An unusual presentation of pediatric acute lymphoblastic leukemia

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Abstract Acute lymphoblastic leukemia (ALL) is one of the most common hematological malignancies occurring in children. We report an interesting case of ALL with an unusual presentation. This 3-year-old boy came with a 6 month history of multiple pathological fractures, generalized osteopenia and vertebral compression. All the possible causes responsible for this condition were ruled out. His complete blood count which was normal initially evolved into cytopenias. His physical examination revealed generalized lymphadenopathy and hepatosplenomegaly. The complete blood count showed pancytopenia with blasts in peripheral smear. Bone marrow aspirate was suggestive of B ALL. Pediatric ALL patients usually present with symptoms due to cytopenias, fever and bone pains. Although asymptomatic skeletal involvement may be seen in 40–60% of patients at presentation, pathological fractures and vertebral compressions are very rare. Therefore a high index of suspicion is needed to diagnose such cases. Moreover, these patients are usually associated with good prognostic features.

Keywords ALL · Fracture · Osteoporosis

Introduction

Acute Lymphoblastic Leukemia is one of the most common malignancies in children, accounting for 30% of all the cancers. It is four times more common than Acute Non Lymphoblastic leukemia. Children present with symptoms due to cytopenias, organomegaly, lymphadenopathy and bone pains. Skeletal manifestations presenting in the form of bone pains, refusal to walk etc may be seen in 40–60% of patients. A variety of skeletal lesions have been described. However there are very few reports of childhood ALL presenting with severe osteopenia and pathological fractures. We report an interesting case of a 3-year-old boy who presented with multiple pathological fractures and vertebral compression.

Case summary

This 3-year-old boy was symptomatic for 6 months before he came to us. He had a small undisplaced closed fracture of lower end of tibia following trivial trauma 6 months back. He was treated conservatively with a cast application. After one month he sustained a similar fracture in the lower end of femur. Simultaneously he developed pain in lower limbs, backache and later was not able to walk. He also had intermittent fever, generalized weakness and weight loss since 6 months. The parents noticed ecchymoses over the extremities and the trunk in the last 2 months. His motor and mental development was normal for age. There was no significant past and family history.

He was extensively investigated outside. The X rays of lower limbs showed generalized osteopenia with stress fractures in the lower end of right femur and left tibia.

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(Figs. 1 and 2) The dorsolumbar spine and the pelvic X-ray also showed generalized osteopenia with multiple vertebral compressions (Fig. 3). His MRI spine could not be completed because of anaphylactic reaction to anesthesia. The available plates of MRI showed multiple compressions of non contiguous vertebrae in dorsal spine (Fig. 4). His mantoux test was negative. The blood mycobacterial DNA PCR

was negative. His serum calcium, alkaline phosphatase, liver function and renal function tests were normal. Serum LDH, uric acid, vitamin B12 levels and ASO titers were normal. His ophthalmologic examination and color Doppler ECHO in view of suspected osteogenesis imperfecta were normal. The complete hemogram which was normal initially evolved into progressive pancytopenia in the subsequent

Fig. 1 Stress fracture with callus formation of lower end of femur with osteopenia

Fig. 2 Fracture of lower end of tibia with osteopenia

Fig. 3 Generalized osteoporosis of spine with multiple non contiguous vertebral compressions

Fig. 4 MRI spine - Multiple dorsal vertebral compressions

4 months. He was referred to us in view of pancytopenia, for evaluation of Fanconi's anemia. On examination patient had pallor, few ecchymoses over the extremities and generalized lymphadenopathy. He had a palpable liver of 4 cms and spleen of 6 cms. He was bedridden due to severe pain and weakness. However there was no focal neurological deficit. The complete blood counts revealed a hemoglobin of 4.3 gm/dl, total leukocyte count of 3700 with 85% blasts and a platelet count of 30,000/cmm. Bone marrow aspiration revealed hypercellular marrow with more than 90% of the cells being L1 blasts. The blast population expressed CD10, CD19, CD22 and HLADR. The cytogenetic study was normal. The patient received standard risk ALL induction therapy with BFM protocol and on day 8 marrow was found to be hypocellular with 7% blasts. The patient went into complete remission on day 28 of induction 6 months back. Since then the patient is in remission and continuing with his further management.

Discussion

Common manifestations of childhood ALL are fever, bony pains and symptoms due to the cytopenias. Although asymptomatic skeletal involvement may be present in 40–60% of patients, rarely the patient presents with pathological fractures. Therefore a high index of suspicion is needed to diagnose such cases.

Hann IM et al had reported that bone pains and radiological bone changes characteristic of leukemia were present in 30 and 65% respectively in children with newly diagnosed ALL [1]. He found a significant correlation between the severity of bone pains and the number of bones involved on x rays, but no correlation was found between the severity of bone pain as well as extent of radiological involvement and survival or length of first remission. Our patient had near normal hematological values initially, which caused a delay in diagnosis. This correlates with the study of 296 Pediatric ALL patients by Jonsson et al from Texas [2]. He reported that 60% of the patients had no bone pains, 22% had some bone pain and 18% had prominent bone pain. Statistically significant differences were found in the presenting hemoglobin, total leukocyte count, absolute neutrophil count, platelet count, and percentage of circulating blasts in these three groups. Patients with prominent bone pains had near normal hematological values causing a delay in their diagnosis. Freidrich D Shapiro reported a similar case of a 6-year-old boy of ALL who presented with multiple vertebral compressions with generalized spinal osteopenia [3]. The presentation of our patient is unique as he had femur and tibia fractures in addition to vertebral compressions and

osteopenia. Skeletal radiographic changes that can occur in a child with acute leukemia include diffuse osteopenia, metaphyseal bands, periosteal new bone formation, geographic osteolysis, osteosclerosis, mixed osteolysis and sclerosis, and permeative destruction [4]. Our patient had diffuse osteopenia, metaphyseal band, osteosclerosis and multiple pathological fractures.

Muller HL et al studied the impact of skeletal involvement on survival and its correlation with the biological markers [5]. Fifty-nine patients (55%) showed radiographic abnormalities defined as metaphyseal banding (48%), periosteal reactions (11%), osteolysis (33%), osteosclerosis (31%), or osteopenia (22%). Patients with severe skeletal involvement which was quantified using a score had severe radiographic abnormalities, a lower peripheral blast, a more frequent “prednisone good response”, higher DNA index and a higher survival rate than patients without SI. Heinrich SD et al divided the patients of ALL into two prognostic groups on the basis of skeletal involvement [6]. This retrospective analysis of 83 children with acute lymphoblastic leukemia suggests that children without radiographic skeletal abnormalities have an “aggressive” form of leukemia. Children with one to four lesions have an “indolent” form of leukemia that is of short duration. Children with five or more lesions have an indolent form of leukemia that is of longer duration. St. Jude Children's Research Hospital in their series of 1466 patients report vertebral compression fractures at diagnosis in 24 (1.6%) [7]. These were more likely to have good prognostic features, including a leukocyte count of greater than $25 \times 10^9/l$, a leukemic cell DNA index of greater than 1.15, and hyperdiploidy (greater than 50 chromosomes). Complete remission of ALL was induced in all patients, and symptoms of vertebral compression fractures abated following antileukemia therapy. Appell RG et al however did not find any prognostic significance of skeletal involvement in their study of 88 patients of pediatric ALL and NHL [8]. In contrast, G Masera et al reported that children with multiple bone lesions are associated with poor prognosis [9].

We wish to highlight that pathological fractures and vertebral compressions are very rare presenting feature of pediatric ALL and these patients are usually associated with good prognostic factors. Pediatricians and orthopedicians need to keep a high index of suspicion to suspect ALL in such patients.

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