



Childhood Leukemia with Musculoskeletal Characteristics

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STUDY DESCRIPTION

Childhood leukemia with Musculoskeletal (MSK) involvement mimics various conditions, which consequently leads to diagnostic delays. The clinical implication of MSK involvement in this disease on survival outcomes is inconclusive.

Acute leukemia is the most common malignancy of childhood, accounting for one-third of childhood malignancies, with age-standardized incidence rates of 36.1-46.4 per million person-years. Apart from the characteristic symptoms of fever, pallor, bleeding tendency, hepatomegaly, and splenomegaly, there are a number of unusual clinical manifestations including Musculoskeletal (MSK) symptoms. MSK involvement has been reported in childhood leukemia at rates varying from 7.1 to 62.3%. In 2016, a systematic review and meta-analysis reported that MSK symptoms were a prominent clinical presenting feature in childhood leukemia, including limb pain (43%), bone pain (26%), joint pain (15%), and limping (11%). Various special characteristics of childhood leukemia with MSK involvement have been reported in the literature. For example, in some studies, MSK involvement was found to be more frequent in Acute Lymphoblastic Leukemia (ALL), especially B-cell ALL, than Acute Myeloid Leukemia (AML). This subgroup with MSK involvement also had lower rates of hematologic abnormalities, as well as peripheral blast counts at initial presentation. Therefore, childhood leukemia with MSK involvement can mimic rheumatic or orthopedic conditions and lead to delayed diagnosis of leukemia. To date there is no consensus on the prognostic significance of MSK involvement in childhood leukemia.

MSK involvement was defined as bone and/or joint pain (either arthralgia or arthritis). Arthralgia was defined as pain localized in one more joints and arthritis was defined as joint pain with signs of joint inflammation (joint swelling, effusion, redness,

increased heat, or limited range of motion). The pattern of joint involvement was defined as monoarticular (one joint), oligoarticular (2-4 joints), and polyarticular (5 or more joints). Initial bone and joint radiographs of all children who had MSK involvement were reviewed by a radiologist for the characteristics of radiographic bone changes in leukemia including metaphyseal radiolucent bands, osteolytic lesions, osteosclerosis, and periosteal reaction.

Our study found that joint pain was the most common MSK involvement, and the large joints of the extremities, especially the ankles and knees, were the most commonly involved sites. This clinical characteristic of MSK involvement was similarly reported in previous studies. However, most previous studies found that the oligoarticular pattern was the most common presentation.

The prognosis of survival outcomes of MSK involvement in childhood leukemia is controversial. Some studies have reported that children with MSK involvement had better survival outcomes than those without MSK involvement, while many found no difference in survival outcomes and one study reported a poor prognostic in children with severe bone involvement. Propensity score-matching method for balancing risks between the study groups, found that the presence of MSK involvement did not have a significant effect on prognosis in childhood leukemia.

Childhood leukemia with MSK involvement had the notable characteristics of minimal or absent hematologic abnormalities and peripheral blast counts. The survival outcomes were not different between those with and without MSK involvement. As the clinical and laboratory signs of leukemia can be obscured at initial presentation, clinicians should be aware of the possibility of leukemia in children who present with MSK complaints.

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