CASE REPORT

Atypical Presentation of Acute Lymphoblastic Leukemia in a 7 Year Old Child

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Abstract Seven year child, who had intussusception 4 month before, readmitted for fever and walking difficulty. On examination, child had mild pallor and kyphosis of the spine but no organomegaly, lymphadenopathy or bone pain. Further evaluation revealed hypercalcemia, diffuse osteoporosis with vertebral fracture. Peripheral smear showed no blasts or pancytopenia. Bone marrow aspiration turned out to be a pre B cell ALL. This child had many atypical presentations like intussusception, osteoporosis, vertebral collapse and hypercalcemia without any classical features of ALL.

Keywords Acute lymphoblastic leukemia · Osteoporosis · Hypercalcemia · Intussusceptions

Introduction

Acute lymphoblastic leukemia(ALL) is the most common hematological malignancy in children [1]. Children with ALL have good prognosis with overall survival rate of 80 % [1]. A child with ALL usually presents with fever, hepatosplenomegaly, lymphadenopathy, bone pain and bleeding [2]. The peripheral smear shows pancytopenia with or without blasts. However, ALL may be a challenge to the clinician when it presents with an atypical clinical

scenario [3]. Here, we report a 7 year child, who was admitted twice during the last 6 months with fever, intussusceptions and with a vertebral fracture.

Case Report

A 7 year old boy presented with difficulty in walking for 3 months and intermittent fever for 2 months. He also had occasional abdominal pain and vomiting for a week. Four months before, he was operated for ileocecal intussusceptions and mesenteric node biopsy taken during laparotomy was suggestive of reactive lymphoid hyperplasia. On examination, child had mild pallor and kyphosis of the spine, without significant lymphadenopathy or hepatosplenomegaly. Restriction of movement in left knee and hip joint was there without any obvious swelling or deformity. Also, there was no bone tenderness. Other systems were normal. His weight was 14 kg (<3rd centile), and height 115 cm (3rd centile) and the vitals were blood pressure 90/60 mmHg, pulse rate 100/min and respiratory rate 30/min.

On investigation, he was anemic (Hb 7.2 g/dl) with normal leukocyte and platelet count (Table 1). The peripheral smear showed normocytic, normochromic RBCs, with neutrophilic left shift and no blast cells. There was also pre renal azotemia (urea 59 mg/dl, creatinine 1.5 mg/dl), hypercalcemia (serum calcium 12.6 mg %) and hypophosphatemia (5.7 mg/dl). Uric acid was normal (4.5 mg/dl). Blood gas analysis was suggestive of metabolic alkalosis (pH 7.506, bicarbonate 28 meq/litre pO₂ 70.2 mmHg, pCO₂ 36.2 mmHg and base excess 4.9 meq/L). Skeletal X-rays showed multiple translucent lesions in skull and long bones (Figs. 1, 2) with erosion and collapse of vertebrae (Fig. 3). Moreover, computed tomography (CT) scan of spine also revealed multiple patchy lytic

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Table 1 Investigations at admission

Investigation	Patient value
Hemoglobin	7.2 g/dl
Total leucocyte count	$11.6 \times 10^9/L$
Differential count	Neutrophil 80 %, Lymphocyte 17 %
Platelet count	$270 \times 10^3/L$
Urea	59 mg/dl
Creatinine	1.3 mg/dl
Sodium	136 meq/L
Potassium	4.4 meq/L
Calcium	12.6 mg/dl
Magnesium	1.9 mg/dl
Phosphorous	5.7 mg/dl
Uric acid	4.5 mg/dl
ESR	68 mm/1 h
CRP	Negative
Blood culture	Sterile
Urine culture	Sterile
Direct coomb's test	Negative
ANA	Negative
RA factor	Negative
Mantoux	Negative
Gastric aspiration for TB	Negative
LDH	261 IU/dl
HIV	Negative
Ferritin	791 ng/ml
Total protein	7.4 g/dl
Albumin	3.7 g/dl
AST	48 IU/dl
ALT	11 IU/dl
Alkaline phosphatase	338 IU/dl
GGT	17 IU/dl
ECHO heart	Normal study
USG abdomen	Normal, no nephrolithiasis or bulky pancreas
Blood widal	Negative
USG right hip	1 cm thick joint effusion seen
ASLO	<200 IU/dl

lesions in lower thoracic, lumbar vertebrae and posterior iliac bone with collapse and sclerosis of lumbar vertebral bodies whereas CT abdomen was normal. He was initially treated with intravenous fluids and antibiotics and packed red cell transfusion. Hypercalcemia resolved after 72 h with fluid and frusemide therapy. Similarly, azotemia and alkalosis also subsided after fluid treatment. Further, the work up for connective tissue disorder and tuberculosis also were negative. In the view of bone lesions, bone

Fig. 1 X-ray wrist showing metaphyseal lucent band in radius, ulna and metacarpals

marrow aspiration was performed which showed hyper cellular marrow with blast cells, positive for Tdt, CD10, CD99 and PAS stain while negative for CD34, CD3, CD20 and Sudan black B suggestive of precursor B ALL. Hence, Child was started on chemotherapy. Bone lesions also started healing after initiation of chemotherapy.

Discussion

The usual clinical presentation of ALL in children includes fever, hepatosplenomegaly, lymphadenopathy, bone pain and bleeding [2]. Musculoskeletal manifestations are seen in 20–40 % patients with ALL [2, 4]. Osteoporosis and reduced bone mineral density had been described in ALL during diagnosis and treatment and even after completion of chemotherapy [5]. The mechanism for osteoporosis and hypercalcemia is multifactorial [6]. The invasion of leukemic cells disrupts the normal hematopoietic microenvironment resulting in an expansion of osteoclasts causing increased bone resorption and a concomitant reduction of osteoblastic activity [7]. Further, parathyroid hormone related protein (PTHrH) secreted by tumor cells cause bone resorption [8]; but, normal parathyroid hormone is suppressed due to feedback mechanism [9]. In addition, various inflammatory cytokines like tumor necrosis factor alpha (TNF- α), interleukins are released and results in bone erosion [8]. Furthermore, the drugs used for treatment

Fig. 2 X-ray chest showing metaphyseal lucency in both humeral bones

Fig. 3 X-ray thoracolumbar spine lateral view revealing radiolucency and multiple vertebral compressions

mainly steroids, methotrexate and radiotherapy cause osteoporosis in ALL [6, 10]. The radiographic changes described in ALL include osteopenia, metaphyseal bands, periosteal new bone formation, geographic osteolysis, osteosclerosis, mixed osteolysis–sclerosis and permeative destruction [6, 11]. At diagnosis, vertebral fracture is seen

16 % of children with ALL. However, only 55 % of children with vertebral fractures presented with back pain [12]. Gastrointestinal lesions have been reported to occur in 20–25 % of leukemic patient; hematoma and leukemic infiltration of bowel may cause intussusception and intestinal obstruction [13].

This child presented with many atypical features like intussusception, hypercalcemia, diffuse osteoporosis and vertebral fracture. He had no classical symptoms or signs nor peripheral smear suggestive of acute leukemia. The purpose of this case report is to increase awareness about varied presentation of ALL among general pediatrician, since it is important to recognize the skeletal manifestation of acute childhood leukemia because a delay in diagnosis has an adverse effect on survival [6].

References

1. Salim H et al (2014) Osteoporosis resulting from acute lymphoblastic leukemia in a 7-year-old boy: a case report. *J Med Case Rep*. 8:168
2. Sadawaite S et al (2008) An unusual presentation of pediatric acute lymphoblastic leukemia. *Indian J Hematol Blood Transfus* 24(2):59–62
3. Brix N, Rosthoj S (2014) Bone marrow involvement is not manifest in the early stages of childhood acute lymphoblastic leukaemia. *Dan Med J* 61(8):A4883
4. Riccio I et al (2013) Musculoskeletal problems in pediatric acute leukemia. *J Pediatr Orthop B* 22(3):264–269
5. Haddy TB, Mosher RB, Reaman GH (2001) Osteoporosis in survivors of acute lymphoblastic leukemia. *Oncologist* 6(3):278–285
6. Cohan N et al (2011) Initial presentation of acute lymphoblastic leukemia with osteoporosis and multiple spontaneous bone fractures. *Iran Red Crescent Med J* 13(1):52–54
7. Lane SW (2012) Bad to the bone. *Blood* 119(2):323–325
8. Das A, Bansal D, Kumar N (2014) Acute lymphoblastic leukemia mimicking metabolic bone disease. *Indian J Pediatr* 81(8):827–828
9. Kolyva S et al (2014) Hypercalcemia and osteolytic lesions as presenting symptoms of acute lymphoblastic leukemia in childhood. The use of zoledronic acid and review of the literature. *J Pediatr Endocrinol Metab* 27(3–4):349–354
10. Gurney JG et al (2014) Bone mineral density among long-term survivors of childhood acute lymphoblastic leukemia: results from the St. Jude Lifetime Cohort Study. *Pediatr Blood Cancer* 61(7):1270–1276
11. Sinigaglia R et al (2008) Musculoskeletal manifestations in pediatric acute leukemia. *J Pediatr Orthop* 28(1):20–28
12. Halton J et al (2009) Advanced vertebral fracture among newly diagnosed children with acute lymphoblastic leukemia: results of the Canadian Steroid-Associated Osteoporosis in the Pediatric Population (STOPP) research program. *J Bone Miner Res* 24(7):1326–1334
13. Kumari TP et al (1998) Intussusception at the onset of acute lymphoblastic leukemia in a child. *Indian Pediatr* 35(5):470–472