

# Congenital Dyserythropoietic Anemia Type I Presenting as Congestive Cardiac Failure in Neonatal Life

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## Case Report

**Abstract:** Congenital Dyserythropoietic Anemias (CDAs) constitute a heterogeneous group of rare inherited disorders, characterized by moderate to severe anemia due to a markedly ineffective erythropoiesis with an erythroblastic bone-marrow and specific erythroid morphological anomalies. Three major types of CDA and a number of variants have been described. The diagnosis and categorization of these disorders are facilitated by microscopic examination of the blood and bone marrow and by serologic testing. The severity of Anemia varies considerably within and between families. We report a case of CDA type I in a neonate who presented as congestive cardiac failure secondary to severe Anemia who also had PPHN due to LVF. Baby succumbed to death on day 1 of life itself. Clinical profile and laboratory investigations were consistent with CDA type I.

**Key Words:** Congenital Dyserythropoietic Anemia, Congestive cardiac failure.

**Introduction:** The congenital dyserythropoietic anaemia's are heterogeneous group of rare hereditary diseases characterised by ineffective erythropoiesis and dysplastic changes in erythroid precursors. Three major types of CDA (I, II, III) as well as number of variants have been described.<sup>1,2</sup> CDAs are rare, and with only a few hundred cases having been reported worldwide.<sup>3</sup> As the clinical and laboratory findings are not distinctive, it is believed that CDA is often under-diagnosed.<sup>4</sup> Congenital dyserythropoietic anemia type 1 is characterized by autosomal recessive inheritance and macrocytic anemia with dyserythropoietic features such as megaloblastoid changes, multinuclearity, and internuclear chromatin bridges. A recent study has revealed that the gene for CDA type 1 is located on 15q15.1-q15.3, but no distinct responsible gene has been identified. It has been demonstrated that most patients with CDA type 1 have mild to moderate Anemia during the neonatal period<sup>5</sup>. The diagnosis of CDA is often made during childhood, though there is no age limit. It can have an intra-uterine onset with severe Anemia, resulting in cardiac failure or the disease may remain undiscovered until late adult life<sup>5,6</sup>. We present a patient with CDA type 1 who had

developed severe anemia during the neonatal period resulting in cardiac failure, PPHN and death.

**Case Report:** There was no history of consanguinity. The patient was born to a mother who was G<sub>5</sub>P<sub>3</sub>L<sub>1</sub>A<sub>1</sub>D<sub>2</sub> G1- FTND at home-M/Ch-5 yrs.-No anemia.

G2- FTND at home-F/Ch-expired on day 2 of life.

G3- FTND at home-M/Ch-expired on day 5 of life.

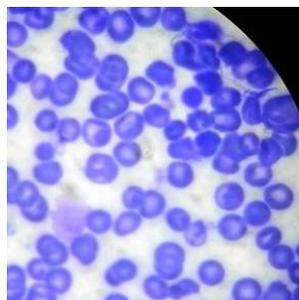
G4- Abortion at 2 MA (All the above events occurred at home only. According to father, 2<sup>nd</sup>& 3<sup>rd</sup> child had similar presentation like our case but we could not get documented information).

G5-Present case

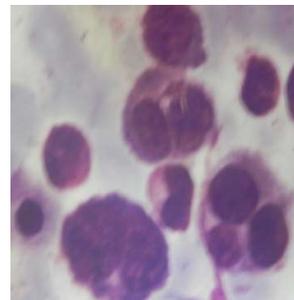
It was a near term vaginal delivery at our institute. Birth weight was 1.9 kg. Apgar score was 2 at 1 min and 5 at 5 mins. After initial resuscitation, baby was admitted to NICU. On examination, severe pallor and oedema were present. There was no obvious evidence of congenital anomaly or skeletal deformity. Per abdominal examination elaborated firm splenomegaly of grade III and firm hepatomegaly measuring 4 cm below right costal margin. CVS examination was showing signs of LVF, tachycardia with hemic murmur of grade II/VI. Baby also had loud P<sub>2</sub>. RS examination revealed basilar crepts suggestive of pulmonary oedema.

Peripheral blood revealed severe anemia with erythroblastemia, macrocytosis, and dyserythropoietic features with multinuclearity, internuclear chromatin bridges (hemoglobin: 5.3 g/dL, red blood cell count:  $1.28 \times 10^6/L$ , hematocrit: 17.3%, mean corpuscular volume: 168.7fL, mean corpuscular haemoglobin: 57.6%, mean corpuscular haemoglobin concentration: 34.1%, RDW-23.1, white blood cell count: 19,600/cmm (P<sub>14</sub>,L<sub>82</sub>,E<sub>2</sub>,M<sub>2</sub>,B<sub>0</sub>), platelet count: 1,60,000/cmm, reticulocyte: 7%, corrected retic count:2.06%, blood group of baby and mother both was A (+ve), serum electrolytes- Na<sup>+</sup>-148.12, K<sup>+</sup>-5.34. An acidified serum lysis test was negative (HEMPAS negative). In view of all the above findings, decision of blood transfusion

was taken and treatment initiated accordingly. But before transfusion baby succumbed to death. Post mortem bone marrow aspiration was done which revealed erythroid hyperplasia and markedly abnormal erythropoiesis (Figure1), including 5-6% of binuclear erythroblasts and occasional trinuclear, tetranuclear



(A)



(B)

**Figure 1:** Optical microscopic morphology of peripheral (A) and bone marrow (B) hematopoiesis. Binucleate erythroblast in peripheral blood (A). Erythroid hyperplasia with marked abnormalities (binucleate, trinucleate, late erythroblasts) (B).

**Discussion:** Our patient had severe Anemia with splenohepatomegaly with PPHN secondary to LVF. Obstetric history was suggestive of genetic and congenital origin of the disease. Recent surveys reveal that symptoms of CDA type 1 cases often developed in the neonatal period, but they improved during the patient's first year of life. Manifestation of congestive heart failure is rare<sup>5</sup>. Though our patient had no obvious evidence of congenital anomalies or skeletal dysplasia, antenatal onset and early neonatal presentation of cardiac insufficiency associated with severe anemia has been reported in CDA type 1 in a case report by Kato K et al.<sup>5</sup> Stillbirth or neonatal death has also been described in other types of CDA's<sup>7-9</sup>. Multinucleated erythroblast and karyorrhexis are seen occasionally in megaloblastic Anemia, iron deficiency, leukemia and haemolytic Anemia, and indicate bone marrow stress. History of consanguinity and affected siblings cases have been reported in earlier studies.<sup>10</sup> Differential diagnosis included thalassemia, some hemoglobinopathies, hereditary sideroblastic Anemia, congenital myelodysplasia, and other forms of CDA<sup>2</sup>. Congenital Anemia such as Blackfan–Diamond Anemia and Fanconi Anemia also should be considered. Our patient showed prominent macrocytosis with dyserythropoiesis, commonly not observed in a case of thalassemia or hemoglobinopathy. No ringed sideroblasts or dysplastic features on the granulocytic/megakaryocytic lineage were seen. Acidified serum lysis was normal. Peripheral blood smears and the bone marrow histology revealed erythroid hyperplasia with megaloblastoid changes and multinuclearity. These findings all favoured a diagnosis of CDA type 1. Because the mother had the stillbirth of unknown cause and other siblings also had similar presentations and CDA type 1 has autosomal recessive inheritance, it was necessary to evaluate the risk for recurrence through

erythroblasts. Occasional chromatin bridges were also seen. Due to rural set up, electron microscopy was not done.

genetic counselling. Accordingly relatives were counselled and referred for genetic studies.

**Conclusion:** CDA type I can present in neonatal life itself with severe Anemia and CCF. It may prove fatal in early life. Further case and genetic studies are required for elaboration of natural course and variations associated with it.

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