

Declining total leucocyte count, an indication of transient abnormal myelopoiesis

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ABSTRACT

Neonates with Down syndrome have an increased predisposition to transient abnormal myelopoiesis, a haematological abnormality which is characterized by uncontrolled proliferation of myeloblasts. The unique ability of this disorder to spontaneously enter in to a state of remission led to the creation of a new class in 2008 World Health Organization (W.H.O.) classification of haemopoietic and lymphoid tumours. It has now been classified as transient abnormal myelopoiesis (TAM). The cause of remission is still not clear although it is possibly linked to the abnormal expression of GATA-1 transcription factor and to a switch from hepatic haematopoiesis to medullary haematopoiesis. Simple laboratory monitoring by serial complete blood count and peripheral smear can give indication of this rare disorder. As very few cases of this disorder exist we share our experience and report a case of transient myeloproliferative disorder in a male newborn having Down syndrome.

Key Words: Down syndrome, megakaryoblastic leukemia, transient abnormal myelopoiesis

INTRODUCTION

Transient abnormal myelopoiesis (TAM) is a haematological abnormality that is characterized by uncontrolled proliferation of myeloblasts in the peripheral blood and bone marrow. In most instances, this disorder has the ability to spontaneously “turn off” the overproduction and enter a state of remission.^[1,2] The disorder is seen especially in infants with Down syndrome in neonatal period and requires supportive treatment in majority of the cases.^[1,2] As very few cases of this disorder exist we share our experience and report a case of transient myeloproliferative disorder in a newborn male with Down syndrome.

CASE REPORT

A new born male child, born at 37 weeks of gestation,

weighed three kilograms at birth and was large for date. Examination revealed features of Down syndrome, pedal edema, hepatosplenomegaly. Antenatal scan revealed pericardial effusion. Ultrasound of the abdomen confirmed hepatosplenomegaly. Haematological examination on day one showed hemoglobin of 15.2 gram percent, Total leucocyte count (TLC) of 78,500 cells per microliter, platelets were 1,41,000 per microliter. Peripheral smear showed cells that measured 12-15 micrometer with round to irregular nuclei and a basophilic cytoplasm along with cytoplasmic blebs and were consistent with blasts. The cytoplasm of blasts cells showed azurophilic granules. These blasts constituted 55% of TLC [Figure 1]. Samples were taken on every day and sent for complete blood count. Samples showed declining TLC till it reached normal level at day ten [Figure 2]. On day ten TLC declined to 12500 which was normal for age and platelets were 1,75,000 per microliter.

The bone marrow examination was done on the day seven, which was diluted with blood and comprised predominately of blasts cells [Figure 3]. Blasts have similar morphology as in the peripheral blood. Cytoplasmic blebs were appreciated in majority of blasts, their cytoplasm contained coarse granules. Mature cells of neutrophilic lineage were reduced.

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Flow cytometry of bone marrow aspirate revealed that the blasts were positive for CD34, CD13, CD33, CD41, and CD61.

Karyotyping done on day seven revealed trisomy at 21 chromosomes [Figure 4].

The reducing TLC along with peripheral smear, bone marrow, karyotyping, flow cytometric findings along with clinical features and physical examination were consistent with a diagnosis of transient myeloproliferative disorder in the infant with Down syndrome.

DISCUSSION

Individuals with Down syndrome have an increased predisposition to acute leukemias, predominantly of myeloid type.^[1,3-6] The major morphological subtype

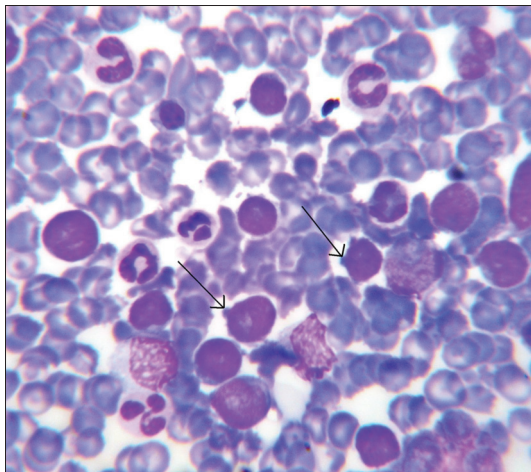


Figure 1: Peripheral smear showing blasts with open chromatin irregular nuclear membrane and scanty basophilic granular cytoplasm revealing blebbing - arrow mark. (Giemsa stain ×1000)

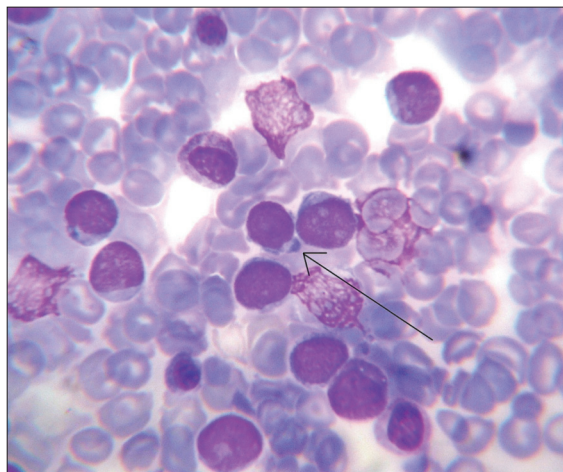


Figure 3: Bone marrow smear was diluted with blood and comprised predominately of blasts cells, note the blebbing in blasts - arrow mark. (Giemsa stain ×1000)

appears to be acute megakaryoblastic leukemia. Sometimes leukemia undergoes spontaneous remission and is referred as transient abnormal myelopoiesis (TAM). TAM is characterized by excessive proliferation of myeloblast in the peripheral blood and bone marrow.^[1,2,6] This unique ability of this disorder to spontaneously enter in to a state of remission led to the creation of new class in 2008 World Health Organization (W.H.O.) classification of haemopoietic and lymphoid tumours.^[6] It's now been classified as TAM with ICD-O code 9898/1, under the category, "myeloid proliferations related to down syndrome".^[6] In the previous W.H.O. classification (2001) it was classified as a variant of acute megakaryoblastic leukemia and was called as transient myeloproliferative disorder.^[7] The lack of GATA-1 transcription factor results in accumulation of abnormally differentiated megakaryocytes without leukemic transformation.^[8] There is a strong association of down syndrome's acute megakaryocytic leukemia to the mutations in X-linked haemopoietic transcription factor GATA-1.^[8] Approximately 10% of infants with Down syndrome have TAM. It is estimated that 25% of these

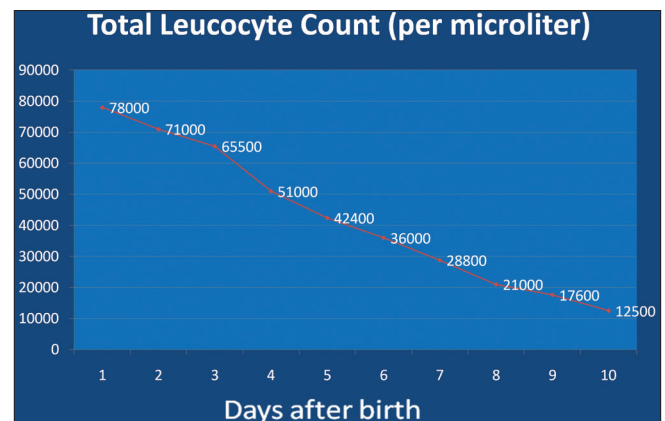


Figure 2: Graph showing declining Total leucocyte count per microliter from day one to day ten after birth

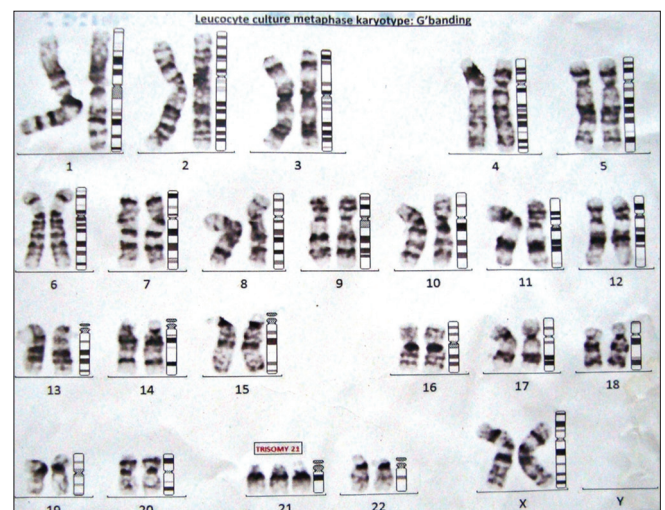


Figure 4: Karyotyping showing trisomy 21

infants, who present with TAM, are likely to develop megakaryoblastic leukemia between the age group of 1 to 3 years.^[1,2] The spontaneous remission of TAM has been linked to switch from hepatic haematopoiesis to medullaryhaematopoiesis.^[1] The initiation of chemotherapy is an important decision for the management, though it is not always required. Supportive care is recommended for TMD during the first few months of life unless the clinical condition requires intervention.^[9] Initial treatment options for TMD include leucopheresis or exchange transfusion. Chemotherapeutic drugs halt tumour cell division and are indicated in hyperviscosity syndrome, organomegaly causing respiratory distress, congestive heart failure, pericardial effusion, hydrops fetalis, liver dysfunction, and disseminated intravascular coagulation.^[9] Low doses of cytosine arabinoside are recommended as the chemotherapeutic agent of choice.^[10] The dose, duration, and frequency of medicine administration are often dependent on the size and type of cancer. The therapeutic effect is not apparent until 3 to 4 days after the initiation of chemotherapy. In this case the disorder spontaneously entered in to the state of remission with out any specific intervention.

A differential diagnosis of septicemia with leukamoid reaction was considered in our case in view of the peripheral smear findings, the diagnosis of transient abnormal myelopoiesis (TAM) was confirmed based on bone marrow and flow cytometric findings.

Simple laboratory monitoring by serial complete blood count and peripheral smear can give indication of this rare disorder. We suggest that extensive research is needed to study the mechanism behind its evolution and management of this disorder.

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