

Case Report

Acute Lymphoblastic Leukemia Presenting as Fanconi Syndrome

Tatsunori Yoshida Hiroshi Tsujimoto Takayuki Ichikawa
Shinji Kounami Hiroyuki Suzuki

Department of Pediatrics, Wakayama Medical University, Wakayama City, Japan

Keywords

Acute lymphoblastic leukemia · Fanconi syndrome · Renal tubular acidosis · Nephromegaly

Abstract

Acute lymphoblastic leukemia (ALL) presenting as Fanconi syndrome (FS) is extremely rare. Here, we report a case of ALL presenting as bilateral nephromegaly following FS. A 2-year-old girl was unexpectedly diagnosed with bilateral nephromegaly. After 2 weeks, she developed general fatigue, thirst, and polyuria. Laboratory examinations revealed renal tubular acidosis, hypokalemia, hypophosphatemia, and aminoaciduria, and FS was diagnosed. Replacement of bicarbonate and potassium did not improve her condition. Two weeks after the onset of FS, leukemic cells appeared on a peripheral blood smear, and the patient was diagnosed with precursor B-cell ALL presenting as nephromegaly and FS. Chemotherapy brought about a prompt resolution of acidosis and electrolyte abnormalities, without renal dysfunction. The patient remains well 4 years after the onset of the disease. Although extremely rare, FS should be recognized as one of the emerging renal complications of ALL.

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Introduction

Proximal tubular dysfunction resulting in renal loss of amino acids, glucose, bicarbonate, phosphate, calcium, uric acid, and other organic compounds is referred to as Fanconi syn-

drome (FS). FS may be caused by various inherited diseases or acquired mainly following the use of exogenous agents such as ifosfamide, valproate, and tenofovir [1]. In hematological malignancies, FS has been described in the context of plasma cell dyscrasias such as multiple myeloma and other monoclonal gammopathies [2] and much less in non-Hodgkin lymphoma [3], but acute lymphoblastic leukemia (ALL) presenting as FS is extremely rare. Here, we report a case of ALL presenting as nephromegaly and FS.

Case Presentation

A 2-year-old girl was referred to a regional hospital because of abdominal tumors. The abdominal tumors were noticed unexpectedly by her general practitioner when she received medications for pharyngitis. The patient had no past history of any significant medical illnesses, including renal diseases, and her family history was unremarkable. She was well, but physical examinations revealed smooth, bilateral abdominal tumors. Ultrasonography and magnetic resonance imaging of the abdomen revealed bilateral nephromegaly (right kidney, 12.2 cm; left kidney, 12 cm; Fig. 1). Blood and urine examinations were normal, except for elevated levels of urinary beta-2 microglobulin (uB2MG, 4,128 µg/L; normal range, <80). After 1 month, she was admitted to the referral hospital because of general fatigue, polydipsia, and polyuria for 2 weeks. Arterial blood gas analysis showed a pH of 7.21, a pCO₂ of 22.9 mm Hg, bicarbonate of 8.9 mEq/L, and base excess of -17.6 mmol/L. Serum chemistry values were as follows: sodium, 139 mEq/L; potassium, 2.2 mEq/L; phosphate, 2.1 mg/dL; uric acid, 2.5 mg/dL; serum creatinine, 0.48 mg/dL; and lactate dehydrogenase, 257 IU/L. Urinalysis was normal, but the uB2MG level was elevated (78,410 µg/L). The complete blood count was normal, and there were no atypical cells on the peripheral blood smear. Although the cause of nephromegaly was obscure, renal tubular acidosis was diagnosed. Intravenous replacement of potassium and bicarbonate was initiated, but the patient's conditions did not improve. Two weeks after admission, the white blood cell count increased to 32.9 × 10⁹/L, with 20% atypical lymphoid cells, and the patient was transferred to our hospital.

At admission, the patient's weight and height were appropriate for her age. She showed -1.2 kg of body weight loss over 1 month. The kidneys were bilaterally palpated as 2 solid masses with a smooth surface. The liver was palpated at 4 cm below the right costal margin. There was no lymphadenopathy. A complete blood count revealed a white blood cell count of 22.9 × 10⁹/L with 22% blasts, a hemoglobin level of 11.2 g/dL, and a platelet count of 6.8 × 10⁹/L. The serum lactate dehydrogenase, creatinine, and uric acid levels were 923 IU/L, 0.36 mg/dL, and 1.5 mg/dL, respectively. Blood gas analysis showed metabolic acidosis (pH, 7.21; HCO₃⁻, 11.9 mmol/L; base excess, -16.5 mmol/L; and anion gap, 15.1). The blood lactate level was 7.6 mmol/L. Serum electrolytes under replacement therapy were as follows: sodium, 135 mEq/L; potassium, 2.1 mEq/L; phosphate, 2.7 mg/dL; calcium, 8.7 mg/dL; and magnesium, 1.4 mg/dL. Urine glucose was positive (154 mg/dL) with a normal blood glucose level (99 mg/dL), and the uB2MG and urinary alpha-1 microglobulin levels were elevated at 24,660 µg/L and 22.76 mg/L (<9.75), respectively. The percentage fractional excretion levels of Na and uric acid were 2% (<1%) and 41.7% (5–11%), respectively. Tubular reabsorption of phosphate was 72.1% (81–90%). Blood amino acid analysis was normal, but urine amino acid analysis revealed severe aminoaciduria. Renal ultrasonography showed bilateral nephromegaly (right kidney, 13.1 cm; left kidney, 13.6 cm). Renal biopsy was deferred owing to thrombocytopenia. Bone marrow aspiration revealed blasts comprising 53.2% of the marrow nucleated cells. The blasts were negative for myeloperoxidase and

nonspecific esterase staining. Flow cytometric analysis revealed that the blasts were positive for CD10, CD19, CD78a, and HLA-DR antigens, but negative for CD3, CD33 antigen, and surface immunoglobulin. Cytogenetic studies of the bone marrow revealed a chromosome abnormality, 46, XX, der(19)t(1;19)(q23;p13.3), and the *E2A/PBX-1* fusion gene was detected. The patient was subsequently diagnosed with precursor B-cell ALL presenting as nephromegaly and FS. Induction chemotherapy for ALL achieved rapid improvement of acidosis and electrolyte abnormalities. Intravenous supplementation of potassium and bicarbonate was discontinued at day 5 and day 21, respectively, after the initiation of chemotherapy. The patient achieved complete hematological remission after 1 month, and the kidney sizes almost returned to normal by this time. Renal dysfunction did not occur throughout the chemotherapy for 2 years, including high-dose methotrexate therapy. Only slight aminoaciduria has been detected until now, and the patient remains well 4 years after the onset of the disease, with no medications.

Discussion

In the present case, palpable bilateral nephromegaly was noticed at first with no evidence of peripheral blood smear abnormalities, followed by FS, and finally, leukemic blasts appeared in the peripheral blood. Although renal infiltration is relatively frequent in ALL, nephromegaly at the onset of the disease is unusual. There have been several case reports of ALL presenting as palpable bilateral nephromegaly [4–7], and Taccone et al. [8] reported that 3 of 117 children with ALL had palpable renal masses at onset. In some cases, renal biopsy made it possible to diagnose ALL [5, 7]. Although the causes of nephromegaly in children vary, including polycystic kidney disease, ALL is an important differential diagnosis of nephromegaly in children.

Leukemic involvement of the kidneys might cause various symptoms, including acute renal failure by hyperuricemia [9] and various life-threatening electrolyte disturbances and acid-base disorders [9, 10]. There have been case reports of patients with acute leukemia presenting features of renal tubular dysfunction, renal tubular acidosis, lactic acidosis, or ketoacidosis [11–13]. Acute leukemia presenting as FS is extremely rare, and, to the best of our knowledge, only a single case has been previously reported in the English literature [14].

FS has been well described in plasma cell dyscrasias, and the deposition of immunoglobulin light chains in the proximal renal tubule is the cause of FS [2]. The pathogenesis of FS in our case might be related to dense leukemic cell infiltration of the kidneys, as evidenced by prominent nephromegaly, although a renal biopsy was not performed. Rapid restoration of renal tubular function following administration of chemotherapy also suggests this mechanism. In previous reports of 2 lymphoma patients with FS, renal biopsy revealed the presence of proximal tubular cell infiltration by lymphomatous cells [3] and compression of the tubular lumen, resulting in tubular atrophy and necrosis due to dense infiltration by lymphoma cells [15].

In conclusion, FS should be added to the list of emerging renal complications of ALL. In ALL patients with nephromegaly, examination for the presence of FS is required.

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Statement of Ethics

The authors have no ethical conflicts to disclose. Patient consent was graciously obtained for the publication needs.

Disclosure Statement

The authors declare that there is no conflict of interest regarding the publication of this paper.

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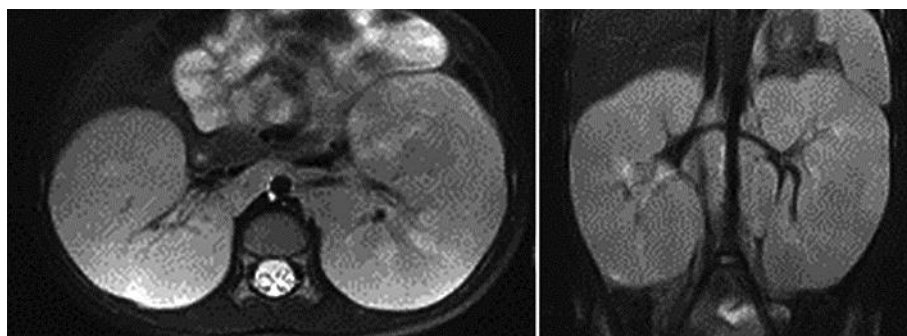


Fig. 1. T2-weighted magnetic resonance imaging of the abdomen showing smooth bilateral nephromegaly with loss of corticomedullary differentiation.