clinical or hematological deterioration rules out TMD. In the present case child was followed up after appropriate chemotherapy was instituted and remission was achieved.

Congenital leukemia is a rare malignancy and a poorly understood disorder which can progress rapidly and be fatal if early and adequate treatment is not instituted, hence it is important to differentiate it from myeloproliferative disorders associated with Down's syndrome which have a complete clinical and hematological recovery within weeks or months of diagnosis.<sup>14</sup> TMD is transient and recovers spontaneously whereas congenital leukemia is fatal, hence it is important to establish early diagnosis and start the therapy in congenital leukemia. A very close follow up is necessary for all such infants.

**References:**

- 1) Bhatt S, Schreck R, Graham JM, Korenberg JR, Hurvitz CG, Fischel-Godsian N. Transient Leukemia with Trisomy 21. *AmJMedgenetics* 1995; **58**:310-314. <http://dx.doi.org/10.1002/ajmg.1320580404> PMid:8533839
- 2) Nathan O. Congenital leukemia. In *Haematology of Infancy and childhood*. 3rd edition. Philadelphia: WBSaunders; 1957. pp.1052-1053
- 3) Li Thio Te V, Bourges Petit E, Capiod JC, Horle B, Micheli J, Morin G, Maingourd Y, Pautard B. Congenital transient leukemia: a case report. *Arch Pediatr* 2008; **15**(1):33-36. PMid:18162385
- 4) Zipursky A, Peeters M, Poon A. Megakaryoblastic leukemia & Down's Syndrome: a review. *PediatrHematolOncol* 1987; **4**(3):211-230. <http://dx.doi.org/10.3109/08880018709141272>
- 5) Moatoshi Aier, Thangura Zadeng, Debdatta Basu, Niranjani Biswal, P.Nalini. Congenital leukemia in Down's syndrome: A case report. *Indian J Pathol Microbiol* 2002; **45**(3):355-357 PMid:12785186
- 6) Prashad HVR, Kumar GN. Congenital leukemia in a two month old boy. *Internet J Pediat Neonatol* 2007; **6**(2):1-2
- 7) Iselius WS, Jacobs P, Morton N. Leukemia & Transient leukemia in Down's Syndrome. *HumanGenetics* 1990; **85**:477-485 PMid:2146208
- 8) Engel RR, Hammond D, Eitzman DV, Pearson H, Krivit W. Transient congenital leukemia in 7 infants with mongolism. *J Pediatr* 1964; **65**:303-335. [http://dx.doi.org/10.1016/S0022-3476\(64\)80535-7](http://dx.doi.org/10.1016/S0022-3476(64)80535-7)
- 9) Dinulos JG, Hawkins DS, Clark BS, Francis JS. Spontaneous remission of congenital leukemia. *J Pediatr* 1997; **131**:300-303. [http://dx.doi.org/10.1016/S0022-3476\(97\)70170-7](http://dx.doi.org/10.1016/S0022-3476(97)70170-7)
- 10) Homans AC, Verissimo Am, Vlacha V. Transient abnormal myelopoiesis of infancy associated with trisomy 21. *Am J Ped Hematol Oncol* 1993; **15**:392-397 PMid:8214361
- 11) Campos L, Nadal N, Flandrin Gresta P, Vasselon C, AAnei C, Berger C, Stephan JL. Congenital acute leukemia with initial indolent presentation: A case report. *Cytometry B Clin Cytom* 2011; **80**(2):130-133 <http://dx.doi.org/10.1002/cyto.b.20578>
- 12) Weizman S, Figure 1: Microphotograph of peripheral smear showing predominance of myeloblasts (Leishman, 40x) & Grant R. Neonatal oncology: Diagnostic & therapeutic dilemmas. *Semin Perinatal* 1997; **21**:102-111. PMid:9190040
- 13) Narayan S, Sharma S, Chandra J, Kulshreshtha R. Clinical hematological profile of congenital leukemia. *Ind J Pediatr* 1994; **71**(10):927-928
- 14) Badhe PB, Sane SY. Congenital Leukemia-organ involvement in six autopsy cases. *J Post Grad Med* 1992; **38**:127 PMid:1303413

**LEGEND:**

Figure 1: Microphotograph of peripheral smear showing predominance of myeloblasts (Leishman, 40x)