CASE REPORT

Bone relapse in T-lineage acute lymphoblastic leukemia in a child

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Abstract

Acute lymphoblastic leukemia (ALL) is the most common malignancy in children. T-cell ALL accounts for 10–15% of cases. ALL can rarely relapse in unusual extramedullary sites like bone. Hereby, we report a case of 7-year-old male child who was being treated for T-cell ALL and then presented with left arm swelling. This swelling was initially thought to be a bone tumor but later it was found to be infiltrated by leukemic blasts. We reviewed all previous cases and suggest that in a patient of ALL presenting with a bone swelling during or after completion of therapy, one should suspect of bone relapse.

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is the most common malignancy in children. It accounts for about one-fourth of all childhood cancers and 72% of childhood leukemia. The majority of pediatric ALL (80–85%) is early B-cell type, 15% is T-cell ALL and ~2% is mature B-cell/Burkitt leukemia [1]. With current advances in treatment, the survival and cure rates of childhood ALL have improved significantly. Despite this progress, medullary and extramedullary relapses remain a concern both during and after therapy. The primary sites of extramedullary relapses are the central nervous system (CNS) and testis. Other location such as eyes, ovary and kidney are the unusual locations and are increasingly observed as long-term survival improves [2].

We present an unusual case of a 7-year-old boy who presented with an early bone relapse in the left humerus during maintenance therapy for ALL. The clinical presentation was initially confused with a bone tumor but was later found to be a relapse of the primary disease.

CASE REPORT

A 7-year-old male child was diagnosed with T-cell ALL in September 2015 when he had presented with fever, hepatosplenomegaly, generalized lymphadenopathy and mediastinal widening. The white blood cell (WBC) count at diagnosis was 2700 per cumm and peripheral smear revealed 32% blasts. The diagnosis was confirmed on bone marrow examination. Immunophenotyping by flowcytometry of the bone marrow aspirate revealed blasts, that were positive for CD3, CD5 and CD7 and negative for CD19, CD20, CD10, CD13, CD14, CD33, anti-MPO and HLA-DR. The cerebrospinal fluid (CSF) was negative for blasts.

He was started on a four drug induction with dexamethasone, L-asparaginase, vincristine and daunorubicin. After completion of 5 weeks of induction therapy, the bone marrow was in remission and the minimal residual disease was negative. Patient was further treated with consolidation therapy consisting of cyclophosphamide, L-asparaginase, cytarabine,
vincristine and 6-mercaptopurine. His course during subsequent chemotherapy, including interim maintenance and delayed intensifications were unremarkable. He was 3 months into maintenance therapy, when he presented with left arm swelling.

The swelling had appeared over lower part of left arm in a week and was progressively increasing. On examination, he had an irregular bony swelling over lower part of left arm that was painful but not associated with fever. The initial blood counts were normal and the X-ray was normal. The child was initially managed with paracetamol and antibiotics. Over the next 2 weeks, swelling gradually increased in size (Fig. 1A). He then underwent a repeat X-ray of left arm that showed a soft tissue swelling (Fig. 1B). The magnetic resonance imaging (MRI) of the arm revealed a soft tissue swelling resembling a malignant infiltration (Fig. 2). Histopathological examination (H&E) shows monomorphic population of intermediate size cells with opened up chromatin and the absence of nucleoli and immunohistochemistry from the swelling was suggestive of T-cell ALL (Fig. 1C), immature lymphoid cells immunopositive for CD3 (Fig. 1D).

He also developed pallor and his physical examination revealed a new splenomegaly. His peripheral smear showed pancytopenia. Bone marrow aspiration showed complete replacement of cellularity by blasts on examination. The CSF did not reveal any blasts. The family was counseled regarding further treatment options and prognosis and they opted for palliative care due to personal and financial reasons.

DISCUSSION

Patients with T-ALL have significantly higher rates of induction failure, early relapse and a shorter median time to relapse compared to B-ALL [3]. T-cell ALL is ~ 10–15% of all pediatric ALL and, compared with those of B-ALL, they have a worse prognosis. Historically, T-cell ALL which was considered high-risk had overall survivals around 60%. With more aggressive modern regimens, however, many patients with T-ALL have up-front survival approaching that of B-ALL. Unfortunately, T-ALL patients continue to experience a lower risk of survival after relapse. Whereas, even after relapse, 50–60% of B-ALL can be cured, it is only ~30–40% for T-ALL [4]. Relapses in leukemia

Figure 1: (A) Swelling over lower part of left arm; (B) X-ray left arm showing soft tissue swelling; (C) Microphotograph shows monomorphic population of intermediate size cells with opened up chromatin and absence of nucleoli; (D) Immature lymphoid cell immunopositive for CD3.

Figure 2: (MRI left arm): (A, T2 fat saturated axial; B, T2 coronal) MRI shows bulky and T2 hyper intense muscles of arm with altered marrow signal intensity in the visualized bone likely infiltration by malignant cell and soft tissue swelling arising from bone with bone marrow edema.
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occur most commonly in the bone marrow followed by CNS and the testes. Other extramedullary sites reported in the literature include the breast, bone, skin and subcutaneous tissue, pancreas, prostate, epididymis, head and neck, uterus and adnexa, gut, kidney, eye and lungs [5–9].

The pathogenesis of bone relapse and other forms of extramedullary leukemia is incompletely understood. The extramedullary relapse could be due to poor penetration of chemotherapy at anatomic sites of leukemic proliferation [10]. Although, non-total body radiation (TBI) containing regimens for allogenic stem cell transplant regimens for relapsed ALL are known to be associated with a higher risk of second relapse, it is unlikely that omission of radiation from up-front ALL regimens may be responsible for the relapses [11].

Murray et al. [12] reviewed 11 cases of isolated bone relapse in ALL. They found that the median age of diagnosis of relapse was 7 years and the median time from diagnosis to relapse in the bone was also 7 years. The most common bone affected was the mandible (n = 5) followed by femur (n = 3), fibula (n = 1), rib (n = 1) and the metatarsal (n = 1). Out of 11, 9 patients received chemotherapy plus radiation, 1 patient received chemotherapy only and another 1 patient received chemotherapy plus radiation and autologous bone marrow transplantation. Out of 11, 6 patients died (5 due to disease and 1 due to sepsis), 4 patients achieved second remission and 1 patient had bone marrow relapse after 1 year of second remission.

Padmanjali et al. [13] from India similarly reported a 6.5-years-old male child with T-cell ALL, who presented with a relapse in the left tibia 7 months after completion of therapy.

The overall prognosis of patients of isolated bone relapse in ALL is poor. Hence, isolated ALL bone relapses in children should be treated aggressively with chemoradiotherapy and bone marrow transplantation [12].

CONCLUSION

In a patient of ALL presenting with a bone swelling during or after completion of therapy, one should suspect of bone relapse.

CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING

None.

ETHICAL APPROVAL

Not applicable.

CONSENT

Informed written consent was taken from mother.

GUARANTOR

Meena Jagdish Prasad.

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