Rare Presentation of Pediatric Acute Lymphoblastic Leukemia: Nephromegaly at Time of Diagnosis

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Abstract Renal involvement is a fairly frequent development in children with acute lymphoblastic leukemia, but palpable renal enlargement at time of diagnosis is very unusual. We report the case of a young girl who presented with enlarged kidneys and was diagnosed with this form of leukemia. This case is of interest because of the rarity of this presentation. The importance of renal biopsy in identifying the etiology of this patient's nephromegaly is emphasized.

Keywords Leukemia · Nephromegaly · Child

Introduction

The proliferative nature of leukemia usually manifests as lymphadenopathy, splenomegaly and hepatomegaly. The kidneys may also be infiltrated with leukemic cells and this form of involvement is fairly common in pediatric

leukemia; however, there are only a few reports of children with palpable renal enlargement at initial presentation [1–3]. We report the case of a young girl who presented with unexplained bilateral renal enlargement. The patient was preliminarily diagnosed with polycystic kidney disease (PKD) at another center, but further investigation revealed acute lymphoblastic leukemia (ALL).

Case Report

A 5-year-old girl was referred to our center with urinary tract infection, anemia and an initial diagnosis of PKD based on ultrasonography at the referring hospital. The patient had a history of dysuria, weight loss and abdominal swelling in the month prior to presentation. She was referred to our pediatric nephrology department for further investigation of bilateral kidney enlargement.

On physical examination, the child was pale, irritable and tachycardic. Her abdomen was distended but not tender, and palpation revealed bilateral symmetrical masses. The patient weighed 13.2 kg (3–10th percentile) and was 82 cm tall (10th percentile). Her blood pressure was in the normal range for her age. Laboratory testing revealed bicytopenia with the following specific findings: white blood cell count 5200/μl, neutrophils 180/μl, lymphocytes 4800/μl, platelets 149,000/μl, hemoglobin 4.5 g/dl, mean corpuscular volume 87 fl, C-reactive protein 14.7 mg/l, erythrocyte sedimentation rate 137 mm/h, urea 24 mg/dl, and creatinine 0.4 mg/dl. There were no atypical cells on a peripheral blood smear. Serum electrolytes, lactate dehydrogenase, uric acid, bicarbonate levels, and results of liver function tests and coagulation tests were in the normal range. Urinalysis was also normal. Ultrasonography of the abdomen revealed bilateral renal enlargement, with the

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right kidney measuring 100×43 mm and the left measuring 111×45 mm. The length and width of both kidneys were more than two standard deviations greater than normal for age. Ultrasound confirmed normal anatomical location and configuration, and the corticomedullary differentiation was within normal limits. Computed tomography (CT) of the abdomen also showed bilateral diffuse renal enlargement (Fig. 1). Percutaneous kidney biopsies were done and histopathological examination revealed diffuse interstitial high-grade hematolymphoid malignant infiltration (Fig. 2). Simultaneously bone marrow aspiration was done which showed 90% lymphoblasts that were positive for CD10 and CD19 and negative for myeloperoxidase. Findings on immunohistochemistry staining and immunophenotyping were consistent with precursor B-cell ALL and L1 morphology based on the FAB classification. Cerebrospinal fluid cytology was negative. So, patient was started on a CCG-1881 protocol. Two months into treatment, follow-up ultrasonography showed that the dimensions of both kidneys had returned to normal range. The patient was still in remission 2 years after diagnosis.

Discussion

The causes of nephromegaly in childhood include PKD, renal vein thrombosis, deposit diseases such as amyloidosis, duplication of the pelvicalyceal system, kidney tumors, and neoplastic infiltration as occurs in leukemia. Leukemic infiltration of the kidneys is more common in the late stage of ALL in all age groups, and is reported to occur in 7–42% of childhood leukemia cases [3–6]. In contrast, isolated bilateral symmetrical renal enlargement as a primary

Fig. 1 Abdominal computed tomographic scanning with contrast showed diffuse enlargement of both kidneys

Fig. 2 Diffuse interstitial infiltration with lymphoblasts forming a distinct ring around a glomerulus

finding in children with ALL is rare [1, 2]. Sometimes leukemic infiltration of the kidneys is detected incidentally by imaging during the course of disease or during testing prior to treatment. Hilmes et al. [7] retrospectively investigated 12 children with leukemia who were found to have renal leukemic involvement on contrast-enhanced abdominal CT. They detected focal renal parenchymal abnormalities, mostly bilateral and multifocal, more frequently than nephromegaly. Although leukemic infiltration of the kidneys is more common late in the course of ALL, this may already be present at time of leukemia diagnosis [8, 9]. This was the situation in our case, where ultrasound and abdominal CT revealed bilateral renal enlargement.

Banday et al. [10] studied 81 adults with established hematological malignancies. Of the 37 individuals diagnosed with leukemia, 21 (57%) had evidence of leukemic infiltration of the kidneys. Renal leukemic involvement does not usually cause acute renal failure; this occurs in only 1% of children with ALL [11]. Fortunately, our pediatric patient had no evidence of acute renal failure before or after she started therapy.

In our case, leukemic infiltration of renal tissue was detected in kidney biopsies, which are not routinely done in cases of ALL. Interestingly, our patient's peripheral blood smear showed no abnormal cell morphology but the combined findings of bicytopenia and nephromegaly led us to suspect renal leukemic infiltration. Histopathological and immunohistochemical examination of the biopsies confirmed leukemia as the cause of her bilateral kidney enlargement. Microscopically, renal leukemic infiltration can be either diffuse or nodular, but in children the diffuse pattern is more common [8, 12]. In all age groups, the pathological findings of infiltration are mainly limited to the renal cortex [8], and in our case we observed infiltrates surrounding the glomeruli (Fig. 2).

There are different opinions about prognosis for children with leukemic renal involvement and resultant nephromegaly. D'Angelo et al. [13] 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. [14] 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. At the time our patient was diagnosed with ALL, she had none of the well-known prognostic factors for this disorder, such as central nervous system involvement, age younger than 1 year or older than 10 years, or leukocytosis. Within months after starting treatment, ultrasound showed that both kidneys had returned to normal size.

In conclusion, this case of pediatric ALL is important in that the child presented with a rare manifestation of isolated bilateral nephromegaly with no evidence of peripheral blood smear abnormalities and none of the classical clinical findings of ALL. Lymphoblastic infiltration should be suspected in any child who presents with enlarged kidneys. Renal biopsy is important in differential diagnosis of renal involvement and renal biopsy should be done for diagnosis and therapy.

Conflict of interest None

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