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Infant Acute Lymphoblastic Leukemia with Bilateral Nephromegaly: Report of an unusual Combination

[1]Balogun TM, [2]Salisu MA

[1]Haematology and Paediatrics Department, Lagos State University Teaching Hospital, Ikeja, Lagos, Nigeria.
[2]GPO, Ikeja, Lagos, Nigeria
taiwo_modupe @ yahoo.com

Abstract:

Introduction: *Infant acute lymphoblastic leukemia is an extremely rare haematological malignancy which has an aggressive clinical presentation in a susceptible host. Also nephromegaly is an unusual form of presentation in this pathology.*

Methods: *A nine month old male infant presented to us with recurrent high grade fever, generalized lymphadenopathy, flank swelling, and severe anaemia . The diagnosis of acute leukemia was made from a peripheral blood film appearance and it was confirmed with a bone marrow aspirate finding. The nephromegaly was confirmed with abdominal ultrasound scan.*

Result: *An unusual case of an infant acute lymphoblastic leukemia with bilateral nephromegaly was found. Possible risk factors for infant leukemia are discussed.*

Conclusion: *Infant acute lymphoblastic leukemia is rare and its association with nephromegaly is unusual but it is a possibility that needs to be ruled out on suspicion.*

Keywords: *Infant leukemia, nephromegaly, case report.*

1. INTRODUCTION

Infant acute lymphoblastic leukemia (ALL) is an extremely rare haematological malignancy with an aggressive clinical presentation in a susceptible host. Also, nephromegaly is an unusual form of presentation in infant ALL. A Previous research in the USA, found that infant ALL accounts for about 5 % of childhood leukemia.[1] Mantan et al reported that 3- 5% of ALL is associated with nephromegaly. [2] In the United Kingdom, acute leukemia is reportedly the most common cancer in children.[3] In Kano, North central Nigeria, acute leukemia has been reported to be among the most common paediatric cancers and was found to be 16.9% of paediatric malignancies.[4] We present a rare case of a 9 month old infant with ALL and unusual bilateral nephromegaly, the disease had an aggressive clinical course with a rapidly fatal outcome.

2. CASE REPORT

We report a nine month old infant boy who presented with a history of recurrent high grade fever of four months duration, severe anaemia, occasional cough, vomiting and bloody loose stools. Mother was not exposed to X-irradiation in pregnancy and didn't smoke cigarette. Baby was on breastfeeding and had started on some cereals.

At general examination, patient looked acutely ill and febrile with moderate clinical pallor, generalised firm, non tender mobile lymphadenopathy which involved the cervical, submandibular, axillary and inguinal body areas. Examination of the respiratory system revealed normal findings. Abdominal examination revealed slight distension, non tender hepatomegaly of 10cm, spleen not palpable, left palpably enlarged kidney.

Laboratory investigations showed the following:

Complete Blood Count with Packed Cell Volume of 28%, Total white cell count 61.1× 109/dl and Platelet count was 10×109/dl. Peripheral blood film morphology showed red cells that were normochromic normocytic. There was moderate leukocytosis with peripheral lymphoblasts count of

10%. Platelets were markedly reduced on film 0-1/high per field. Haemoglobin electrophoresis was genotype AA .Bone Marrow aspiration confirmed ALL with depressed normoblastic erythropoiesis. Myelopoiesis was also depressed. Lymphoblasts comprised 30% of nucleated marrow cells. No megakaryocytes were seen.

Abdominal Ultrasound revealed normal size and span of the liver, smooth outline and normal homogeneous echo pattern of the spleen. There was no abnormality detected in the gall bladder, pancreas, intestines as well as the right and left iliac fossae. The right and left kidneys were enlarged. The right kidney measured 101mm x 49mm while the left measured 97mm x 51mm in sizes with increased echogenecity of renal sinus noted. However, Blane et al reported normal average infant kidney length as 3.1mm for the right and 3.3mm for the left respectively [5] No retroperitoneal lymph node enlargement was reported. Renal biopsies and abdominopelvic computed tomographic scan were not done since diagnosis had been made from blood film and bone marrow aspirate. No cytogenetic studies were done because of lack of facility. The patient was given supportive care in form of red cell transfusions, platelet concentrates, antibiotics, antifungal agents. Unfortunately, the patient died two weeks after presentation from intracranial bleeding and this was prior to initiation of chemotherapy

3. DISCUSSION

Our report is of a 9 month old male infant who was diagnosed for acute lymphoblastic leukemia (ALL) with bilateral nephromegaly and the case had an aggressive rapidly fatal outcome. Generally, infant leukemia refers to acute lymphoblastic or acute myeloblastic leukemia (AML) diagnosed in a child less than one year old. However, congenital leukemia is diagnosed in the newborn less than a month old. Our case report is of a male patient, which is contrary to previous documentation that females have a higher risk of developing infant leukemia than males.[6] this patient was 9 months old and had a high total white cell count with peripheral blood lymphoblasts at diagnosis. The younger age, male gender and high white cell count are independent poor prognostic factors from previous research findings; indicating that the younger infants, male and those with higher white cell counts have poorer outcomes in acute lymphoblastic leukemia. [1,7] The symmetrical bilateral nephromegaly in our case report is an infrequent finding in infant ALL .Acute lymphoblastic leukemia associated with nephromegaly is an unusual form of presentation which has been reported to have poorer prognosis than leukemia alone.[7, 8] Also, it's been found out that renal enlargement due to leukemia is usually as a result of acute lymphoblastic leukemia. [9] The clinical presentation in children with acute leukemia include fever which could be high grade, bone pain, clinical pallor, easy bruising, mucosal bleeding, diarrhea, failure to gain weight and life threatening infections.[1, 10] The most common sites of extramedullary spread of acute lymphoblastic leukemia are the lymph nodes, spleen, liver, CNS, skin, testes, ocular anterior chamber, pleural and pericardial spaces, kidneys and ovaries but renal infiltration and the resulting nephromegaly is a rare finding. [11, 12] However, in a previous study, 30% of patients with ALL had renal involvement while 10% presented with bilateral nephromegaly.[13]

Our patient got red cells and platelet transfusions, broad spectrum antibiotics and antifungal medications. A previous study in Morocco by Depasse et al has emphasized the importance of supportive care in low income countries to reduce the high rate of infectious deaths in leukemia compared to that reported in high income countries.[14]

In the USA, ALL has been documented to be commoner than AML in infants.1 However, Linden et al reported that in neonates, AML has been found to be more frequent than ALL and that high mortality rates in leukemia are observed in this age group. [15] In the United Kingdom, acute leukemia is reportedly the most common cancer in children and the cause of the disease in the majority of cases are unknown, but has been associated with chromosomal rearrangements. [3] Ochicha et al found that 16.9% of paediatric malignancies were acute leukemia and that it is among the most common paediatric cancers in Kano, North central Nigeria; AML was slightly more prevalent than ALL in this study.[4] The United States Cancer Group reported Leukemia as the most common cancer in children less than 15years of age accounting for 32% of all childhood malignancies.[16] No cytogenetic or molecular studies were carried out on our case report on account of lack of facilities. However, cytogenetic studies are crucial in leukemias as the analysis has therapeutic and prognostic significance. The causes of acute leukemia in the majority of cases are unknown, but have been associated with chromosomal abnormalities. These specific chromosome rearrangements include constitutional duplications, deletions, translocations, breakages, aneuploidy and point mutations.[17- 19] Children with trisomy 21 (Down syndrome) have been found to have about 20 times increased risk of

developing acute leukemia than non Down syndrome children.[20] It has also been documented that almost 10% of Down syndrome patients are born with transient abnormal myelopoiesis (TAM) which is a transient self-limiting leukemia.[20] Fanconi anaemia which is an inherited autosomal recessive disorder has been associated with solid and haematological malignancies as well as progressive bone marrow failure and congenital malformations.[21-23] Mushtaq et al found out that among children with Fanconi anaemia, AML is the commonest hematological malignancy followed by myelodysplastic syndromes, while transformation to ALL is a rare phenomenon in this genetic disorder.[20, 23]Maternal exposure in pregnancy to dietary flavonoids may contribute to the risk of Mixed Lineage Leukemia-rearrangement (MLL-r) infant leukemia.[2] Chemical exposures into a child's environment including parental smoking, pesticides, traffic fumes, paint and household chemicals possibly predispose to acute leukemia.[24] Maternal exposures to X-irradiation and smoking in pregnancy have been independently associated with a risk of ALL.[25] Longer duration of formula feeding and later age of introduction to solid foods were independently associated with increased risk of ALL, so also is rapid fetal growth (high birth weight), but the mechanisms are not understood. [26]

In summary, we have presented a rare case of a 9 month old infant with ALL and unusual bilateral nephromegaly, the disease had a rapidly fatal course. The rapidly fatal course of disease in our case may be attributed to the early age of onset of acute leukemia, male gender, associated bilateral nephromegaly which is a manifestation of disseminated and late presentation of the disease. Though rare, acute infant leukemia with nephromegaly is possible a differential diagnosis in babies that have symptoms and signs that are suggestive.

We recommend that our hospitals in low income countries be equipped with facilities for cytogenetic studies, quality supportive care especially blood products and newer less toxic cytotoxic agents FREE of charge for children who have acute leukemia.

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