Renal Presentation in Pediatric Acute Leukemia

Report of 2 Cases

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INTRODUCTION

Acute leukemia is the most common malignancy in children. It accounts for 30% of all cancer diagnosed in children younger than 15 years. Leukemic infiltration is most frequently seen in bone marrow, spleen, lymph nodes, and liver. Extra-medullary involvement of the kidneys is uncommon finding at diagnosis. There are only a few reports of children with palpable renal enlargement at initial presentation. We report a case of a young girl who presented with unexplained bilateral renal enlargement and further investigation revealed acute lymphoblastic leukemia.

Acute renal failure has a large variety of etiologies but when associated with acute leukemia it is typically due to leukemic infiltration of the kidneys, therapy-related side effects, metabolic changes arising from chemotherapy, nephrotoxic drugs, and septicemias. Hyperuricemia, as a manifestation of tumor lysis syndrome, is a well-recognized complication, it occurs before chemotherapy (due to large tumor burden) or after the initiation of chemotherapy. However, initial presentation of acute leukemia as bilateral renal enlargement with renal failure is rather rare.

Here, we report a child who presented with bilateral nephromegaly, acute renal failure, and hyperuricemia and was subsequently diagnosed to have biphenotypic leukemia. The study was approved by the research and ethical committee of Faculty of Medicine, Zagazig University, Egypt.

CASE REPORTS

Case 1

A 4-year-old girl was referred to our Pediatric Hematology and Oncology Unit, Zagazig University Hospitals, on March 2011, with pallor and abdominal distension. She had been suffering from abdominal pain, fever, and abdominal enlargement for the last 6 weeks. The diagnosis of urinary tract infection was established at private clinic and several antibiotics were given without improvements. On examination, she had pallor and her blood pressure was 95/65 mm Hg. She had bilateral enlarged cervical and axillary lymph nodes. Abdominal examination revealed no hepatosplenomegaly but there was a bilateral mass in renal regions. Complete blood picture (CBC) revealed white blood cell (WBC) count 11 × 10^9/L, hemoglobin (HB) 8.7 g/dL, and platelet count 197 × 10^9/L with no abnormal cell in peripheral blood smear. Serum creatinine was 0.85 mg/dL, blood urea was 20 mg/dL, erythrocyte sedimentation rate in first hour was 42 mm and in second hour was 74 mm while lactate dehydrogenase (LDH) was 1130 IU/L. Markedly elevated serum LDH recorded in our patient is suggestive of increased cell proliferation and turnover. Other chemistry and coagulation parameters were in normal range except serum uric acid was increased (9.5 mg/dL) which suggest spontaneous tumor lysis. Urine analysis was normal. Serological tests including cytomegalovirus, human immunodeficiency virus, Epstein–Barr virus and hepatitis B and C markers were all normal.
Abdominal ultrasonography revealed bilateral renal enlargement with hyperechogenic pattern and poor corticomedullary differentiation. The right kidney was measuring 8.5 cm × 3.5 cm and the left kidney was measuring 7.8 cm × 3.1 cm. Also magnetic resonance imaging (MRI) of the abdomen revealed bilateral symmetrical homogenous enlargement of both kidneys and poor corticomedullary differentiation while the pelvicalyceal systems were not dilated with patent both renal arteries and veins. There were no other abnormal MRI findings (Figure 1). Bone marrow aspirate was done and revealed 95% blast cells of L1 morphology based on FAB classification cell lineage. Immunophenotypic analysis of bone marrow blast showed that blast cells positive for CD10+, CD19+, CD79a+, HLA DHR+, TdT+ve, and myeloperoxidase negative. Finding consistent with precursor B-cell acute lymphoblastic leukemia (ALL). Cerebrospinal fluid cytology was negative. Patient started on modified CCG 1991 standard risk protocol. Patient achieved complete remission at the end of induction and abdominal ultrasonography showed that the dimension of both kidneys had returned to normal range. The patient was in complete remission for 11 months after therapy but unfortunately she developed extramedullary central nervous system (CNS) relapse. She stared R16 protocol of ALL relapse and now in complete remission.

Case 2

A 13-month-old girl was referred to our hospital on April 2015 with history of fever, vomiting, and oliguria for 2 days. On examination the child was pale, irritable, and dyspneic with rapid and deep breathing. Her blood pressure was 60/40 mm Hg, heart rate 140 beat/min, respiratory rate 60 cycle/minute and temperature 39°C. Her abdomen was distended but not tender with bilateral palpable renal masses. Her CBC revealed bicytopenia with the following specific findings: WBCs 11 × 10⁹/L, Hb 8.2 mg/dL, platelets 32 × 10⁹/L, C-reactive protein 10 mg/L, erythrocyte sedimentation rate first hour 15 mm and second hour 45 mm and LDH 1242 IU/L. Coagulation parameters (prothrombin time, activated partial thromboplastin) were normal while D dimer was 1533 ng/mL. Blood gas analysis revealed severe metabolic acidosis where pH 7.25, PCO₂ 14 mm Hg, HCO₃ 10 mmol/L. Renal function tests showed blood urea nitrogen 51 mg/dL and serum creatinine 1.2. Uric acid was 23 mg/dL. Serum electrolytes were within normal range. Urine analysis showed no proteinuria, hematuria, or pyuria. Pelvic-abdominal sonography revealed markedly enlarged both kidneys with mild increased renal parenchymal echogenicity. Right kidney measuring 12.3 cm × 5.5 cm and left kidney measuring 12.2 cm × 5.7 cm. Multislice computed tomography of the abdomen and pelvis also showed bilateral diffuse renal enlargements and significantly thickened renal capsule with dilated both pelvicalyceal systems (Figure 2). In view of fever, cytopenia involving 2 cell lineage (anemia and thrombocytopenia) elevated LDH and uric acid, bone marrow aspirate was performed which showed 92% blast cells of L2 morphology based on FAB classification and it was positive for CD3, CD5, CD33, TdT, and MPO. Finding on immunohistochemistry staining and immunophenotyping were consistent with biphenotypic leukemia. Unfortunately cerebrospinal fluid analysis was positive for blast cells. On the basis of those findings, she was diagnosed as biphenotypic leukemia with CNS and renal infiltration. Patient was admitted to the intensive care unit and received supportive measures with hydration, alkalinization, allopurinol, and started chemotherapy according to modified CCG 1961 high-risk augmented arm. Due to the risk of tumor lysis treatment was initiated with small dose of prednisolone. Renal parameters normalized within 1 week of therapy. The child achieved complete remission at day 28 with marked reduction of kidney size but unfortunately she died from sepsis in consolidation phase of therapy.

DISCUSSION

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% to 42% of childhood leukemia cases.5,9,10 In contrast, bilateral symmetrical renal enlargement at the time of diagnosis of ALL is an infrequent finding, being present in 3% to 5% of cases.11 A potential mechanism in the trafficking of leukemia cells is the interaction of the chemokine receptor CXCR4,
which is expressed on ALL cells, and its ligand stromal cell-derived factor-1 (SDF-1), produced by stromal cells in bone marrow and extramedullary organs. As high expression of the chemokine receptor CXCR4 predicts extramedullary organ infiltration in ALL, Crazzolara et al report that CXCR4 and its ligand play an important role in extramedullary invasion.

The presence of renal leukemic involvement does not commonly cause renal dysfunction, although few cases of renal failure secondary to diffuse bilateral infiltration have been reported.

Fortunately, our first case had no evidence of acute renal failure at diagnosis or after initiation of therapy. Findings of fever, lymphadenopathy, bilateral symmetrical homogenous enlarged kidney, and elevated LDH and serum uric acid suggest the diagnosis of acute leukemia with renal infiltration. Other investigations as renal biopsy were not done because the suspicion of acute leukemia was confirmed by bone marrow examination that revealed 95% lymphoblast.

Acute renal failure in patients with hematological malignancies can present a major clinical problem, and generally develops as a direct invasion of the hematological malignant cells, for example, obstruction of the ureters, or renal artery or vein thrombosis. Other more indirect causes of renal failure include glomerulonephritis due to immunologic reactions, sep- sis, hemolysis, treatment with nephrotoxic antibiotic, radiation nephropathy, and antileukemic therapy. Tumor lysis syndrome, either before chemotherapy or after initiation of chemotherapy, can cause renal failure.

Interestingly, our second patient’s peripheral blood smear showed no abnormal cell morphology but the combined findings of bicytopenia, bilateral nephromegaly, elevated LDH and evidence of tumor lysis as hyperuricemia, on admission led us to suspect renal leukemic infiltration. So bone marrow aspiration was performed and showed 92% blast cells of biphenotypic nature. Renal impairment in our patients can be explained by bilateral renal infiltration of leukemic cells and tumor lysis syndrome and uric acid nephropathy.

There are different opinions regarding prognosis for children with leukemic renal infiltration and resultant nephromegaly. Some authors demonstrated no prognostic significance for the outcome when analyzed after adjustment for the known prognostic factors. Whereas, renal involvement may be associated with shorter survival in other studies.

Unfortunately, our first case relapsed 11 months from the end of chemotherapy and the second case had well-known poor prognostic factor which is CNS involvement, biphenotypic leukemia and died in consolidation phase. This work suggests that renal infiltration may be suggested as a poor prognostic factor in childhood ALL that needs intensive treatment, although further investigation is needed. As a conclusion, few cases of bilateral nephromegaly in childhood acute leukemia were reported in literature. Renal involvement of acute leukemia should be considered in child presenting with unexplained bilateral renal enlargement with or without renal function abnormalities and bone marrow examination should be included in the workup.

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