Case Report

Acute megakaryocytic leukemia (m7) in a newborn with down syndrome

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Abstract

Patient with Down's syndrome (DS) are found to have an increased risk of developing various hematological disorders. There is 46 to 83 fold increased risk of acute myeloid leukemia (AML) and 10 to 27 fold increased risk of acute lymphoid leukemia (ALL). One of the most characteristics feature of Down syndrome associated AML (DS-AML) is that vast majority of case (70%) of AML in DS are megakaryoblastic leukemia i.e. M7 as per FAB classification (DS- AMKL). Virtually, all cases of DS-AMKL occur within the first 5 years of life. The median age of presentation of AMKL is 1.8 years. We report a case of AMKL in a newborn with Down's syndrome.

Key words

Acute myeloid leukemia, Acute megakaryocytic leukemia, Down's syndrome.

Introduction

Downs syndrome (DS) is the most common post natally viable chromosomal anomaly. It has an incidence of about 1 in 700 live births [1]. Certain malignancies occur more frequently in patients with Downs syndrome as compared to others. They include leukemias, gonadal and extragonadal germ cell tumors and retinoblastomas [2, 3]. Children and adolescents with Downs Syndrome have a 10-30 fold increased incidence of leukemia [1]. This suggests an important role for some chromosome 21 genes located in leukemogenesis [2]. Notably, the AML 1 gene, a critical regulator of normal hematopoiesis located at 21q22 is involved in 25% of childhood acute Lymphoblastic Leukemia (ALL) and 15% of acute Myeloblastic Leukemia (AML) [2, 3]. The age of onset for leukemia in Downs syndrome is bimodal, peaking first in the newborn period and again at 3-6 years [4]. AML in Downs syndrome almost exclusively presents before the age of 4 years and the commonest type is acute megakaryoblastic (AMKL) which is...
extremely rare in non-Downs syndrome children [1, 3, 5]. Recent reports indicate that Down syndrome children with AML especially AMKL have exceptionally high cure rates with event free survival (EFS) rates ranging from 80-100%. This is in contrast to EFS less than 35% for non-Downs syndrome children [6, 7].

Case report

The patient presented to the Pediatric Department of the Dhiraj Hospital, Vadodara State in Gujarat at the age of 16 months. The patient was showing phenotype of Down’s syndrome, which was confirmed by karyotyping (Photograph - 1). He presented with a history of recurrent cough and running nose and decrease acitivity, increase sleepiness, not tacking feeds well, not playing well and fever of 5 days duration. On presentation, the child was pale, febrile with dysmorphic features e.g. flat occiput, upward slanting eye webbed neck, flattened nasal bridge, low set ears and protruding tongue (Photograph - 2). He had a mild distended abdomen and on palpation with hepatomegaly and splenomegaly present. An assessment of possible Downs syndrome with bronchopneumonia and acyanotic congenital heart disease was made. He was admitted in NICU for 3 days due to hyperbilirubinamia and weight loss.

Photograph – 1: Karyotyping with trisomy 21 (Down syndrome).

A complete blood count was done on admission revealed a Hb-5.1 gm/dl, Packed Cell Volume (PCV) of 12.6%, Platelets count-18000/cmm, Total White cell count (WBC)-19400/cmm, WBC differential count showed neutrophils-21% lymphocytes-20%, monocytes-1%, eosinophils-2% and blast 56%. He was transfused with fresh whole blood. Peripheral blood smear findings showed RBCs with severe anisopoiikilocytosis, polychromasia, tear drop cells, elliptocytes and target cells. Total WBC count was increased on smear with presence of blast cells with high N:C ratio, fine chromatin, prominent 1-2 nucleoli and scanty cytoplasm with some having blebs (Photograph - 3). An impression of Acute leukaemia with Downs syndrome was made. We had advised for bone marrow aspiration (BMA), bone marrow biopsy (BMB) and flow cytometry. Bone marrow aspiration revealed depressed erythropoiesis, multiple megakaryoblasts with cytoplasmic blebbing constituting about 60% of marrow nucleated cells (Photograph - 4). BMB showed marrow infiltrate by blast cells, apoptotic bodies and mitosis (Photograph - 5). Immunophenotyping revealed markers positive for CD34, CD45, CD33, CD13, CD117, CD36, aberrant CD7, CytoCD61, CD5 negative for CD10, CD19, CytoCD3, CytoCD79, CD14, CD64, CD11b, CD11a, CytoMPO and CD5 suggestive of AML M7 type. An impression of acute megakaryoblastic leukaemia (AML-M7) by morphology and immunophenotypically was made.

Photograph – 3: Peripheral smear with blast cells and cytoplasmic bleb (Leishman stain, 40X).

Photograph – 4: Bone marrow aspiration (Leishman stain, 40X).

Photograph – 5: Bone marrow biopsy showed infiltration of blast cells (H&E stain, 10X).

The parents were counseled on the nature of the child’s disease, management options and prognosis and the child was subsequently worked up for chemotherapy.

Discussion

The association between Downs syndrome (DS) and malignancy has been established for over 90 years [1-7]. A major diagnostic challenge in DS patients with acute leukemia is posed by the presence of transient myeloproliferative disorder (TMD), also called transient leukemia. It occurs in about 10% of DS patients [2]. TMD is usually recognized by the presence of megakaryoblasts in the peripheral blood, liver and bone marrow. Typically, most cases present at birth or shortly after and remit by three months, though a few cases persist beyond this [2, 8, 9]. After spontaneous remission of TMD, 10-30% of cases develop AML after 1-30 months [8, 9].

Transient abnormal myelopoiesis (TAM) and acute myeloid leukemia of Down syndrome (AML-DS) are disorders associated with trisomy 21; these conditions almost always develop before the age of 5 years. In individuals with Down syndrome (DS), the risk of developing AML-DS is increased 150 to 500 fold [10], compared to a 30-fold increase of developing acute lymphoblastic leukemia (ALL). Approximately 1%-2% of children with DS develop acute myeloid leukemia, with a large majority of cases (70%) being acute megakaryoblastic leukemia (AML French-American-British [FAB] classification: M7). TAM is a disorder that predominantly occurs in newborns with Down syndrome. It is characterized by an increase in the number of circulating blasts that have acquired mutations in the transcription factor gene GATA1 [2]. In the present case our patient also had more than 50% blast cells. The circulating blasts in TAM generally have the morphologic and immunophenotypic features of megakaryoblasts [11, 12].

A majority of TAM cases resolve spontaneously; however, a significant percentage persist (20-30%) and progress to acute megakaryoblastic leukemia within 1-3 years. As mentioned above, AML-DS is most often of the acute megakaryoblastic type, AML-FAB M7. It should
be recognized that both myelodysplastic syndrome associated with Down syndrome (MDS-DS) and AML-DS are classified as myeloid leukemia associated with Down syndrome [13].

References