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Arthritis as a Presenting Manifestation of Acute Leukemia in Children

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Abstract

This study included 15 children coded as acute leukemia presenting with arthritis. This arthritis had no evident cause other than leukemia. It was present solely or as a part of a group of signs and symptoms. Thirteen children of them had acute lymphoblastic leukemia (ALL) while the other two had acute myeloblastic leukemia (AML). They were 6 males and 9 females. The patients' ages ranged between 3-14 years (mean 8.2 ± 3.4). The duration of their arthritis on initial examination ranged between 4-24 weeks (mean 11.2 ± 6.7). This arthritis was persistent symmetrical polyarticular in 73.3% of patients and migratory in 26.7% of them. The knees, ankles and wrists were the most frequently affected joints. Radiological changes suggestive of leukemia were detected in only 5 patients (33.3%). Laboratory investigations including the erythrocyte sedimentation rate, rheumatoid factor and anti-streptolysin O-titre were of no help for differentiating this group of patients from others with rheumatic diseases. This demonstrates the importance of considering leukemia as a possible etiological diagnosis in children presenting with arthritis.

Introduction

LEUKEMIA is the most common malignancy in children which may present with diverse symptoms and signs[1].

Arthritis may be a prominent feature of acute leukemia, and leukemic arthritis

can be mistaken for various rheumatic diseases[2]. Confusion with rheumatic diseases particularly juvenile rheumatoid arthritis and acute rheumatic fever may arise when musculoskeletal complaints or arthritis dominate the early course of leukemia[3].

Joint manifestations have been attributed to leukemic synovial infiltration, hemorrhage into joints or periarticular structures, synovial reaction to adjacent bony or capsular lesions and crystal induced synovitis[4].

Although the incidence of malignant disease in children is relatively low, the impact of cancer on the child makes it imperative that all professionals handling children have a high index of suspicion of cancer[2].

The aim of this study is to emphasize the influence of the presenting arthritis on making the diagnosis of leukemia in children.

Material and Methods

This study is an analysis of the clinical presentation in 155 children coded as acute leukemia presented at the pediatric Oncology Unit, National Cancer Institute, Cairo, during the period from 1991-1992. Fifteen children of these patients had arthritis as an initial manifestation of their leukemia. These cases were referred from Benha, Cairo and Suez Canal University Hospitals.

The diagnosis of acute leukemia was confirmed by complete history taking, physical examination as well as the routine leukemia work-up including a complete blood count and bone marrow aspirate. Plain radiographs of the involved joints were obtained.

Laboratory analyses for the rheumatoid factor, antistreptolysin O-titre and ery-

throcyte sedimentation rate were also included. In addition, each case was carefully reviewed by the rheumatologist to note the extent of evaluation for their arthritis.

Results

Fifteen children (9.7%) out of 155 leukemic patients presented with arthritis as an initial manifestation of their acute leukemia. They were 9 females (60%) and 6 males (40%), with a female to male ratio of 3:2. Their ages ranged between 3-14 years (mean 8.2 ± 3.4 years). Thirteen patients (86.7%) had acute lymphoblastic leukemia (ALL) and the other two (13.3%) had acute myeloblastic leukemia (AML).

The presenting arthritis was almost always symmetrical polyarticular (> 5 joints) in 11 patients (73.3%), while it was migratory in 4 patients (26.7%). The involved joints were painful, hot and tender. Synovial effusion was detected in 4 patients (26.7%).

The duration of arthritis on initial examination ranged from 4-24 weeks (mean 11.2 ± 6.7 weeks). Recurrent attacks were reported by 5 patients (33.3%). Seven patients (46.7%) claimed partial relief of their symptoms on non steroidal anti-inflammatory drugs.

Thirteen patients had fever which was high intermittent in 6 children (40%) and low grade in 7 children (46.7%) Two children (13.3%) had no documented fever.

Table (1) : The Main Clinical Findings in Children with Acute Leukemia Presenting with Arthritis.

Case No.	Age (Yrs)	Sex	Duration of arthritis (weeks)	Joints affected	Type of arthritis	Enlarged liver, spleen and/or lymph nodes
1	3	F	4	Knees, ankles, elbows wrists	Persistent	Yes
2	3	F	24	Lt-knee, Lt-wrist	Persistent	No
3	5	M	8	Knees, ankles	Persistent	No
4	5.5	F	6	Small joints of both hands	Persistent	No
5	6	M	4	Knees, wrists	Persistent	Yes
6	7	M	4	Lt-knee, ankles.	Migratory	Yes
7	8	M	4	Small joints of hands, knees	Persistent	No
8	8	F	16	Knees, ankles	Persistent	No
9	9	F	12	Knees, Lt. ankle	Persistent	No
10	9	F	16	Small joints of both hands	Migratory	Yes
11	10	M	20	Rt. shoulder, hips	Persistent	Yes
12	11	M	12	Small joints of both hands	Persistent	Yes
13	12	F	10	Rt. knee, ankles, Rt-wrist	Migratory	Yes
14	13	F	20	Elbows, wrists	Migratory	Yes
15	14	F	8	Shoulders, hips, sacroiliacs	Persistent	No

Table (2) : Laboratory Findings in Patients with Acute Leukemia Presenting with Arthritis.

Case No.	Diagnosis	Hemtocrit (%)	WBCs/mm ³	Platelets	ESR mm/hour	RF	ASO
1	ALL	36	7000	N	15	—VE	N
2	ALL	25	10000	N	40	+VE	N
3	AML	35	12000 abnormal cells	LOW	25	—VE	N
4	ALL	13.5	2600	LOW	15	—VE	N
5	ALL	30	14100 abnormal cells	LOW	150	—VE	N
6	ALL	30	22000 abnormal cells	N	60	+VE	N
7	AML	30	5200	N	55	—VE	N
8	ALL	40	6000	N	20	+VE	N
9	ALL	39	7300	N	44	—VE	N
10	ALL	22	13000 abnormal cells	LOW	100	—VE	N
11	ALL	44	12000	LOW	110	—VE	N
12	ALL	25	21000 abnormal cells	LOW	130	—VE	N
13	ALL	15	4000	N	130	+VE	N
14	ALL	22	1500	LOW	40	—VE	N
15	ALL	25	300	N	140	—VE	N

ALL = Acute lymphoblastic leukemia.

AML = Acute myeloid leukemia.

WBCs = White blood Cells.

ESR = Erythrocyte sedimentation rate.

RF = Rheumatoid factor.

ASO = Anti-streptolysin O-titre.

N. = Normal.

Table (3) : Extent of Presenting Joint Involvement in Children with Acute Leukemia.

Joint	Percentage
— Knees	60.0%
— Ankles	40.0%
— Wrists	33.3%
— Small joints of the hand	26.7%
— Shoulder	13.3%
— Elbow	6.7%
— Hip	6.7%
— Sacroiliac	6.7%

Radiological changes suggestive of leukemia (metaphyseal rarefaction, osteolytic deposits or periosteal reactions) were detected in 5 patients (33.3%). Nine children (60%) had non specific radiographic changes (osteoporosis and periarticular soft tissue swelling). No patient had evidence of secondary gouty arthritis or septic arthritis.

Hepatosplenomegaly and/or lymphadenopathy were encountered in 8 patients (53.3%). The hematocrit value of these patients ranged between 15-44% (Mean 28.8 ± 8.9). It was low ($< 30\%$) in 10 patients (66.7%). The white blood cells ranged between 300-22000/mm³ (mean 92000 ± 6555). It was low (< 4000) in 3 patients (20%), while it was high (> 10000) in 7 patients (46.7%). Abnormal blood cells were found in 5 patients (33.3%) Platelet counts were low in 7 patients (46.7%), while it was normal in other patients (53.3%). The erythrocyte sedimentation rate (ESR) ran-

ged between 15-150 mm/hour (mean 71.6 ± 49.5). It was highly elevated (> 100 mm/hour) in 6 patients (40%). The rheumatoid factor was positive in 4 patients (26.7%) while, the anti-streptolysin O-titre was normal in all patients.

Discussion

Malignancy may assume various guises, some of which pertain to the musculoskeletal system[4].

Arthritis is the presenting feature in 13.5% of patients with leukemia, the majority of whom have acute leukemia[5]. Arthritis or arthralgias have been said to occur in 60% of children with acute lymphoblastic leukemia[6]. The overall incidence is probably less (10-20%), though it is often difficult to ascertain in a sick, miserable child[7].

In our study 97% of children with acute leukemia presented with arthritis, 86.7% of these patients had ALL, the other 13.3% had acute myeloid leukemia (AML).

The presenting arthritis in our study was symmetrical polyarticular in most of the patients (73.3%). This was also reported by Caldwell[7], while Guyton and Koopman[4] stated that the arthritis of acute leukemia tends to be asymmetric, additive and polyarticular.

Holt[6], found that the knee and wrist regions are frequent sites of involvement, while the ankles, shoulders, fingers and other small joints are less frequently affected and tenosynovitis is rare. This coincided with our results, although the

ankles were more frequently involved and tenosynovitis could not be detected in any of our patients.

Joint manifestations in leukemia were noted to occur without evident bone involvement as reported by Spilberg and Meyer[8], which was also confirmed in our work.

Hematological abnormalities (anemia, thrombocytopenia, leukopenia, leukocytosis or abnormal leukocytes in the peripheral blood) were detected in 66.7% of our patients, while this was found in 70% of children studied by Costello et al[9].

Hepatosplenomegaly and/or lymphadenopathy were reported by Caldwell[7], in 60% of children, while it occurred in 53.3% of our patients.

Harden et al[10], found that the sedimentation rate (ESR) was of no help in distinguishing patients with leukemia presenting with arthritis. This also coincided with the presentation in our patients where the ESR was highly elevated (> 100 mm/hour) in only 40% of cases.

Rheumatoid factor positivity has been reported by Caldwell[7], as well as in 13.4% of our patients.

From our study it is concluded that the presence of anemia or leukopenia or a non diagnostic bone radiograph in a child with arthritis should prompt the physician to examine the bone marrow. Clinical findings and constitutional complaints were of no help to differentiate arthritis of leukemia from other rheumatic diseases which demonstrates the importance

of considering leukemia in the differential diagnosis of arthritis in children.

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