Atypical Presentation of Acute Lymphoid Leukemia as Hypercalcemia and Bilateral Renal Calculi

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Abstract

The presentations of acute leukemias in children are varied. Here, we report a child who presented with severe hypercalcemia with bilateral renal calculi who was later diagnosed to have acute leukemia. Intravenous Pamidronate is an effective and safe therapy for acute management of severe hypercalcemia in acute leukemias.

Keywords: Acute leukemia; hypercalcemia; Renal calculi; Pamidronate

Introduction

Hypercalcemia presenting as acute leukemia is a rare but an important complication in childhood leukemia. Hypercalcemia usually results in nonspecific constitutional symptoms, although it can also manifest as a life-threatening metabolic emergency [1]. Hypercalcemia alone or combined with osteolytic lesions can be the only presenting symptom of Acute Lymphoblastic Leukemia (ALL) in children. Here, we report a child who presented with severe hypercalcemia with bilateral renal calculi who was later diagnosed to have acute leukemia.

Case History

A 4yr 8-month-old boy was brought with the complaints of moderate to high grade fever on and off since last 9 months. Preceding this, the boy had a fracture of spine following fall from stairs for which he was treated conservatively. He had history of vomiting, 3-4 episodes per day, decreased appetite and weight loss in the last 9 months. He also had constipation, pain abdomen, frequent passing of urine, bone pains and generalized weakness. On examination, he was wasted and emaciated. He weighed 10 kgs with a height of 87cms, head circumference of 47cms and midarm circumference of 10cms. Systemic examination findings were within the normal limits. His WBC counts were 13,000/cmm, neutrophils-59.4%, lymphocytes-35.8%, RBC counts were 3.72 million cells/cmm, Hb-9.4g/dl. Peripheral smear showed normocytic hypochromic with neutrophilia. No blast cells were seen in peripheral smear. His renal functions and liver functions were normal. Serum Sodium -131mEq/l, Serum Potassium-4.1mEq/l, Serum Chloride-94mEq/l, and Serum Calcium was 19mg/dl (reconfirmed with a repeat test). Urine routine and microscopy examination were unremarkable.

Other metabolic investigations like random plasma glucose was 125mg/dl, serum phosphorus 5.4mg/dl, serum uric acid 9.9mg/dl, serum magnesium- 1.58mg/dl. In view of severe hypercalcemia, he was treated with saline diuresis followed by intravenous Pamidronate infusion over 4 hours (1mg/kg). 24-hours later serum calcium level decreased from 19mg/dl to 12.7mg/dl. 48-h later serum calcium was 10.2mg/dl. Further evaluation revealed a parathormone levels of 6.8pg/ml. USG abdomen showed normal sized kidneys with loss of corticomedullary differentiation in both the kidneys and multiple renal calculi in both kidneys, largest measuring 4 mm and was reported as grade II medical renal disease with non-obstructing bilateral renal calculi. Skeletal survey showed multiple osteolytic lesions all over the body as shown in Figure 1.

Figure 1: X-ray showing osteolytic lesions at the upper ends of the both humerus.

In view of the above findings, hematological malignancy was suspected, and bone marrow aspiration was done. This showed normal erythroid maturation, myeloid series markedly suppressed, and eosinophils are mildly increased. Lymphoid series show many atypical cells which large cells with high N/C ratio are, coarse chromatin, 0-1 nucleoli and scant cytoplasm, a few of these cells show nuclear convolutions which was reported as ALL. Bone marrow biopsy was inconclusive. Other tests like flowcytometry and chromosomal studies were advised to find out the type of ALL. However, the parents deferred any further evaluation and treatment despite counseling.

Discussion

We report a rare case of ALL presenting with hypercalcemia. In contrast to adults, hypercalcemia is very rare in children with cancer (0.4%). Incidence of hypercalcemia in children with acute leukemia or lymphoma at diagnosis is < 0.3% [2]. A higher incidence (4.8%) of hypercalcemia occurs in children with early pre-B-cell ALL [3]. An association of t(17;19) with hypercalcemia has also been reported among children with ALL [4-6]. However, we could not get the exact typing and genetic studies in our patient. In contrast to children with ordinary ALL, gastrointestinal symptoms (nausea, vomiting, abdominal pain) and skeletal symptoms (bone pain, gait disturbance) are the predominant presenting complaints in ALL children with hypercalcemia [1]. Most of the described cases of hypercalcemia in ALL children have been characterized by absence of blasts in peripheral blood film and are associated with multiple osteolytic lesions [1,7]. Our patient also had similar features. The unique finding in our patient was the presence of bilateral renal calculi. The long-standing hypercalcemia and hypercalciuria had led to formation of renal calculi. Although, urolithiasis has been reported as a complication of ALL therapy, to the best of our knowledge, this is the first case of pediatric ALL to have multiple renal calculi before initiation of chemotherapy [8].

Severe Hypercalcemia with serum calcium level as high as 20.8 mg/dl have been reported in children with ALL [4]. Hypercalcemia in ALL is of multifactorial origin. It may result from markedly increased osteoclastic resorption in the areas surrounding malignant cells within the marrow space (local osteolytic hypercalcemia) or production of humoral factors like PTHrP by tumour cells which increase bone resorption and retention of calcium through kidney (humoral hypercalcemia of malignancy) or very rarely in association with true PTH dependent hypercalcemia [9]. PTHrP should be

measured in conditions where hyper calcaemia is an uncommon association as it may help confirm a paraneoplastic aetiology. Chemotherapy normalizes hypercalcemia in most patients with ALL. Additional measures like saline diuresis, calcitonin, corticosteroids and bisphosphonates may be used in moderate to severe cases of hypercalcemia. Pamidronate at a dose of 1mg/kg is a safe and effective treatment for severe, refractory hypercalcemia of malignancy in children [10].

Conclusion

This rare case highlights the presence of severe hypercalcemia with multiple renal calculi at the initial presentation of acute leukemia in the absence of blasts in the peripheral blood film. Intravenous Pamidronate is an effective and safe therapy for acute management of severe hypercalcemia in acute leukemias.

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