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Case report

Acute leukemia case presented with hypercalcemia

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Abstract. An 8-year-old girl patient referred to our emergency clinic with articular pain, stomachache and fever complaints. Past history revealed that she was suffering from pain in both knees and ankle joints for 8 days. The joint temperature increased and swelling did not accompany articular pain. Family history was unremarkable. In the physical examination, there was sensitivity in the knees, elbows and ankles during movement. The patient had normal complete blood cell count, and no blast or atypical cells were observed in peripheral smear. Serum electrolytes, liver and kidney function tests were normal except for hypercalcemia. The 25 (OH) vitamin D and 1-25 $(OH)_2$ vitamin D levels were within normal range. In bone marrow aspiration, infiltration of cells with lymphoblastic and homogenous cellular features was observed. With positivity of cCD79, CD19, CD45, the case was considered as preB cell leukemia. Body bone scintigraphy performed for bone metastasis was normal. After the chemotherapy, hydration and furosemid treatment, the calcium level returned to normal. This case emphasized on the fact that, children with hypercalcemia should undergo a detailed examination for malignancies even though no blast or atypical lymphocyte are observed in their peripheral blood smear before steroid treatment is applied and if necessary, bone marrow aspiration should be taken into account.

Keywords: Acute leukemia, hypercalcemia, childhood malignancy

Introduction

Hypercalcemia and its presentation are rare situations among malignancies of childhood. In children, leukemia, rabdomyosarcomas, malignant rabdoid tumors, Hodgkin and non-Hodgkin tumors, hepatoblastoma, neuroblastoma and Ewing sarcoma may be mentioned among malignancies presenting hypercalcemia as complications [1]. In acute leukemia, hypercalcemia is more frequent than in solid tumors as a cause of presentation. While symptomatic hypercalcemia in acute leukemia is usually not resistant to treatment, hypercalcemia that develops more often in the later phases of the disease in solid tumors is resistant to treatment [2]. The treatment includes intravenous hydration, loop diuretics, calcitonine, mitramycine and the subjacent treatment. In the cases where no clue is obtained, biphosphonates are used [1].

We present a case of an 8-year-old girl admitted to our emergency unit for articular pain, stomachache and fever and presented with hypercalcemia and acute leukemia.

Case Presentation

An 8-year-old girl patient applied to our emergency clinic for articular pain and stomachache and fever complaints. Her past history showed that she was suffering from pain in both knees and ankle articulations for 8 days. It was determined that joint temperature increase and swelling do not accompany articular pain. The patient suffered from stomachache like cramps associated with intermittent fever three days later. In the physical examination there was no particular feature in personal and familiar history. Her body weight was 24 kg (25-50 p), her height was 123 cm (25-50 p). A sensibility was observed in knees, elbows and ankles during movement, with stable vital observations. The other physical examination features were normal. The complete blood cell counts were as follows: Hg: 13.5 g/dL, leucocytes: 14400/mm^3, hematocrit 37.4%, MCV: 76.1 fL, platelet 208.000/mm^3. In the results of the peripheral blood smear were as follows: 34% lymphocyte, 63% neutrophiles, 2% monocytes, 1% eosinophiles, trombocytes were in mass and no blast or atypical cell have been observed. Biochemical evaluations showed that serum calcium (Ca) was 14.23 mg/dL, phosphor (P) was 4.97 mg/dL, alkaline phosphatase (Alp) was 305 U/L, lactic dehydrogenase was 1000 U/L. Other biochemical examinations (serum electrolytes, liver and renal function test, pre-prandial blood glucose level) were

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within normal ranges. While the erythrocyte sedimentation rate was 40 mm/hour, C-reactive protein level was 41 mg/L (N:< 3 mg/L). prothrombin time (14.4 sec), activated partial tromboplastin time (29.4 sec), fibrinogen (395 mg/dL) levels were normal. Moreover, parathormone (PTH) level was 9.7 U/L, 25 (OH) vitamin D level was 30 ug/L (N:10-60 ug/L) and 1-25 $(OH)_2$ vitamin D level was 57pg/ml (30-50 pg/ml). Homogenous cellular with lymphoblast type infiltration was observed in bone marrow aspiration. This case with positivity of cCD79, CD19, CD45 (respectively 94.6%, 37.9%, 100%) was considered as preB cell leukemia. Body bone scintigraphy performed for bone metastasis was normal. After the chemotherapy and hydration (3000 ml/m^2/day), prednisolone 2 mg/kg/day and furosemid treatment (1 mg/kg) were administered and the calcium levels returned to the normal level.

Disscussion

Hypercalcemia is rare but has severe complications that should be treated immediately. In malignancies, the incidence of hypercalcaemia was reported to be between 0.2% and 0.7% [1-4]. Childhood acute lymphoblastic leukemia is one of the most frequent malignancies presenting with hypercalcemia. The incidence is known as 0.39% [2, 3, 5].

Hypercalcemia associated with malignancy develops as a result of excessive secretion of interleukin-1 (IL-1), IL-2, IL-6, transforming growth factor beta, 1,25$(OH)_2$ vitamin D, direct bone invasion, parathormone associated proteins (PTH-rP) and prostaglandin E2 and rarely excessive secretion of parathormone [6, 7]. PTH and PTH-rP can directly be secreted from lymphoblasts. PTH and PTH-rP leads to hypercalcemia by causing bone resorption. In these cases, hypercalcemia is present in peripheral blood frequently [1]. In our case, in the studies performed for the determination of hypercalcemia etiology, parathormone, 25 $(OH)_2$ and 1,25 $(OH)_2$ vitamin D levels, total body scintigraphy and bone survey were normal. No blast was present in peripheral blood. The absence of bone resorption showed that in hypercalcemia etiology, PTH-rP and PTH had no role. İn our case, as IL-1, IL-2, IL-6 and TGF-beta have not been studied, these factors are supposed to be efficient in hypercalcemia etiology.

In the treatment of hypercalcemia associated with malignancy, the classic treatment of hypercalcemia has been used. The scheme of this treatment includes intravenous hydration, furosemid, corticosteroids and calcitonine. When the treatment is not efficient or when it cannot be applied due to cardiac or renal problems, biphosphonates should be taken into consideration as an alternate treatment possibility [1]. Biphosphonates are quite efficient in hypercalcemia associated with malignancy. There are few studies about the use of biphosphonates in the treatment of hypercalcemia associated with malignancy in children. After IV administration of biphosphonates, a temporary hypocalcemia, hypophosphatemia and hypomagnesemia may develop [8]. Moreover, fever and grip–like symptoms are among the other side effects [9]. In our case, steroid, IV hydration and furosemid treatment and BFM ALL treatment protocol were used to ensure normocalcemia. biphosphonates were not used.

In conclusion, this study emphasizes on the fact that children with hypercalcemia should undergo a detailed examination for malignancies even no blast or atypical lymphocyte are observed in peripheral smear, before steroid treatment is performed and if necessary bone marrow aspiration should be taken into account.

Conflict of interest

The authors declare no conflicts of interest.

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