

## Acute lymphoblastic leukemia presenting as nephromegaly in a child: A rare case report

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**SUMMARY:** Arora SK, Swarnim S, Hemal A, Bidhuri N. Acute lymphoblastic leukemia presenting as nephromegaly in a child: A rare case report. Turk J Pediatr 2019; 61: 97-101.

Acute leukemia is the commonest pediatric malignancy with acute lymphoblastic leukemia (ALL) constituting about 75% of all leukemias. ALL commonly presents as fever, bleeding, bone pains, anemia, lymphadenopathy and hepatosplenomegaly. The liver, spleen or lymph nodes are the most common sites of extramedullary involvement in ALL, with renal involvement being relatively uncommon. The usual differential diagnosis of acquired massive bilateral nephromegaly in children includes pyelonephritis, obstructive uropathy, infections such as HIV nephropathy, mucormycosis, glycogen storage diseases, myelofibrosis with extramedullary hematopoiesis, kidney tumors and rarely hematological malignancies like ALL.

Here we report a 2 years old child who presented with abdominal distention, low grade fever and constipation. Clinical examination revealed massive bilateral nephromegaly. Preliminary investigations showed severe anemia and slightly elevated WBC counts with presence of reactive changes in lymphocytes along with few atypical cells (9%). Abdominal ultrasonography revealed bilaterally enlarged kidneys which was later confirmed by CT abdomen.

He was eventually diagnosed with CALLA positive B cell ALL for which treatment was started in accordance with the International network for cancer treatment and research (INCTR) protocol 02 04. At present, he is on maintenance phase and responding well to the treatment with regression of kidney size to normal on follow up ultrasonogram.

Thus, leukemia should be considered in a child presenting with bilateral nephromegaly after exclusion of above mentioned differential diagnosis. Bone marrow aspiration must be done before doing a more invasive investigation like renal biopsy.

*Key words:* acute lymphoblastic leukemia, kidney, nephromegaly.

Acute lymphoblastic leukemia (ALL) is the most common malignancy in children. It commonly manifests with symptoms like fever, bleeding, bone pains, anemia, lymphadenopathy and hepatosplenomegaly.<sup>1</sup> Some less common manifestations include oral ulcers, arthritis, testicular enlargement and central nervous system involvement.<sup>1</sup> Clinically palpable bilateral nephromegaly is rarely seen in ALL at presentation. The common causes of nephromegaly in early infancy include autosomal recessive polycystic

kidneys, congenital hydronephrosis, storage disorders, primary renal tumors and renal vein thrombosis.<sup>2</sup> The differential diagnoses in older children include pyelonephritis, obstructive uropathy, HIV nephropathy, mucormycosis, glycogen storage diseases, myelofibrosis with extramedullary hematopoiesis, and primary kidney tumors.<sup>3</sup> Rarely nephromegaly may arise due to massive neoplastic infiltration by lymphoma or leukemia cells.

There are a few case reports of children having ALL with clinically palpable nephromegaly to

date (Table I).<sup>4-12</sup>

We report a 2 years old child who presented with bilateral nephromegaly and was eventually diagnosed with ALL on bone marrow examination.

### Case Report

A 2 years 4 months old male child presented to the hospital with the chief complaints of generalized abdominal distention for the past 2 months, low grade fever on and off for the last month and constipation for the last 20 days. There was no history of persistent vomiting, loose stools, abdominal pain, weight loss or loss of appetite. There was no significant past or family history. On examination the child was stable, afebrile other vitals being: Heart rate 98/min, pulses well palpable, Respiratory rate 24/min; blood pressure was 88/56 mm Hg. His anthropometry revealed normal nutritional status, weight was 12 Kg (50th centile) and length 89 cm (50th centile). General physical examination revealed severe pallor but there was no icterus, cyanosis, lymphadenopathy, clubbing or pedal edema. There were no petechiae, purpura, ecchymosis or bony tenderness. Abdominal examination revealed bilaterally palpable and ballotable kidneys. The child also had soft hepatomegaly 5 cm below costal margin with a liver span of 13 cm and splenomegaly 1 cm below left costal margin. Rest of the systemic examination was unremarkable.

Preliminary investigations revealed presence of severe anemia (Hb = 2.9 g/dL) and slightly elevated WBC counts ( $14.2 \times 10^9/L$ ) with a normal differential leucocyte count (DLC: Neutrophils 39%, Lymphocytes 45%, Eosinophils 3%, Monocytes 2%) and platelet count ( $200 \times 10^9/L$ ). Peripheral smear showed presence of reactive changes in lymphocytes along with few atypical cells (9%, small mature lymphocytes with scant amount of pale agranular cytoplasm, nucleus was round with irregular nuclear membrane, opened up chromatin, 0-1 inconspicuous nucleoli). Urine analysis was normal. The liver and kidney function tests were normal but serum LDH was elevated (2079 U/L). HIV serology was non-reactive. Abdominal ultrasonography revealed bilaterally enlarged kidneys with right kidney measuring 110x51mm and left kidney

123x61mm without any focal lesion. The cortico-medullary differentiation was maintained on both sides with mild prominence of bilateral pelvicalyceal system. Abdominal computed tomography with contrast enhancement further confirmed these findings (Fig 1). It showed bilateral enlarged kidneys (right kidney 110x54 mm and left kidney 108x56mm) with normal attenuation. No post contrast enhancement was



Fig. 1 (a). CT abdomen depicting bilateral nephromegaly in coronal section.

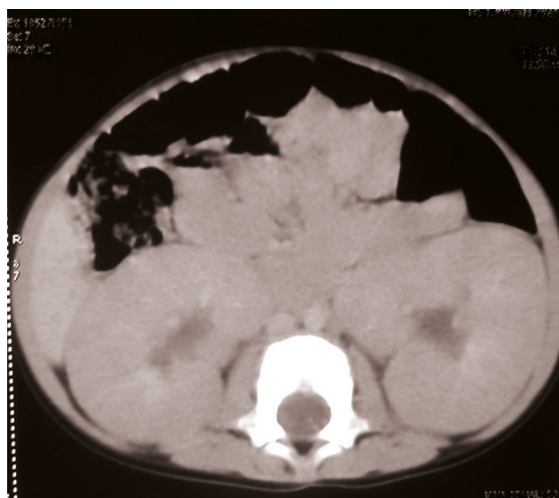


Fig 1.(b). CT abdomen depicting bilateral nephromegaly in transverse section

**Table I.** Previously Reported Cases of Nephromegaly in ALL.

Author	Patient Characteristics	Clinical Presentation	Diagnosis of Leukemia
Sabui et al. <sup>4</sup>	2 years 6 moths, Male	Fever, arthritis, bilateral nephromegaly.	Bone marrow aspiration: pre-B ALL. Renal biopsy: No leukemic infiltration.
Erdem et al. <sup>5</sup>	5 year, female	Anemia, dysuria, weight loss and palpable kidneys.	Bone marrow aspiration: ALL Percutaneous kidney biopsies: diffuse interstitial high-grade hematolymphoid malignant Infiltration.
Boueva et al. <sup>6</sup>	1year 4 months, Male	Nephromegaly, nonoliguric acute renal failure and recurrent infections.	Peripheral smear: normal Bone marrow examination: normal. Surgical renal biopsy: precursor Bcell ALL.
Saha A et al. <sup>7</sup>	6 moths, Female	Bilateral palpable nephromegaly and parotid enlargement.	Diagnosed with ALL on renal biopsy and BMA
Aguayo et al. <sup>8</sup>	1 year 3 months, Male	Incidental detection of massive bilateral nephromegaly on well baby examination.	Renal biopsy: infiltration of the renal parenchyma with precursor B-cells.
Pradeep R et al. <sup>9</sup>	7 years, Male	Fever, abdominal pain and palpable bilateral renal masses on examination.	Bone marrow aspiration: pre-B ALL FNAC of both kidneys: blasts with similar morphology as in bone marrow.
Mantan et al. <sup>10</sup>	7 months, Female	Fever, facial palsy, hemiparesis and palpable nephromegaly.	Bone marrow aspirate: ALL CT abdomen: enlarged smooth kidneys with maintained corticomedullary differentiation.
Dogan et al. <sup>11</sup>	14 years, Male	Fever, weightloss, pallor, petechiae and palpable bilateral kidneys.	Bone marrow examination: ALL
Basker et al. <sup>12</sup>	4 years, Male	Anorexia, arthritis, anemia, hepatosplenomegaly and nephromegaly.	Bone marrow examination: ALL Trucut renal biopsy: ALL

ALL: Acute lymphoblastic leukemia, BMA: Bone marrow aspiration

seen in peripheral region of renal cortex. Mild compression of pelvicalyceal system on both sides was observed. Bone marrow aspiration and biopsy was planned in view of severe anemia and presence of few atypical cells in blood smear. BM Examination revealed :

BM Imprint smear: 72% blast (individual blasts were 2 times the size of small mature lymphocytes with scant amount of pale agranular cytoplasm, nucleus was round with irregular nuclear membrane, opened up chromatin, 0-1 inconspicuous nucleoli), Lymphocytes -25

%, Neutrophils -2 %, Metamyelocyte- 1 %. Erythroid and myeloid series are markedly suppressed. No megakaryocytes were seen.

BM aspiration: MPO negative Acute leukemia.

BM biopsy: CALLA positive B cell acute lymphoblastic leukemia.

A diagnosis of CALLA positive B cell acute lymphoblastic leukemia was made that was confirmed with flowcytometry. "Chemotherapy for leukemia was started with Prednisolone, L- Asparaginase, Vincristine, methotrexate (MTX), daunorubicin, dexamethasone, 6 - mercaptopurine, cyclophosphamide and cytarabine given during induction and consolidation phases. Presently the child is in maintenance phase receiving daily 6-Mercaptopurine and weekly methotrexate after a short course of prednisolone and L-asparaginase. He is in remission and responding well to the treatment. Repeat ultrasonography done after 1 month of starting therapy showed a reduction in size of both the kidneys to normal.

Informed written consent was obtained from the parents for reporting the case.

## Discussion

The usual presenting symptoms of ALL include infections caused by neutropenia,

bruising or bleeding due to thrombocytopenia and pallor and fatigue from anemia. In

50–60% of patients with ALL, fever is the most common presenting symptom<sup>1</sup>. Leukemic infiltration of the liver, spleen, lymph nodes, and mediastinum is common at diagnosis. However, isolated bilateral symmetrical renal enlargement as a primary finding in children with ALL is rare. Extensive literature search revealed around 9 cases of pediatric ALL with clinically palpable nephromegaly reported in English language to date (Table I).<sup>4-12</sup>

The possible causes of nephromegaly in ALL can be due to leukemic infiltration or may be simple hypertrophy or hyperplasia. Leukemic infiltration of the liver, spleen, lymph nodes, and mediastinum is more common at diagnosis. Reports quote microscopic leukemic infiltration of kidney in 7-42% cases of ALL and it is more common in late stages of the disease.<sup>4</sup> Histopathologically, renal leukaemic infiltration

can be either diffuse or nodular in nature but in children diffuse pattern is more common.<sup>13</sup> The infiltrates are reported to be mainly confined to the cortex with minimal involvement of the medulla.<sup>14</sup> Renal involvement in ALL is generally asymptomatic until nephromegaly is large enough to cause pressure symptoms as in the present case. Renal insufficiency with acidosis and electrolyte imbalance at presentation is reported in less than 1% of cases of ALL.<sup>15</sup>

Most common CT finding in patients with renal involvement is of multiple bilateral masses whereas focal solitary masses are less common. However, a variety of patterns of renal involvement in children with ALL have been reported to include diffuse bilateral involvement, diffuse unilateral involvement, discrete intrarenal masses, or hilar masses.<sup>16</sup>

The relationship of nephromegaly on prognosis in ALL is inconclusive. D'Angelo et al.<sup>17</sup> assessed the prognostic value of nephromegaly in children at time of diagnosis with ALL. They reported poorer event free survival in a group with nephromegaly that was treated with non-intensive protocols than in a group without nephromegaly that was treated with the same protocols. Contradicting these findings, Neglia et al.<sup>18</sup> found that, when kidney size was analyzed as a single variable and when it was considered after adjustment for the known prognostic factors of age, sex, and initial white blood cell count; enlarged kidney size at diagnosis of ALL in childhood was not associated with overall poorer survival.<sup>18</sup>

Leukemia should be considered in the differential diagnosis in a child presenting with bilateral nephromegaly. In case the initial workup is inconclusive, a bone marrow aspiration must be done before doing renal biopsy which is a more invasive and risky procedure. Additionally, there is no role of renal biopsy in a child diagnosed with ALL, with or without nephromegaly, as it has no therapeutic or prognostic significance.

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