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Case Report

Neonatal Leukaemia: A Case Report and Review of the Literature

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Abstract

Background: Acute leukemia has a particularly bad prognosis in the newborn era. Its prognosis is significantly poorer than in older youngsters. The occurrence of leukaemia in the neonatal period can present diagnostic challenges due to the rarity of the condition and its clinical presentation, which may be misleading or inconspicuous. *Case report:* A case of neonatal acute myeloblastic leukaemia (AML) in a newborn with trisomy 21 is presented herein. The patient was admitted with respiratory distress and a clinical examination revealed a facial dysmorphic syndrome, pallor, hepatosplenomegaly, and a bone marrow failure syndrome with bone marrow invasion by 36% myeloblasts, confirming the diagnosis of AML. The immunophenotyping results indicated that the patient had AML0, with a low CD13+ and CD33+ MPO myeloid population. During the patient's hospitalisation, a multi-resistant Klebsiella pneumoniae urinary tract infection was diagnosed, and septic shock was diagnosed after four days. *Conclusion:* Acute neonatal leukaemia is a rare and complex condition that requires the expertise of both neonatologists and paediatric haematologists.

Keywords

Leukaemia, Neonatal, Trisomy 21, Blasts

1. Introduction

Neonatal acute leukaemias are rare, accounting for less than 1% of all childhood leukaemias, such incidents may occur at birth or during the first 28 days of life. [1-3]. They often present clinically with hepatosplenomegaly and skin involvement (cutaneous leukaemia), sometimes in the absence of bone marrow involvement. Newborns with trisomy 21 have an increased incidence of acute leukaemia.

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characterised by the presence of skin infiltrates, hepatomegaly and splenomegaly, while lymphadenopathy is rare

Congenital leukaemia, also known as neonatal leukaemia, constitutes less than 1% of all childhood leukaemia cases. The clinical features of congenital leukaemia include hepatomegaly, splenomegaly, and skin infiltrates, with lymphadenopathy being less common [1].

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The largest historical series demonstrates an overall survival rate of approximately 35%, which is an unfavourable prognosis for this condition. Due to the advanced age at which the disease first manifested, chemotherapy is not a viable option. Consequently, other ethical and therapeutic considerations must be made [4].

2. Case Report

The infant was a male newborn, 15 days old, born to a mother who had not attended to her pregnancy, estimated to be at term by vaginal delivery at home. The pregnancy had been uneventful, and the patient's family history was unremarkable. The infant was admitted with respiratory distress. A clinical examination revealed that the newborn was trisomic and had a weight of: The infant weighed 2,470 grams (10%-50%), was 43 centimetres in length (3%-10%), and had an occipitofrontal circumference of: The infant's temperature was 32.5 degrees Celsius (50% of the normal range). The infant's temperature was 37.4 ℃, and its heart rate was: The infant's heart rate was 140 beats per minute, while the respiratory rate was: The infant's respiratory rate was 57 breaths per minute, and the blood pressure was 66/36 mm Hg. The oxygen saturation was 90%. The pleuropulmonary examination revealed subcutaneous chest indrawing and audible whining through the stethoscope.

The abdominal examination revealed 5 cm of hepatomegaly and 4 cm of splenomegaly with a rib margin on the mid-clavicular lines. The neurological examination yielded normal results.

A complete blood count (CBC) was performed, which revealed a haemoglobin concentration of 90 g/l, a white blood cell count of 100 g/l, and a platelet count of 45 giga/l. A blood smear demonstrated the presence of 30% blast cells (Figure 1). A myelogram was ordered and revealed an amegakaryocytic marrow, infiltrated by 36% large blasts with a high nucleocytoplasmic ratio, irregularly shaped nuclei, fine nucleated chromatin and non-granular basophilic cytoplasm with low myeloperocytase estimated at 2% in all blasts. Lactate dehydrogenase (LDH) levels were found to be elevated at 900 IU/L.

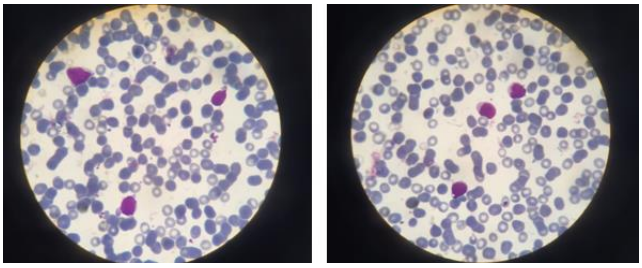

Figure 1. *A blood smear demonstrated the blast cells.*

The diagnostic work-up was completed by karyotype analysis, which revealed trisomy 21.

The immunophenotyping results indicated that the patient had AML0, with a low CD13+ and CD33+ MPO myeloid population.

During the patient's hospitalisation, a multi-resistant Klebsiella pneumoniae urinary tract infection was diagnosed, and septic shock was diagnosed after four days.

3. Discussion

The incidence of congenital leukaemia, a rare disease affecting newborns, is 4.7 cases per million births [3]. The diagnostic criteria include:

1. Appearance during the initial four weeks of life;
2. Immature myeloid, lymphoid, or erythroid cell proliferation;
3. Immature cell infiltration into non-hematopoietic organs;
4. Lack of other illnesses to explain the proliferation. [5, 6].

A number of potential contributing factors have been identified, including maternal irradiation during pregnancy, birth weights in excess of 4 kg, the presence of insulin-dependent growth factors or exposure to topo-diuretic topoisomerase II inhibitors contained in tea, coffee or chocolate or certain soya derivatives [7].

Gender does not significantly differ [1].

Children with trisomy 21 have a 10 to 20 fold increased risk of developing leukemia compared to children in the general population. Acute lymphoblastic leukaemia (ALL) is less prevalent in newborns than acute myeloid leukaemia (AML), with respective percentages of 38% and 56%. AML7 is the most predominant form of trisomy 21 AML [8].

The most prevalent clinical symptoms are hepatomegaly, splenomegaly, and skin lesions (leukemia cutis) [9]. Approximately 50% of cases present with central nervous system (CNS) infiltration, which may manifest as bulging fontanelles, papilloedema, retinal haemorrhages, and decreased consciousness. This latter symptom may also be caused by leucostasis linked to hyperleucocytosis. In addition to cardiac and renal failure, infants with hyperleucocytosis may experience respiratory distress with hypoxia and acidosis [10].

In approximately two-thirds of cases of acute myeloid leukaemia (AML) in newborns, cutaneous infiltrates are observed, which can develop independently of involvement of the bone marrow or peripheral circulation [9]. A common symptom of leukemia cutis is a widespread, firm nodule that can be blue, red, brown, or purple in colour. The appearance has been referred to as a "blueberry muffin rash," but it is not exclusive to neonatal leukemia; it can also occur in neuroblastoma, congenital infections, and non-malignant conditions like severe hemolytic anemias that are linked to extramedullary hemopoiesis. It can take several months for a neonate with leukemia cutis to progress to a systemic condition. It is estimated that approximately 50% of newborns with acute lymphoblastic leukaemia (ALL) also have skin

infiltration [11].

The range of haematologic results may vary considerably, from normal levels to severe anaemia, thrombocytopenia and leukocytosis, with the presence of leukaemic blasts identified in the peripheral blood [12]. Hyperviscosity and leukostasis, which can result in impairment of the heart, lungs, and central nervous system, can arise from leukocytosis. Furthermore, elevated uric acid and lactate dehydrogenase are additional test abnormalities. Significant hepatic infiltration is indicative of impaired liver function [13]. To confirm the diagnosis, flow cytometry, skin biopsy, and/or bone marrow aspirate and biopsy are commonly employed. The majority of cases of congenital leukaemia have a myelogenous origin, with the most prevalent subtypes being acute myelomonocytic (M4) and monocytic (M5) [14].

The utilisation of flow cytometry to identify cellular markers serves to confirm the myeloid or lymphoid nature of blasts and to distinguish between sub-groups. Flow cytometry appears to be the technique of choice for immunophenotyping acute leukaemia [15]. In the diagnosis of MPO-negative AML, CD13 and/or CD33 expression serves as the reference criterion for membership of the myeloid lineage, with expression observed in between 80% and 85% of poorly differentiated acute myeloid leukaemias (AML0) [16].

The immunophenotypic characteristics of neonatal leukaemia are reflective of the underlying molecular abnormalities. Acute myeloid leukaemia (AML) is most commonly of an acute monocytic/monoblastic or myelomonocytic type, due to the frequent involvement of the KMT2A gene (formerly known as MLL) and the less frequent relationship with t (8; 16) (p11.2; p13.3)/KAT6A-CREBBP. The immunophenotypic subtype associated with t(1;22) (p13.3; q13.1) in acute megakaryoblastic leukaemia represents the second most common subtype, accounting for 17% of cases [17].

Initial treatment is supportive include transfusons to address anemia, thrombocytopenia, and coagulopathy [18].

In the absence of chemotherapy, the prognosis for patients with congenital leukaemia is invariably fatal. The disease progresses rapidly, leading to death from bleeding or infection [19]. High leukocyte count and extramedullary infiltration including the CNS, are indicative of a poor prognosis [20].

Despite its rarity, spontaneous remission has been documented in cases of congenital AML [21]. The overall three-year survival rate in a study of newborns with leukaemia (AML and ALL) was 26%. The prognosis was more favourable for AML (35%) than ALL (9%) [22].

4. Conclusion

Acute neonatal leukaemia is a rare and complex condition that requires the expertise of both neonatologists and paediatric haematologists. It is of the utmost importance to rapidly gather prognostic information (immunophenotyping, cytogenetic study of blasts) in order to inform the decision-making process with the parents regarding the nature of the treatment.

Abbreviations

ALL	Acute Lymphoblastic Leukaemia
AML	Acute Myeloid Leukaemia
M4	Acute Myelomonocytic
M5	Monocytic
CNS	Central Nervous System
KMT2A	Lysine Methyltransferase 2A

Conflicts of Interest

The authors declare no conflicts of interest.

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