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A Case Report on Acute Lymphoblastic Leukemia in A 10 Days Old Neonate

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Abstract Although leukemia's are the most common malignant disease seen in children, it occurs rarely in neonates. Only few cases of congenital leukemia have been reported in literature. We report here a rare case of congenital lymphoblastic leukemia in a 10 days old full term male neonate of normal home delivery who presented in the hospital with complaints of fast breathing and fever of 1 day duration. Initial clinical manifestation was that of Multi organ dysfunction syndrome due to late onset neonatal sepsis but was found to have acute leukemia on subsequent investigations.

Keywords: *Neonate, Infants, Acute lymphoblastic leukemia, malignancy*

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1. Introduction

Acute lymphoblastic leukemia (ALL) in early infancy usually occurs during the first year of life. Leukemia during infancy accounts for 2.5% to 5% of acute lymphoblastic leukemia (ALL) and 6% to 14% of acute myeloid leukemia (AML) of all pediatric cases [1]. Although leukemia is common malignant disease seen in children, it occurs rarely in neonates. Reaman *et al.* reported that only 2 of the 115 cases entered on children cancer group had congenital leukemia [2]. Both acute and long-term complications of treatment for infant acute lymphoblastic leukemia are also frequent. Several studies have shown that infant ALL has poor prognosis. However, the number of survivors has increased with the recent treatment protocols [3].

2. Case Presentation

Here is the case of a 10 day's old full term male neonate of normal home delivery who presented in the hospital with chief complaints of fast breathing with fever since 1 day. The baby was a referred case from the nearby hospital for neonatal intensive care (NICU).

The neonate belonged to the lower socio-economic class muslim family from Siraha district, eastern region of Nepal. The mother had not been to any antenatal checkups and no significant maternal medication and medical history was disclosed upon interview. The baby was said to be apparently well during first week after birth. On physical examination, the baby was tachypnoic, dehydrated with toxic look and naso-gastric tube in-situ. Pallor, icterus and peripheral cyanosis were present. The vitals record during admission were heart rate (HR) 136 bpm, respiratory rate (RR)-52 bpm, temperature 97.6°F, Spo_2 (oxygen saturation) 63% without oxygen, Cappillary refill time, CRT < 3s ; Bilateral crepts were present on chest. Cardiovascular findings were normal. Baby also had soft distended abdomen with hepato-splenomegaly (Liver- 5 cm below right subcostal margin (RSCM); Spleen- 4 cm below left subcostal margin (LSCM) with decreased reflex activity and tone (Figure 1). Laboratory investigation reports from referred hospital showed increased random blood sugar (240 mg/dl), total serum billirubin (10.9 mg/dl), blood urea (96 mg/dl), potassium (8 mmol/l), total leucocyte count (1,20,000/cumm), monocytes (24%) value and decreased Haemoglobin (10.5 gm%) value. Arterial blood gas analysis demonstrate decreased P^H (7.229) and partial oxygen pressure PO2 (62.5) with no significant alteration in other metabolic values.

Baby was admitted in the NICU with provisional diagnosis of late onset neonatal sepsis with Multi-organ dysfunction syndrome considering fever, hepatosplenomegaly, diminished renal and respiratory function and others clinical finding and laboratory investigation report. Antibiotics therapy were started with intravenous ceftazidime, vancomycin along with IV fluid and baby was kept in radiant warmer with oxygen via continuous positive airways pressure (CPAP) @ 5 cm

H_2O. Fresh frozen plasma 35 ml and 35 ml of fresh whole blood were transfused. Repeat Laboratory investigation was sent for Renal function test (RFT), liver function test (LFT), complete blood count (CBC), Urine RME (urine rapid microbial examination) and stool examination. Baby was kept under observation.

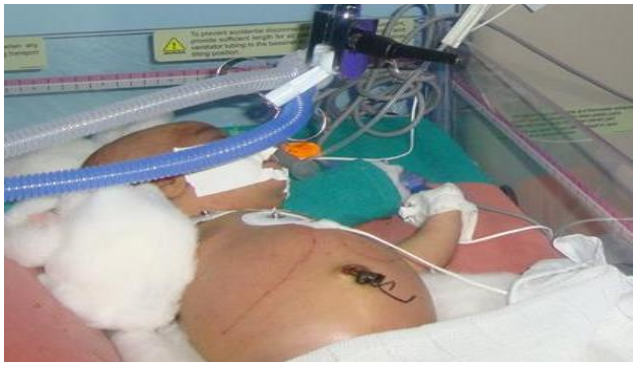

Figure 1. Infants with ALL in NICU having hepato-splenomegaly and distended abdomen

The fever subsided after few hours of therapy however no significant improvement was seen in respiratory rate and other vitals during first 6 hours of admission. Laboratory report revealed significant increase in TLC and blast cells (29%) with decreased platelets count (1, 10,000/mm^3), Increased blood urea (84.4%), potassium (8.3 meq/l) and total serum billirubin (18.9 mg%) level were shown. Urine examination report showed increased pus cells (8-10/ HPF (high power field)), red blood cell (2-4/HPF) with granular cast (2-4/ HPF) and trace albumin. Furthermore, occult blood was seen on stool. No change in treatment plan was made during this period. Test for peripheral blood smear (PBS) was sent suspecting acute leukemia.

After 8 hours in NICU, there was sudden drop of oxygen saturation to 60% with diminished blood pressure after which the oxygen was delivered via bag and mask. The baby was then planned for endotracheal tube intubation for mechanical ventilation (MV). Blood pressure was increased upto 100/60 mm Hg after 30 minutes in ventilator. Baby also had single episodes of Seizure. Oxygen saturation was kept more than 95% along with closed monitoring however no significant clinical improvements was seen till 48 hrs of MV.

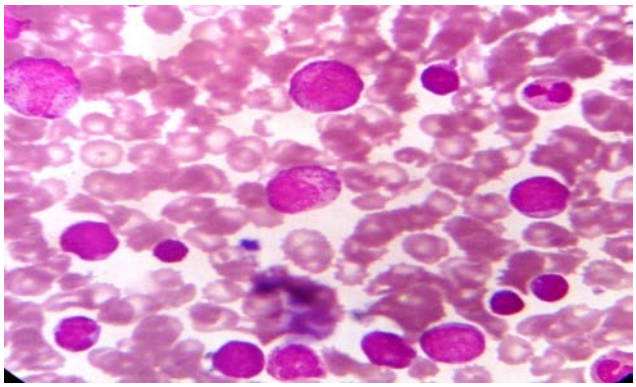

Figure 2. Peripheral Blood Smear Image with increased number of blast cell and leucocytosis

Reports of PBS outline impression of acute lymphoid leukemia (considering presence of 60% blast cell with leukocytosis) (Figure 2). Bone marrow aspiration cytology was planned but on parents' request, the baby was referred to higher oncology center under bag and mask ventilation, for further evaluation and management.

3. Discussion

Although overall incidence is rare, leukemia is the most common type of childhood cancer. It accounts for 30% of all cancers diagnosed in children younger than 15 years. Epidemiologic studies of acute leukemias in children have examined possible risk factors, including genetic, infectious, and environmental, in an attempt to determine etiology. The environmental risk factors include ionizing radiation, nonionizing radiation, hydrocarbons, pesticides, alcohol use, cigarette smoking, and illicit drug use. Genetic conditions such as Down's syndrome, eurofibromatosis, Shwachman syndrome, Bloom syndrome, Ataxia telangiectasia are also found associated in many studies [4]. In this case, though maternal exposure to certain environmental risk factors such as UV radiation, pesticides and smoke was disclosed on interview, whole genome sequencing of the parents were not examined to outline the presence of any possible genetic predisposition factors in neonates.

Studies had showed that acute leukemia in infants present a unique biological and clinical characteristic than that found in adults. Leukemia in infants is characterized by the presence of high leukocyte counts (>50%) at diagnosis, massive organomegaly, central nervous system involvement, CD10 negative, and sometimes with aberrant expression of monocytoid differentiation [3,5]. These characteristics seen in infant ALs are inter-correlated, and their presence is inversely associated with age. Infants diagnosed with acute leukemia with chromosomes 11q23 rearrangement also known as mixed lineage leukemia (MLL), have a particularly poor prognosis when compared to other children with acute leukemia [6].

In this Case, the infant had showed characteristics manifestation of acute leukemia involving fever, high leukocyte count, jaundice, uremia, internal GI bleeding, hepato-splenomegaly and diminished respiratory and renal function which initially had some contrasting evidence of sepsis. The positive peripheral blood smear report for lymphoid leukemia confirms the diagnosis of leukemia later without difficulty.

Our case also resembles in some aspect with the case report of congenital leukemia by Sethi et al., [7] where the neonate was febrile and tachypnoeic, had rales in the chest and manifested with hepato-splenomegaly with increased leukocytes and lymphoblast cells. The report discussed that the course of congenital leukemia is one of rapid deterioration and death from hemorrhage and infection and that it is a more aggressive disease with increased incidence of leukocytosis, massive hepatosplenomegaly, CNS involvement, thrombocytopenia, hypo-gammaglobinemia, and less frequent remission induction by 14 days of age. The report also addresses that treatment outcome is significantly poorer in infants with ALL younger than 1 year at diagnosis (23% disease free survival compared with 70% for older children) and may be even lower in newborns [7].

Historically, treatments for infants with ALL were treated on risk-adapted childhood ALL protocols. These studies had a crucial role in identifying the need for infant-specific protocols, outlying prognostic categories and the requirement for a more interrogated approach for treatment for ALL. Development of collaborative infant-specific studies as Landmark outcomes and Universal prospective identification of independent adverse prognostic factors, including presence of a mixed lineage leukemia rearrangement and young age, has established the basis for risk stratification within current trials. Despite variations in therapeutic intensity, there has been no recent improvement in survival due to the equilibrium between relapse and toxicity [8].

Moreover, Recent understanding of the genetic and epigenetic makeup of high-risk pediatric leukemia has led the opportunity to develop targeted therapies that promise to be both more effective and less toxic than current chemotherapy [9]. Current novel approaches to targeting pediatric ALL includes targeting oncogenetic kinases such as protein tyrosine kinase inhibition, Fms-like Tyrosine (FLT3) receptor tyrosine kinase inhibition, mammalian target of rapamycin (mTOR) kinase inhibitors, The Janus kinase (JAK) tyrosine kinase inhibition etc. and other oncogenic targets, various apoptotic pathway, epigenitics and other non oncogenic surface targets are in evaluation for treatment of acute ALL in pediatrics under various clinical trials and laboratory based research [10]. Some Studies had also investigated therapeutic potential of pharmacologic inhibition of bromodomains in hematologic malignancies (ALL, MLL). Bromodomain and extraterminal domain (BET) protein inhibition result in a potent suppression of *MYC* transcription and activity as well as decreases expression of the cytokine receptor *IL7R* (interleukin 7 receptor) in *CRLF2* (cytokine receptor subunit) rearranged and other B cell acute lymphoblastic leukemia (B-ALL) cell [11]. Bromodomain inhibition posses promising therapeutic strategy for B-ALL as well as other conditions including mixed lineage leukemia.

4. Conclusion

Acute lymphoblastic leukemia in neonates is fetal form of malignant diseases having varying clinical presentation yet its exact cause is still not fully understood. The further research investigation is suggested to explore the possible causative factors and out lay a better preventive and treatment strategy.

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