

# Mature B Cell Acute Lymphoblastic Leukemia Presenting with Hypercalcemia

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## Abstract

Hypercalcemia is rarely observed in acute lymphoblastic leukemia. So far, all cases presenting with hypercalcemia are pre-B cell ALL. In this case, a mature B-cell ALL patient presenting with hypercalcemia is discussed. A three-year-old boy had a history of fever, weakness, swelling and pain in both knees. In the patient's blood smear, 93% L3 type blasts were seen and 90% L3 type large blasts with vacuoles were seen in the bone marrow aspiration smear. The flow cytometry results were as follows: CD10: 87%; CD19: 85%; KAPPA: 66%; and Lambda: 35% was compliant with mature B cell ALL. His calcium level: 15 mg/dl. Although previous cases imply that hypercalcemia is usually treated with pamidronate, calcium levels gradually decreased to normal levels within five days with intravenous fluid therapy, furosemide, and steroids in our case.

Conclusion: Hypercalcemia is rare in leukemia. So far, all cases presenting with hypercalcemia are pre-B cell ALL. It is important to know that hypercalcemia could be seen in the mature B-cell ALL.

**Keywords:** Acute lymphoblastic leukemia; Parathyroid hormone-related protein; Hypercalcemia; Lymphomas

**Abbreviations:** ALL: Acute Lymphoblastic Leukemia; ALP: Alkaline Phosphatase; Ca: Calcium; P: Phosphor; PTHrP: Parathyroid Hormone-Related Protein

## Introduction

The most common causes of hypercalcemia in childhood are vitamin D intoxication, primary hyperparathyroidism, malignancies, and granulomatous diseases [1]. In children, malignancy dependent hypercalcemia has most frequently been seen in solid tumors such as rhabdomyosarcoma, neuroblastoma, hepatoblastoma, and lymphomas. Hypercalcemia is rarely observed in acute lymphoblastic leukemia and the treatment is easier compared to that for the patients with solid tumors [2]. The pathophysiology of hypercalcemia due to malignancy is explained by two main mechanisms. First, the bone metastasis of the tumor cells by activating osteoclasts are formed by the breakdown of bone. The second mechanism is parathyroid hormone-related protein secreted from the tumor cells to activate osteoclastic bone resorption and to increase calcium reabsorption from the distal tubule [3]. Hypercalcemia observed in ALL is thought to be due to the effect of PTHrP and leads to weakness, fatigue, abdominal pain, vomiting, polyuria, constipation, hypertension, arrhythmias, seizures, renal failure, and acidosis. Intravenous fluid therapy, furosemide, steroids, and bisphosphonates are used in the treatment of hypercalcemia [1]. Osteolytic lesions of the skull and long bones can be seen in radiological images [4]. In this article, a patient with mature B-cell ALL presenting with hypercalcemia is discussed.

## Case

A three-year-old male came to the hospital with a history of fever, weakness, swelling, and pain in both knees. During the physical examination, a rash, petechiae, and purpura were not observed. He had fever of 39°C and a pale appearance. The oral-pharyngeal examination was normal, and cervical, axillary, and inguinal lymphadenopathy was not detected. Examinations of the cardiovascular and respiratory systems were normal. Minimal hepatomegaly but no splenomegaly

were detected in the abdomen examination. There were joint pains and limited movement in both hips and knees. The right knee and left knee were both measured as 21 cm.

The laboratory test results were white blood cells: 7780/mm<sup>3</sup>; hemoglobin: 9.1 g/dL, platelets: 86.000/mm<sup>3</sup>; C-reactive protein: 0.8 mg/dL; erythrocyte sedimentation rate: 100/h; urea: 32 mg/dL; creatinine: 0.32 mg/dL; sodium: 137 mmol/L; potassium: 3.3 mmol/L; calcium: 15 mg/dl; total protein: 6.6 g/dL; albumin: 4 g/dL; alkaline phosphatase: 142 IU/L; phosphor: 4.2 mg/dl, lactate dehydrogenase: 266 U/L; and uric acid: 10 mg/dl. In the patient's blood smear, 93% L3 type blasts were seen and 90% L3 type large blasts with vacuoles were seen in the bone marrow aspiration smear. The flow cytometry results were as follows: CD10: 87%; CD19: 85%; KAPPA: 66%; and Lambda: 35% was compliant with mature B cell ALL. Other results included 25-OH D vitamin: 13.6 ng/ml; parathormone: 4.62 pg/ml (15-65); and spot urine calcium/creatinine: 0.44. Osteolytic lesions were not seen in the radiographs of his long bones and cranium. Intravenous hydration 3000 cc/m<sup>2</sup>/day, sodium bicarbonate 20 mEq/L, allopurinol 10 mg/kg/day, and furosemide 1 mg/kg/dose three times/day were started for the treatment of hypercalcemia and tumor lizis syndrome. Daily follow-up calcium levels decreased to normal values in five days with hydration, furosemide, and steroid treatment (Table 1).

## Discussion

Hypercalcemia is rare in childhood leukemia. Until now, the largest study at St. Jude Hospital examined 2,816 children with leukemia, and

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DAY	Ca (mg/dl)	P (mg/dl)	ALP (IU/L)
1	15	42	142
2	14.5	3.6	139
3	13.4	3.8	137
4	13.7	3.7	118
5	10.7	4.2	108

Table 1: Daily Ca, P and ALP levels in the first 5 days of treatment.

hypercalcemia was found in 11 patients [2]. In Japan, a study was conducted over a period of 15 years and hypercalcemia was found at the beginning of the disease in 22 children with pre B cell ALL. In the literature, the median age of the children at presentation on available data is eight years. Most patients do not have a strikingly deranged blood count and the absence of blasts in the peripheral blood film is not uncommon [5]. But our patient, only three years old, has bicytopenia and 96% L3 type blast was seen in peripheral blood smear examination.

Osteolytic lesions of the skull and long bones can be seen in hypercalcemic malignancies. In the literature, osteolytic lesions have been reported in patients with ALL who presented with hypercalcemia [4,6]. In our case, although osteopenia was detected, osteolytic lesions were not seen in the head and extremity radiographs.

Intravenous fluid therapy, furosemide, steroids, and bisphosphonates are used in the treatment of hypercalcemia. Pamidronate is the most frequently used of the bisphosphonates [7]. Although previous cases [8,9] imply that hypercalcemia is usually treated with pamidronate, calcium levels gradually decreased to normal levels within five days with intravenous fluid therapy, furosemide, and steroids in our case.

A large proportion of patients with leukemia presenting with hypercalcemia have been diagnosed pre-B cell ALL and CD10, CD34 positive, CD19 negative was found in the flow cytometry investigations [10,11]. Flow cytometry examination of our patient resulted in CD10: 87%; CD19: 85%; KAPPA: 66%; and Lambda: 35% functioning, and mature B-cell ALL was diagnosed.

Inukawi et al. reported t(17,19) in five of 22 patients and relapses have been seen in all five [5]. In another study, t(17,19) was observed in two of 10 patients with ALL presenting with hypercalcemia [2]. In our case, t(17, 19) could not be observed.

We present this report because this is the only case report in the literature describing mature B-cell ALL presenting with hypercalcemia. Consequently, hypercalcemia is rare in leukemia. So far, all cases presenting with hypercalcemia are pre-B cell ALL. It is important to know that hypercalcemia could be seen in the mature B-cell ALL.

## Conflict of Interest

Yasemin Isik Balci declares that she has no conflict of interest. Aziz Polat declares that he has no conflict of interest. Hakan Sarbay declares that he has no conflict of interest. Bayram Ozhan declares that he has no conflict of interest. Mehmet Akin declares that he has no conflict of interest. Selin Guler declares that she has no conflict of interest.

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors. Additional informed consent was obtained from the patient for whom identifying information is included in this article.

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