

# An unusual diagnosis in a child presenting with hypercalcemia: acute lymphoblastic leukemia

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## SUMMARY

Hypercalcemia is a rare complication of acute lymphoblastic leukemia in childhood. We report a 4-year-old boy who presented with hypercalcemia and was diagnosed to have acute leukemia. The laboratory tests for main causes of hypercalcemia (Hyperparathyroidism, hypervitaminosis A and D, hyperthyroidism) were within normal limits. Hypercalcemia was treated with intravenous isotonic sodium chloride solution, furosemide and corticosteroids. In repeat laboratory tests performed on day 4 of admission, a normal complete blood cell count was found, but peripheral blood smear examination at this time revealed atypical lymphocytes. A bone marrow aspiration was performed, and 80% lymphoblasts were determined. The diagnosis of acute leukemia cannot be excluded in a patient with hypercalcemia and normal complete blood cell count and peripheral blood smear examination results. Repeat laboratory and detailed peripheral blood smear examinations are necessary to make a correct diagnosis in such cases.

**Key words:** Acute lymphoblastic leukemia, childhood, hypercalcemia

## ÖZET

**Hiperkalsemi nedeni ile başvuran bir çocukta nadir bir neden: akut lenfoblastik lösemi**

Hiperkalsemi çocukluk çağı akut lenfoblastik lösemilerinde nadir bir komplikasyondur. Bu yazıda hiperkalsemi ile başvuran ve akut lösemi tanısı konulan 4 yaşında bir erkek olgu sunulmuştur. Hiperkalseminin ana nedenlerine (hiperparatroidi, vitamin A veya D aşırı alımı, hipertiroidizm) yönelik laboratuvar testler normal bulundu. Hiperkalsemi, intravenöz izotonik sodyum klorür, furosemid ve steroidler ile tedavi edildi. İzleminin dördüncü gününde tekrarlanan laboratuvar testlerinde tam kan sayımı normal olarak bulundu, fakat periferik yayma incelemesinde atipik lenfositler tespit edildi. Yapılan kemik iliği aspirasyon incelemesinde %80 oranında lenfoblast belirlendi. Tam kan sayımı ve periferik yayma incelemesinin normal olduğu hiperkalsemili bir hastada akut lösemi tanısı ekarte edilemez. Böyle olgularda laboratuvar tetkiklerinin ve periferik yayma incelemelerinin tekrarlanması doğru tanı koyma açısından önemlidir.

**Anahtar kelimeler:** Akut lenfoblastik lösemi, çocukluk çağı, hiperkalsemi

## Introduction

Acute lymphoblastic leukemia (ALL) is the most common form of acute leukemia in children. ALL commonly presents with nonspecific features such as fever, bleeding, musculoskeletal pain or lymphadenopathy (1). ALL in childhood is rarely associated with hypercalcemia (2).

Hyperparathyroidism, hypervitaminosis A and D, hyperthyroidism, immobilization and malignancies are the major causes of hypercalcemia. This case report demonstrates that ALL may present in an atypical form with nonspecific symptoms such as hypercalcemia. Repeat laboratory and peripheral blood smear examinations are important in cases of hypercalcemia.

## Case Report

A 4-year-old boy was admitted to our hospital because of nausea, vomiting, fever, fatigue, weight loss and an increased intake of water lasting for the last 10 days. His complaints increased significantly on the last 2 days. His vomiting was non-bloody and commonly occurred after eating. He had no prenatal follow up and was born in a hospital. His immunizations were up-to date. The family history was unremarkable.

Physical examination on admission showed lethargy and apathy. His pulse rate was 126/min, axillary temperature 37.2 °C, blood pressure 82/58 mmHg, respiratory rate 26/min, weight 15 kg (25th percentile) and height 99 cm (10-25th percentile). His scleras and oropharynx were hyperemic, and the oral mucosa was dry. No hepatomegaly, splenomegaly or lymphadenopathy were detected. The rest of his physical examination findings was unremarkable.

The laboratory investigations on admission revealed hemoglobin (Hb) 11.4 gr/dl, white blood cell (WBC) count 23.400/µl, with neutrophils 40%, lymphocytes 58%, monocytes 2%, platelets 302.000/µl. Urea level was 76 mg/dl, creatinine 1.1 mg/dl, so-

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dium 136 mmol/L, potassium 2.8 mmol/L, lactate dehydrogenase (LDH) 320 U/L, alkaline phosphatase 236 U/L, clor 98 mmol/L, parathyroid hormone 12.8 pg/ml (15-65), urine calcium/creatinine ratio 0.4 mg/mg and serum calcium (Ca) 20.2 mg/dl. Alanine aminotransferase, aspartate aminotransferase, 25-OH-VitD3, albumin, magnesium, electrocardiogram, renal ultrasonography, bone radiographs and thyroid function tests were normal. The peripheral blood smear examination was normal.

Hypercalcemia was treated with intravenous isotonic sodium chloride solution, furosemide and corticosteroid. On day 4 of admission, WBC count of 8400/ $\mu$ l, Hb level of 12 gr/dl, platelet count of 269.000/ $\mu$ l, Ca 13.5 mg/dl, urea 35 mg/dl, creatinine 0.8 mg/dl, LDH 840 U/L were detected, and peripheral blood smear examination at this time revealed atypical lymphocytes. A bone marrow aspiration was performed, which showed the presence of 80% lymphoblasts. After cytogenetic and flow cytometric analysis, the patient was diagnosed with ALL of the B-cell type.

## Discussion

ALL in childhood is rarely associated with hypercalcemia (3). Hypercalcemia has been described in children with hematologic malignancies and solid tumors (1). Case reports of hypercalcemia with one of the presenting clinical findings in patients with acute leukemia have been reported previously (4-6).

Gastrointestinal (nausea, vomiting, anorexia, constipation), neuromuscular (lethargy, fatigue, hypotonia, stupor, coma) and cardiovascular (bradycardia, arrhythmia) symptoms characterize the clinical spectrum of malignant hypercalcemia (7). Buonuomo et al. reported a 9-year-old girl who was referred for abdominal pain, nausea, vomiting, loss of weight and muscle aches, without polydipsia, polyuria or constipation. They found hepatomegaly on physical examination (8). Our patient presented with nausea, vomiting, fever, fatigue, weight loss, increased intake of water, and no cardiovascular symptoms, polyuria, constipation or organomegaly were detected.

Laboratory and radiological findings may be a clue to the presence of a malignancy as the underlying diagnosis of hypercalcemia. In the initial laboratory results, radiologic findings and peripheral blood smear examination of our patient, malignancy was not detected. On day 4 of admission, a WBC count of 8400 u/l, Hb level of 12 gr/dl, platelet count of 269000/ $\mu$ l, LDH 840 U/L were noted, and peripheral blood smear examination at this time revealed atypical lymphocytes.

The initial treatment for hypercalcemia is intensive hydration and diuretics. If this treatment fails, corticosteroids may be useful (8). Loop diuretics (e.g., furosemide) may be used after correction of dehydration, with strict fluid and electrolyte monitoring to further augment urinary calcium excretion (9). An alternative therapy is the administration of biphosphonates, which are very powerful inhibitors of bone resorption (1,10). In our case, hypercalcemia was treated with intensive hydration, furosemide and corticosteroids. Biphosphonates were not used.

In conclusion, hypercalcemia may be a presenting laboratory finding of ALL in childhood. The physical examination and laboratory results (history, physical examination, laboratory, radiology) may be atypical for ALL at presentation and a normal complete blood cell count may be found. Physicians should be aware of this rare presentation of ALL. Repeat laboratory and peripheral blood smear examinations are important for differential diagnosis of hypercalcemia.

## References

1. Mittal MK. Severe hypercalcemia as a harbinger of acute lymphoblastic leukemia. *Pediatr Emerg Care* 2007; 23: 397-400.
2. McKay C, Furman WL. Hypercalcemia complicating childhood malignancies. *Cancer* 1993; 72: 256-260.
3. Hibi S, Funaki H, Ichaiai-Kanai R, Todo S, Sawada T, Imashuku S. Hypercalcemia in children presenting with acute lymphoblastic leukemia. *Int J Hematol* 1997; 66: 353-357.
4. Turker M, Oren H, Yilmaz S, Cakmakci H, Demircioglu F, Irken G. Unusual presentation of childhood acute lymphoblastic leukemia: a case presenting with hypercalcemia symptoms only. *J Pediatr Hematol Oncol* 2004; 26: 116-117.
5. Soni PN. Hypercalcemia and multiple osteolytic lesions in childhood acute lymphoblastic leukemia. *Postgrad Med J* 1993; 69: 483-485.
6. Ohoishi S, Koshibu T, Kazama H, Shinomiya N, Aoki T. Common acute lymphoblastic leukemia preceded by hypercalcemia in an infant. *Acta Paediatr Jpn* 1996; 38: 549-552.
7. Harguindey S, DeCastro L, Barcos M, Getaz EP, Henderson ES, Freeman A. Hypercalcemia complicating childhood malignancies: a report of seven cases with some pathophysiological considerations. *Cancer* 1979; 44: 2280-2290.
8. Buonuomo PS, Ruggiero A, Piastra M, Riccardi R, Polidori G, Chiaretti A. A case of acute lymphoblastic leukemia presenting as severe hypercalcemia. *Pediatr Hematol Oncol* 2004; 21: 475-479.
9. Ariyan CE, Sosa JA. Assessment and management of patients with abnormal calcium. *Crit Care Med* 2004; 32: 146-154.
10. Andiran N, Alikasifoglu A, Kupeli S, Yetgin S. Use of bisphosphonates for resistant hypercalcemia in children with acute lymphoblastic leukemia: report of two cases and review of the literature. *Turk J Pediatr* 2006; 48: 248-252.