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ORTHOPAEDIC MANIFESTATIONS OF ACUTE LEUKEMIA IN CHILDREN - A CASE SERIES

Orthopedics

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ABSTRACT

Usually acute leukemia in children presents with constitutional symptoms and abnormalities in blood investigations. But in certain proportion of cases leukemia can mimic certain orthopedic diseases like septic arthritis, osteomyelitis, juvenile rheumatoid arthritis and transient synovitis. Since the musculoskeletal manifestations are not pathognomonic, it will result in a delay in diagnosis and initiating treatment. The purpose of this review is to highlight the importance of considering acute leukemia as a differential diagnosis in children presenting with atypical and persistent musculoskeletal symptoms and signs.

KEYWORDS

Acute leukemia, orthopedic manifestations, bone pain.

INTRODUCTION

The most common malignancy in childhood is acute leukemia accounting for nearly 40% [1]. The cases presenting with a history of symptoms for less than 6 weeks is included as acute leukemia. The most common subtype is the acute lymphoblastic leukemia(ALL) with a peak incidence at 2 to 6 years. The children usually present with signs and symptoms like pallor, fever, anorexia, lethargy, lymphadenopathy, hepatosplenomegaly and various blood dyscrasias. Similarly, a certain proportion of patients with ALL may present with symptoms associated with musculoskeletal system [1,2]. The orthopedic presentations can mimic septic arthritis, osteomyelitis, transient synovitis and juvenile rheumatoid arthritis[2]. Diffuse or localized bone pain, arthritis, myalgia, limping and inability to use the extremities are the common orthopedic symptoms.

The ALL presenting with musculoskeletal manifestations are difficult to diagnose as both the clinical features and associated hematological and radiological findings are not pathognomonic. The hematological abnormalities may be subtle or even absent. This will lead to delay in commencing correct treatment and may also cause an inappropriate intervention[3].

We present three ALL cases initially presented with musculoskeletal manifestations with mild blood abnormalities and has resulted in a diagnostic difficulty. We also review the various musculoskeletal manifestations and radiological abnormalities in children with ALL.

CASE 1

2-year-old girl child presented with a history of fall and supracondylar fracture of right femur. She was treated with long leg cast for one month and on removal of the cast child has difficulty in walking and pain around knee joint. Over the next one-week she developed edema over the entire right leg and foot which was progressively increasing to include the opposite leg and both upper limbs. She also had intermittent low-grade fever and a history of loss of weight. Physical examination revealed pallor, cervical lymphadenopathy. No organom egaly was detected.

Routine blood examinations revealed, hemoglobin 8.1 gm/dl, white cell count 5800/mm^3, platelets 3.2 lakhs/mm^3 and ESR 142 mm/hr. Mantoux test and sickling test was negative. Xrays showed healing supracondylar fracture right femur, thickened band of sclerosis in distal femoral and proximal tibial epiphysis and radiolucent band in metaphysis. There was osteolytic lesions and metaphyseal radiolucent band in radius. Peripheral smear showed normocytic normochromic anemia with predominant lymphocytic picture and presence of atypical cells. Bone marrow aspiration study showed cellular marrow with predominant blast cells and confirmed the diagnosis of acute leukemia. The patient was referred to regional cancer centre and was started on induction therapy for ALL.

CASE 2

7-year-old male child with swelling and superficial wounds around the right knee joint after a fall and developed high grade fever after two days. An initial diagnosis of septic arthritis was made, and aspiration of the joint was done which happens to be negative. The swelling gradually spread to the thigh region. The physical examination showed pallor, abdominal wall edema and no organomegaly. His initial blood examinations showed hemoglobin 9.2 gm/dl, white cell count 3300/mm^3, platelets 26000/mm^3 and ESR 70 mm/hr. Xrays showed sclerotic bands in the epiphyses around knee. Peripheral smear showed anisocytosis with 16 % blasts and 3.2 % reticulocytes. Bone marrow aspiration study revealed two populations of blast cells with MPO (myeloperoxidase) positive and CD 3 positive blasts. Mixed phenotype acute lymphoblastic leukemia was diagnosed and started on induction therapy from regional cancer centre.

CASE 3

2-year old male child presented with intermittent low-grade fever for 2 months with an infected wound and generalized edema in the left lower limb. The patient was initially treated with parenteral antibiotics, but he developed multiple septic foci over the trunk and limbs. On physical examination there was mild pallor and liver was palpable 3 cm below right costal margin and no lymphadenopathy. His blood investigations showed hemoglobin 8.2 gm/dl, white cell count 3600/mm^3, platelets 45000/mm^3. Bone marrow imprint showed scattered blasts and lymphoid cells. Bone marrow aspiration study confirmed acute lymphoblastic leukemia and patient referred to regional cancer centre and started on induction therapy.

Figure 1: Thickened band of sclerosis

Figure 2: Osteolytic lesions and metaphyseal changes

DISCUSSION

The commonest malignancy of childhood is leukemia in which the predominant variety is acute lymphoblastic leukemia(ALL) with a peak incidence between 2 to 6 years of age [2]. It is the malignant disease of marrow in which the precursors of lymphoid cells proliferate and gradually replace the hematopoietic cells of bone marrow [3]. Although

most of the patients comes with medullary signs and symptoms with abnormal blood parameters, nearly one third will initially show orthopedic complaints with minimal abnormalities in blood investigations. The commonest symptoms include bone pain especially in the lower limbs, joint pain usually associated with effusion or swelling, low grade to high grade fever and back pain. These symptoms are due to the massive proliferation of bone marrow or direct leukemic infiltration of bone or periosteum [4,5,6]. It is more frequently seen in children as the child's small marrow reserve can be rapidly replaced [3]. The clinical presentation will mimic osteomyelitis, juvenile rheumatoid arthritis, septic arthritis or transient synovitis.

The most common radiological abnormalities are metaphyseal radiolucent bands (leukemic bands), osteopenia, lytic osseous lesions, and sclerotic lesions. The leukemic bands are seen in upto 90 % of cases and are due to generalized metabolic dysfunction of epiphyseal growth plate. These bands are commonly seen in proximal tibia, distal femur, proximal humerus and distal radius [1,7,8]. Periosteal new bone formation can be seen in 2-50 % cases [7,8] and are associated with osteolytic lesions. The leukemic infiltration of the marrow cavity extends and lifts the periosteum and results in sub periosteal new bone formation. Osteopenia or lytic bone lesions are reported in 10-50 % of cases [7,9]. The lytic lesions are well demarcated, multiple and usually seen in the metaphyseal area of long bones such as proximal humerus and tibia. Osteosclerotic lesions are less common, which is reported in only 3-7 % of cases [1]. These lesions are due to reactive bone formation secondary to osseous infarction or leukemic cell infiltration. But these radiological abnormalities are not pathognomonic of ALL [1,2]. So the diagnostic importance lies mainly in clinical suspicion and hematological investigations rather than radiological changes.

The diagnosis of ALL in this group of children presenting with musculoskeletal manifestations and nearly normal blood investigations are often difficult. There are no specific guidelines for early detection [1]. Even though the radiological findings are not confirmatory X ray examination should be done in those children with persistent bone pain which arises clinical suspicion. The MRI and bone scan may be helpful but not consistent in arriving a diagnosis. The presence of blast cells or atypical cells in peripheral blood smears are strongly suggestive of leukemia and should be confirmed by bone marrow biopsy [3]. The biopsy of synovium of affected joints will not reveal leukemic infiltration [2,11].

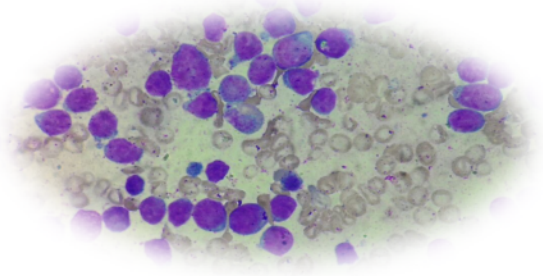

Figure 3: Bone marrow aspiration

The prognostic implications of early skeletal involvement are still unclear. But a reasonable delay in diagnosis in these children has less impact on prognosis due to their more favorable age and minimal involvement of other organ systems [2,10]. These patients usually belong to a subgroup of ALL called precursor -B cell ALL with a good prognosis [1,12]. Precursor- B cell ALL starts in the bone marrow and interferes with bone metabolism in the initial course itself. This is the reason for early musculoskeletal symptoms. Because of the large impact on the diagnosis and treatment, bone marrow examination should not be postponed in any child with atypical musculoskeletal manifestations causing clinical suspicion, with or without hematological abnormalities.

CONCLUSION

Acute leukemia should be considered in children presenting with persistent atypical musculoskeletal manifestations with or without radiological lesions, even though they have only mild hematological abnormalities. ALL mimics various orthopedic conditions, so a combination of clinical, laboratory and radiological evaluations will be helpful in arriving at an appropriate diagnosis. The presence of anemia, leukopenia, thrombocytopenia and blast/atypical cells in peripheral smears should increase clinical suspicion and is an indication for confirmatory bone marrow biopsy.

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