

Case Report

A rare presentation of Congenital Leukemia in Down's Syndrome

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Abstract: One day old preterm newborn presented at 10 hours of life with respiratory distress, cyanosis, shock and poor suck. Detailed examination revealed Down's facies, hepato-splenomegaly and severe pallor suggestive of sepsis. Peripheral blood smear revealed hyperleukocytosis, thrombocytopenia and presence of myeloblasts, also, the bone marrow study revealed an increase in myeloblasts. Other causes of leukemoid reaction were ruled out and a final diagnosis of congenital leukaemia was confirmed by immunophenotyping.

Keywords: Congenital leukemia, Down's syndrome, Myeloproliferative disorders

INTRODUCTION

Congenital leukemia is a rare condition often associated with fatal outcomes [1]. Its incidence is reported to be 1 per 5 million [2]. Most of the neonatal cases reported have acute non-lymphoblastic leukemia, in contrast to the predominance of acute lymphoblastic leukemia found in later childhood.

Congenital leukemia (CL) is occasionally associated with a number of congenital anomalies and with chromosomal disorders such as Down's syndrome. Neonates with Down's syndrome have an increased risk of Congenital leukemia, and a 20 fold increased risk of developing acute leukemia is reported elsewhere [3]. It's seen that inherent unstable hematopoiesis resulting from chromosomal aberration, in children with Down's syndrome can present with transient myeloproliferative disorder, mimicking leukemia which can undergo a fortunate spontaneous recovery [4]. But on the other extreme, congenital leukemia (CL) is very aggressive and has a poor prognosis [5]. Hence, it is important to differentiate CL from the milder transient myeloproliferative disorder (TMD) associated with Down's syndrome [6-8]. All cytogenetic types of Down's syndrome predispose to leukemia. Only few cases of congenital leukemia with Down's syndromes have been reported in the literature [9]. We herewith report a newborn with features of Down's syndrome, who presented as congenital leukemia.

CASE REPORT

A preterm male born to 34 years old mother of non-consanguineous marriage presented at Assam Medical College and Hospital immediately after delivery. It was a normal vaginal delivery with no history of cytotoxic drug intake or exposure to radiation during antenatal period. Special emphasis was given to elicit the history of maternal fever, rash or lymphadenopathy in the mother in the first trimester to rule out TORCH infection. There was a history of maternal chorioamnionitis with prolonged preterm premature rupture of membranes. The baby had cried immediately after birth. But at 10hrs of life, baby presented with respiratory distress, cyanosis and shock. On examination child looked cyanosed and tachypnic with Downe's score of 2/10 and prolonged capillary refilling time. Physical examination revealed features of Down's syndrome (mongoloid facies, epicanthic folds, hypotonia, and simian crease in hands) and mild pallor was also noticed. Cardiovascular examination showed cardiomegaly with pansystolic murmur over apex. Liver was just palpable and spleen was 5 cm below left costal margin. No lymph nodes were palpable. Peripheral blood smear revealed mild hypochromia; there was leukocytosis with presence of myeloblasts above 30%. Total white cell count was 48000/cmm with blasts 34%, myelocytes 09% metamyelocytes 02% and promyelocytes 03% (Fig. 1). Bone marrow aspiration done from tibia showed markedly hypercellular smears and fragments. Myeloid series showed moderate hyperplasia with maturation shift to left, myeloblasts being 23% (Fig. 2). The case

was provisionally labeled as Acute Myeloid leukaemia for further workup (AML-M2). Immunophenotyping was done from the peripheral blood sample, and gated population of blasts showed positivity for CD-33, CD-117, CYTO.MPO (Myeloid Series), Immunophenotyping also shows positivity for CD-41, CD-42, CD-61 (Megakaryocytic Series) (Fig. 3). Tests done to rule out congenital infections such as TORCH, WR and VDRL were within normal limits.

Chromosomal analysis revealed a 47XX+21 karyotype, confirming the diagnosis of Down's syndrome. Cerebrospinal fluid study was normal, while echocardiography showed a Ventricular Septal Defect but, the thyroid profile was normal. The mother's blood group was B+ve, the baby's blood group was AB+ve, and the Glucose 6 phosphatase dehydrogenase enzyme levels were within normal limits.

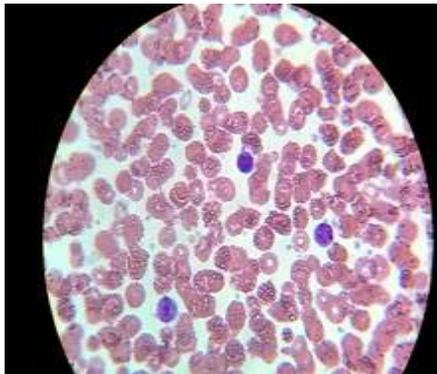


Fig. 1: Peripheral blood smear

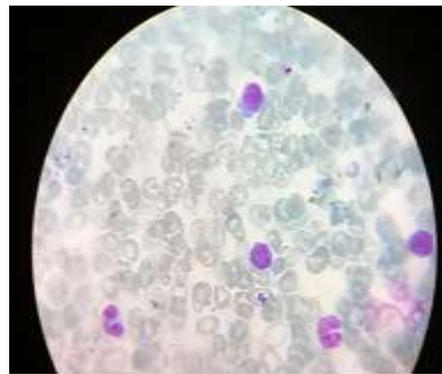
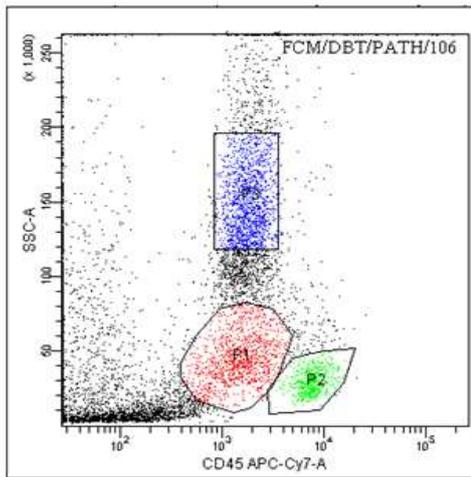
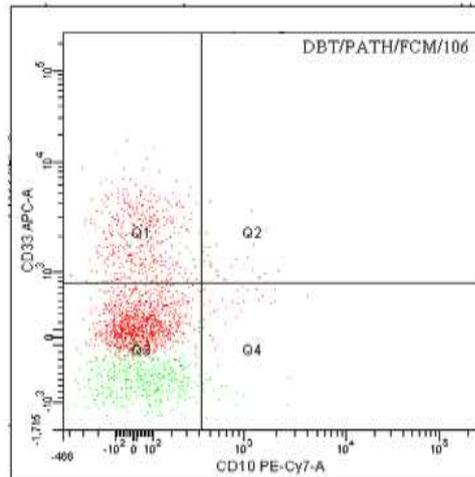


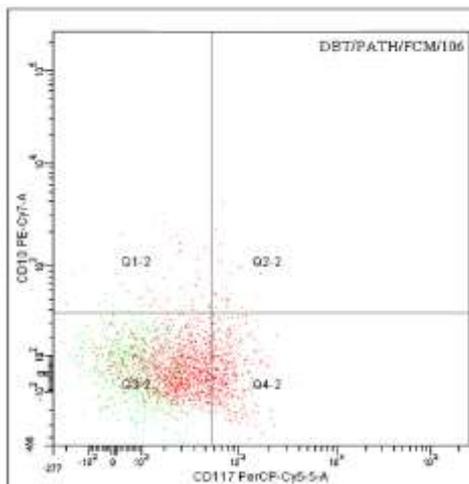
Fig. 2: Myeloid



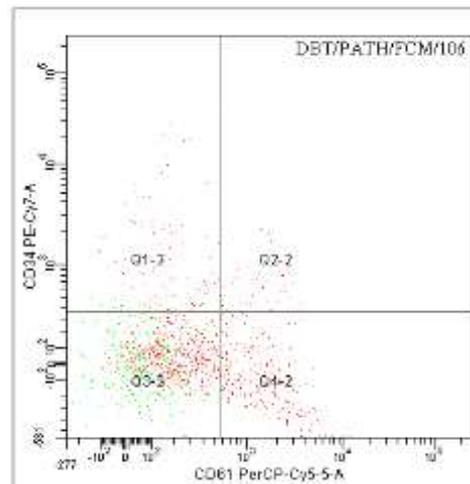
I.SSC vs CD45



II.CD33 vs CD10



III.CD10 vs CD117



IV.CD34 vs CD61

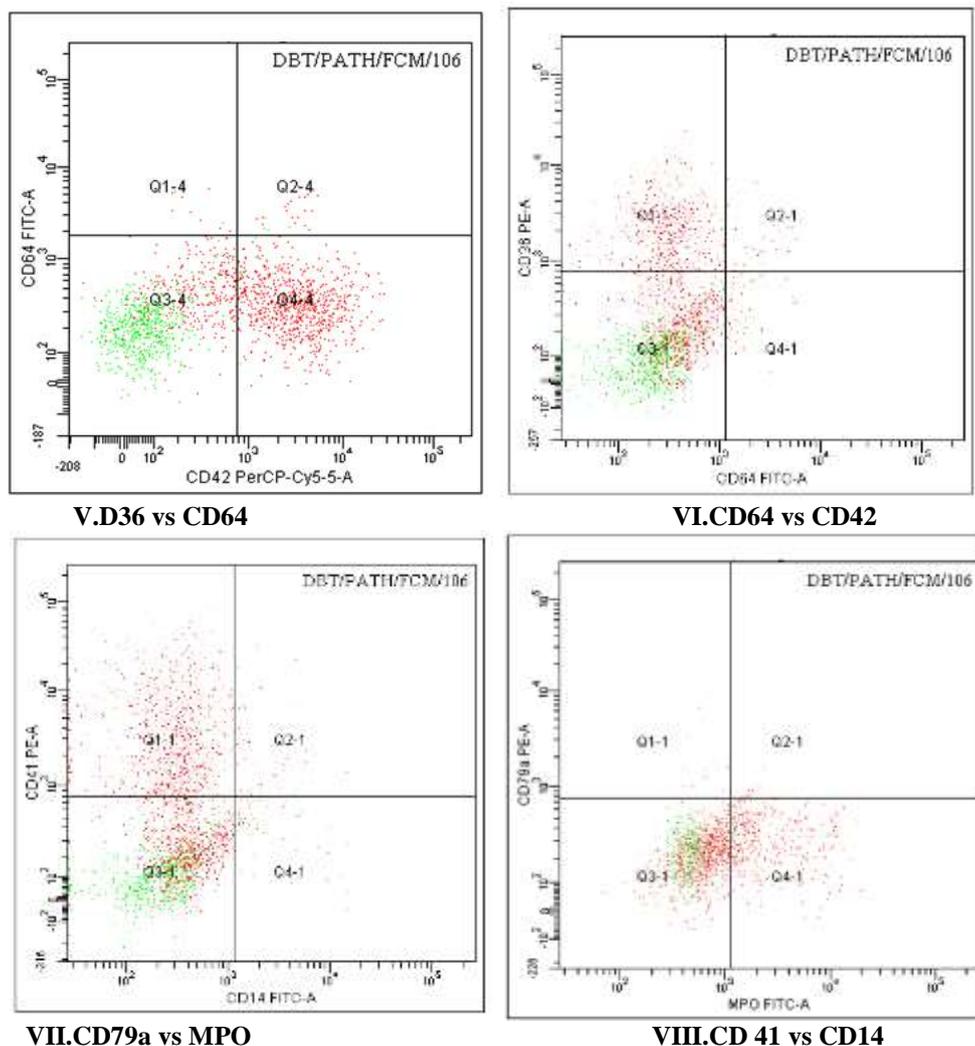


Fig. 3: SERIES I - VIII showing the immunophenotyping

DISCUSSION

Leukemia is classified as congenital when diagnosed at birth, as neonatal leukemia during the first month of life and as leukemia of infancy after one month of life [10]. However the diagnosis of congenital leukemia has been applied to those cases developing symptoms within first 3-6 weeks of life [11]. Congenital leukemia is often a rare disease and the prognosis for neonates is poor as most of them do not survive beyond infancy [12]. It is characterized by non-specific symptoms requiring a high index of suspicion for further investigations and diagnosis.

Diagnosis of congenital leukemia is more stringent than the adult because of the lability of infant's hemopoietic system that on exposure to stressors can mimic leukemia [13]. The differential diagnosis includes leukemoid reactions, congenital infections, severe erythroblastosis and neonatal neuroblastoma [14]. It has been advocated that the following criteria must be fulfilled for the diagnosis of congenital leukemia viz. (a): Proliferation of immature white cells, (b): Infiltration of these cells into bone marrow, (c): Absence of any other disease that can

cause leukemoid reaction mimicking leukemia like congenital syphilis, blood group incompatibility or TORCH infection [15]. Our child fulfilled all three criteria i.e. evidence of blasts in peripheral smear and infiltrate of blasts in the hemopoietic tissue (bone marrow) hence we confirmed the clinical suspicion with immunophenotyping.

Another additional criterion reported to be a requisite for the diagnosis is the absence of constitutional disorders that may be associated with unstable hematopoiesis such as trisomy 21 [16].

CONCLUSION

Congenital leukemia is a rare condition, diagnosed from birth to 6 weeks of life that causes rapid deterioration and death from haemorrhage and infection. During diagnosis condition of transient myeloproliferative syndrome should always be kept in mind. We feel that, while diagnosing congenital Leukemia with Down's syndrome, immunophenotyping can prove as a useful adjunct in confirmatory diagnosis.

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