Case Report

IMPORTANCE OF PERIPHERAL SMEAR IN DOWN'S SYNDROME WITH TRANSIENT MYELOPROLIFERATIVE DISORDER

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ABSTRACT

One day old female child presented with respiratory distress, cyanosis, abdominal distention and dysmorphic facies. On detailed clinical examination she had features suggestive of downs syndrome with hepatosplenomegaly and severe pallor. Peripheral blood smear revealed marked hyperleukocytosis, thrombocytosis and presence of blast cells. Appropriate therapy was initiated immediately that resulted in a good outcome.

INTRODUCTION

Approximately 5 to 30 percent of infants with Down syndrome are born with transient leukaemia of Down syndrome (TL-DS), which is also known as transient myeloproliferative disorder (TMD) or transient abnormal myelopoiesis (TAM). It is a clonal disorder characterised by circulating blasts and dysplastic changes in blood cells[1,2,3]. TL-DS is a result of mutations in GATA1 a haematopoietic transcription factor gene associated with trisomy 21, which is either constitutional or acquired. TAM may present with apparent clinical features but some cases are only identified through examination of the peripheral blood film and/or by mutation analysis of GATA1 gene [4,3]. TAM is recognized shortly after birth or in neonatal period and is characterized by leukocytosis with or without thrombocytopenia. Though many cases resolve spontaneously, TAM may result in early death in around 15– 23% cases and 20–23% of survivors will develop acute myeloid leukaemia of Down syndrome (ML-DS) during the first 4 years of life. Generally TAM has an event-free survival of 63–68%[4,5,6]. Here we report our experience of one such case along with review of literature.

CASE REPORT

A 2300g female child was born via LSCS to a 23 years old mother with uncomplicated pregnancy, cried immediately after birth and required no active resuscitation. After 14 hours of delivery the baby developed respiratory distress and was referred to our center for further management. Physical examination revealed hypotonia, mongoloid slant, low set ears, high arched palate, short neck, short and broad hand, and a sandal gap suggestive of downs syndrome. Pallor was also noticed. Cardiovascular examination revealed a short systolic murmur over apex. On abdominal examination liver was enlarged 6cm below left costal margin and spleen was just palpable 2cm below left costal margin. No lymph nodes were palpable. On respiratory system examination the baby had respiratory distress with a SAS score of 6 and acrocyanosis. Complete blood count showed Hb 9.3g/dl, platelet count of 6.24 lakhs, white blood cell count (WBC) was 140300/cu mm with presence of blast cells. SGOT & SGPT were 1504 and 474 u/l respectively and serum potassium was 7.7 mg/dl. The baby was managed for suspected tumor lysis syndrome with hyperhydration, lasix and allopurinol along with oxygen therapy. Sepsis work up was negative. Flowcytometry was done from the peripheral blood sample, and gated population of blasts showed positivity for CD 33, CD 7, Cy CD 61, CD 56

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and CD 38 markers. The findings were consistent with TAM. Echocardiography showed a PDA of 3mm. The baby was started on low dose cytarabine at the dose of 10mg/m² IV twice a day for 7 days in view of leukocytosis, hepatomegaly, respiratory compromise. Careful monitoring of tumor lysis markers was done along with strict fluid balance management. Subsequent hemogram showed gradual decrease in WBC and liver enzymes. On Day 5 of life hemogram showed a WBC of 23100/cumm, Platelets counts of 3.33 lakhs/cumm and SGOT and SGPT 39 and 134 u/l respectively. On day 6 of life the parents took leave against medical advice and the child was lost to follow up. Chromosomal analysis later revealed a 46XX+rob (14;21)(q10;q10)+21 karyotype, confirming the diagnosis of Down’s syndrome.

DISCUSSION

TMD is a unique phenomenon seen in newborns with trisomy 21. The incidence is approximately 10% [7,8]. This disorder is detected in approximately 80% of the cases during the third trimester, and in the rest of the cases it is confirmed after birth. Findings during ultrasonography can be hepatosplenomegaly (79.5%), fetal hydrops (30.8%), pericardial effusion (23.1%) and alteration in the volume of amniotic fluid (15.4%). Diagnosis during perinatal period requires a high index of suspicion and therefore have poor prognosis and has high mortality [9]. Its clinical expression is not consistent, although there are asymptomatic cases, other patients present symptoms caused by organ infiltration or tumor lysis, accompanied by leukocytosis, leukostasis, organic failure with hemodynamic and respiratory compromise [7,10]. The circulating blasts cells in the peripheral blood show immunophenotypic markers of myeloblastic, megakaryoblastic and erythroblastic precursors. The clinical course is generally self-limiting during the first six months of life. Around 30% of patients may develop acute leukemia (MAM-M7) or a myelodysplastic syndrome during the first five years of life [9,11]. Hence it is very necessary to consider differential diagnosis with other diseases that may produce a leukemoid reactions, thrombocytopenia and anemia, such as neonatal hemolytic processes (Rh incompatibility), congenital viral infections (TORCH), neonatal leukemia, histiocytosis, neuroblastoma or situations that occur with perinatal hypoxia [1,12,13]. The initial treatment is supportive. Chemotherapy is used in patients with evidence of compromised liver or cardiorespiratory function that are accompanied by visceromegaly or serious effusion, as well as severe leukocytosis [14]. The exact incidence of TAM is very tough to determine without performing a screening of all infants with down syndrome. Although the diagnosis of transient abnormal myelopoesis is generally made with clinical features along haematological findings, a molecular diagnosis by finding the GATA1 mutation(s) will clinch the diagnosis in clinical and hematologically silent cases [10]. Given the varied clinical presentation of TAM, it is important to identify the factors that dependably predict the consequence and, therefore, the patients who are likely to be gained from the treatment. It will also important to consider which babies deserve treatment and to establish the most effective treatment regimens [10,11].

CONCLUSION

All infants with either known, or having a high suspicion of, down syndrome must be examined for other features suggestive of TL-DS (organomegaly, cholestasis and hepatopathy, skin rash, pericardial and pleural effusions) & they must have a complete blood count and peripheral blood film examination and requested with a formal assessment of the blast cell percentage in peripheral blood. Neonates who have clinical findings and blast cell percentage indicative of TL-DS should undergo additional investigation such as liver function tests, chest X-ray, echocardiogram, abdominal ultrasound and flowcytometry should be considered and banking on which further treatment should be planned.

References


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