Transient Leukaemia: Leukaemia or Leukaemoid? A Diagnostic Dilemma

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Abstract We report a case of a newborn male who had mongoloid slant and was hypotonic at birth. Routine investigations revealed leucocytosis (WBC > 70,000/cmm) with 50% blasts in peripheral blood film. Marrow examination confirmed the excess of blasts. Karyotyping revealed 47, XY + 21 chromosomes. Due to absence of clinical symptoms, the baby was kept on follow-up without treatment. Within 7 weeks, PBF and bone marrow findings returned to normal, and the child was diagnosed as having Transient leukaemia with Down syndrome.

Keywords Transient leukaemia · Down syndrome · Transient myeloproliferative disorder

Introduction

Children with Down syndrome (DS) are at an increased risk of development of several haematological disorders.

Transient leukaemia (TL) is a disease entity unique to DS newborns, is characterised by high blastosis in peripheral blood and bone marrow and usually resolves without specific therapy in 1–3 months. Many infants may be clinically well at presentation with an incidental finding of circulating blasts in the blood, but in some cases, however, the disease is severe and potentially fatal [1]. Despite its typical transient nature, 20–30% of these patients develop overt acute leukaemia, usually within 3 years and typically of the M₇ phenotype [2].

Case Report

A baby boy was born after 38 weeks of gestation to a 29 year old mother with uncomplicated vaginal delivery. The baby weighed 3.0 kg and cried immediately after birth. Apgar score was six at first minute and eight at fifth minute. On physical examination infant was hypotonic and bore a few stigmata suggestive of DS including rounded facies, mongoloid slant, clinodactyly and increased distance between great toe and first toe. There were no cardiovascular disturbances. The child had no evidence of hepatosplenomegaly or cutaneous bleeds. Karyotyping revealed 47, XY + 21, chromosomes. On routine investigations, haemogram on day one revealed leucocytosis (WBCs, 70,000/cmm) and thrombocytopenia (platelets, 70,000/cmm) with no evidence of anaemia (haemoglobin, 15 g/dl). Differential leucocyte count included 50% of the blast cells along with segmented neutrophils (30%), lymphocytes (17%) and monocytes (3%) (Fig. 1a). The blast cells revealed high nucleus/cytoplasmic ratio, agranular cytoplasm, nuclei with occasional 1 or 2 nucleoli and no auer rods. Only 2–3% of the blast cells were positive for myeloperoxidase and Sudan black B on cytochemical staining.

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Fig. 1 **a** Peripheral blood film showing approximately 50% of the nucleated cells being blasts. (May-Grunwald Giemsa, $\times 400$). **b** Bone marrow smear showing blast cells. (May-Grunwald Giemsa, $\times 400$).

c Peripheral blood smear after 7 weeks revealing normalisation of blood counts. (May-Grunwald Giemsa, $\times 400$)

Bone marrow aspiration was performed which revealed slightly lower percentage of blasts (30%) with similar morphological characteristics (Fig. 1a). There were no morphological abnormalities in the remaining cell population of both the bone marrow and peripheral blood. The diagnosis of acute myeloid leukaemia (AML) was rendered.

Immunophenotyping of the blast cells revealed positivity with CD13, CD33 and CD117 which confirmed myeloid lineage of cells.

Since the clinical picture was silent, the infant was followed and monitored without any specific treatment. The follow-up haemograms revealed decline in circulating blast cells and were not detected after 7 weeks concurrent with normalisation of blood counts (Fig. 1a). The bone marrow repeated after 9 weeks showed normal haematopoietic activity.

Discussion

DS is caused by an extra whole or partial copy of chromosome 21 and is the most common chromosomal abnormality in the live newborn [3]. Other than showing various clinical features, infants with DS may infrequently develop a condition called TL of newborn which is characterised by a high number of circulating blast cells. It has also been referred as transient myeloproliferative disorder (TMD) or transient abnormal myelopoiesis (TAM) and occurs in approximately 10% of DS neonates and in phenotypically normal neonates with trisomy 21 mosaicism [2]. TL is usually detected in the first week of life and spontaneously resolves by 3 months of age.

TL is a unique syndrome that occurs only in newborns with complete or mosaic DS and is defined as the morphologic detection of blasts in DS patients less than 3 months of age [3].

Typically, TL is diagnosed in clinically normal children with DS via the casual detection of leucocytosis with

circulating blast cells. However, in approximately 20% of cases, the disease is severe and life-threatening, manifesting as hydrops fetalis, multiple effusions, and liver or multi-organ system failure resulting in death [4].

In TL, peripheral blood analysis shows variable number of blasts and usually thrombocytopenia; other cytopenias are uncommon. Bone marrow characteristics of TL are, likewise, variable. Sometimes the bone marrow blast differential can be lower than peripheral blood blast differential because these cells are believed to be of foetal derivation and normally reside in organs of foetal haematopoiesis such as liver [3]. The blasts of TL typically show light microscopic, ultrastructural, and flow cytometric evidence of megakaryocytic differentiation [2].

Frequently, TL disappears during the first 3 months of life, but after a period of normal marrow morphology and peripheral blood count recovery, 20–30% of patients develop acute leukaemia (most commonly AML M₇) within the first 4 years of life. Unlike TL, if left untreated, the subsequent leukaemia does not spontaneously regress [1].

The molecular mechanisms that lead to TL are being elucidated. TL blasts contain extra copies of chromosome 21 and occasional additional karyotypic abnormalities. All TL blasts have various somatic mutations in the X linked gene GATA 1 that encodes a transcription factor for normal erythroid and megakaryocytic development [5].

TL can be confused with congenital leukaemia because the two are clinically and haematologically indistinguishable. TL must be differentiated from congenital leukaemia because TL resolves spontaneously without anti-leukemic therapy whereas untreated congenital leukaemia is a fatal disease. Myeloid blasts other than M₇ and lymphoid blasts point towards leukaemia. Patients of congenital leukaemia have a high leukaemic cell load with hepatosplenomegaly, leukaemia cutis and hyperleucocytosis whereas TL patients have fewer signs. Cytogenetic abnormalities are more commonly found in congenital leukaemia patients. On the contrary, TL have few cytogenetic abnormalities apart from +21 [6, 7].

In view of its transient nature, specific antileukaemic therapy is not indicated, unless there is haematological progression of disease [8].

In our case the patient was initially diagnosed as AML. Since blast cells disappeared from both peripheral blood and bone marrow without any treatment, a final diagnosis of TL was made. The child is still under follow-up to look for any development of acute leukaemia.

Conflict of Interest None

References

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