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CASE REPORT

Onubogu UC
Okoh BAN
Eke G
Joboy-okei EA

Acute Lymphoblastic Leukaemia presenting as Juvenile Idiopathic Arthritis in a Nigerian boy

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Onubogu UC (✉)
Department Paediatrics,
Shawsand Medical Center,
Port Harcourt, Rivers State,
Nigeria.
Email: utchayonubogu@yahoo.co.uk
Tel: +234 803 327 9486

Okoh BAN, Eke G
Joboy-okei EA
Department of Paediatrics,
University of Port Harcourt Teaching Hospital, Port Harcourt,
Rivers State,
Nigeria.

Abstract *Background:* Acute Lymphoblastic Leukaemia in children commonly presents with osteo articular manifestations that may mimic Juvenile Idiopathic Arthritis. This may create considerable diagnostic difficulty and lead to delay in commencing appropriate treatment.
Case: An eight year old boy who presented with multiple joint pains and swellings of two months duration, had an elevated Rheumatoid factor and X-ray findings suggestive of Juvenile Idiopathic Arthritis. A blood film and bone marrow aspirate however, confirmed the diagnosis of Acute Lymphoblastic Leukaemia for which he was managed.
Conclusion: This report emphasizes the need for a high index of suspicion in children presenting with osteo articular manifestations of Acute Lymphoblastic Leukaemia in order to make a prompt diagnosis and institute treatment.

Key words: Acute Lymphoblastic Leukaemia, Juvenile Idiopathic Arthritis.

Introduction

Leukaemia is one of the common malignant neoplasms in childhood, accounting for about 41% of all malignancies that occur in children <15year of age and Acute lymphoblastic leukaemia (ALL) accounts for about 77% of cases of childhood leukemias.[1] Bone pain, particularly of the lower extremities is a common manifestation of childhood ALL. Although the initial presentation of childhood ALL is usually nonspecific and relatively brief, symptoms may be of several months duration, may be localized predominantly to the bones or joints, and may include joint swelling.[1] Joint lesions are less frequent but have been reported in at least 10 to 15% of children and 3% of adults with acute leukaemia.[2,3]

Joint manifestations in leukaemia have been attributed to a variety of causes. These include leukaemic synovial infiltrations, haemorrhage into the joint or periarticular structures, synovial reaction to adjacent bony, periosteal or capsular lesions, and crystal induced synovitis.[4]
Radiographic bone abnormalities have been said to occur at presentation in more than half of children with ALL with bone and joint symptoms.[5,6] Radiographs of involved joints may show lesions in the adjacent bone, or show joint effusion.[2,3]
The orthopaedic manifestations of ALL in children may create considerable diagnostic difficulty. This may lead to both a delay in commencing appropriate treatment or inappropriate intervention. We present the case of an 8 year old male who presented with features suggestive of Juvenile Rheumatoid Arthritis (JRA), also known as Juvenile Idiopathic Arthritis (JIA) but was finally diagnosed with ALL.

Case Report

An 8year old male presented with a three month history of recurrent fever, two month history of paleness of the body and joint pains. The fever was high grade and intermittent, with occasional chills. He had two episodes of pallor in the two months preceding presentation and was transfused with blood donated by the father in a private hospital. The Joint pains involved his left shoulder, left elbow, left knees, left ankle and all fingers. Pain was severe enough to make him cry and keep him awake at night. There was associated swelling of the joints. He was initially hospitalized in a private hospital where he received intramuscular injections and blood transfusions. Genotype done there was AS. With no remarkable improvement, he presented to the University of Port Harcourt Teaching Hospital (UPTH). He had a rash on the trunk that lasted for about a week at onset of symptoms. The review of systems showed he had haemoptysis and epistaxis. On physical examination he was moderately pale, febrile with submandibular lymphadenopathy. His left ankle was swollen and he had Swan neck deformity of his left ring and middle fingers. There was diffuse swelling on the middle phalanges on the

right hand with differential warmth and tenderness. He had no organomegaly and ophthalmology examination was normal.

His peripheral blood film showed hypochromic normocytic anaemia with few normoblast, There was leukocytosis with a White Blood Cell count (WBC) of greater than 30 x 10^9/L and greater than 50% were blasts. The Platelets were scanty on the blood film but normal in size, shape and granularity. His serum uric acid was elevated. The X-ray of the hands showed juxtaarticular osteoporosis with soft tissue swelling suggestive of rheumatoid arthritis (Figure 1). The Rheumatoid factor was raised and antinuclear antibodies were negative. The bone marrow aspirate confirmed ALL type L2.
He was treated using the protocol for high risk ALL. He had three cycles of chemotherapy but was yet to achieve remission before he defaulted from treatment. Contact made with the family revealed that he died 2 months after default.

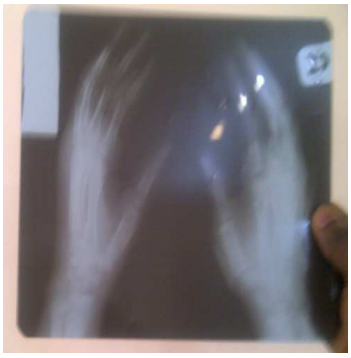

Fig 1: Plain radiograph of both hands of patient showing soft tissue swelling

Discussion

Acute lymphoblastic leukaemia (ALL) is the second most prevalent childhood cancer in Nigeria.[7,8] It is a malignant disease of the bone marrow in which early lymphoid precursors proliferate and replace the normal hematopoietic cells of the marrow. ALL may initially present with osteoarticular manifestation that mimic Juvenile idiopathic arthritis (JIA). Such presentation can occur in 15% to 30% of ALL cases at disease onset, when peripheral blood changes are subtle or even absent.[5] Barbosa et al[9] showed that 8% of patients with leukaemia had been diagnosed with rheumatic fever or JIA before referral, and some of these patients had already received steroids, delaying the commencement of definitive treatment for ALL. In another study[10] on children presenting with musculokeletal symptoms in which occult cancer was found, ALL was the most prevalent (60%), followed by lymphoma (20%).

The cause of the osteoarticular manifestation of acute leukaemia has been attributed to direct extension of leukemic cells from the marrow or to hematogenous dissemination of leukemic cells.[3] The proliferating leukemic cells cause bone destruction, increase intramedullary pressure which interferes with nutrition, or induce osteoclastic or blastic responses. The increased frequency and severity of bone symptoms in children have been attributed to a more active bone metabolism, more red marrow with little reserve marrow space, and a less firmly attached perioteum.[11]

Typically, children with ALL have asymmetric oligoarthritis, particularly in the large joints of the lower limbs in the following descending order of frequency: ankle 63%, knee 59%, and hip 20%. In the upper limbs the descending order is elbow 32%, carpal 16%, and shoulder 8%. In the metacarpophalangeal and interphalangeal small joints of hands 14% and 2% in the tarsometatarsal, small interphalangeal joints of the feet and vertebrae.[3] Our patient however, had polyarticular involvement of the left shoulder, left elbow, left knees, left ankle and all fingers. About 7% of children with ALL with initial musculoskeletal manifestations meet diagnostic criteria for JIA. Our patient met the criteria for polyarticular rheumatoid positive JIA,[12] considering the duration of symptoms (>6weeks), number of joints involved (>6), swan neck deformity of the interphalageal joint, preceeding history of a transient rash and high rheumatoid factor. In such cases, diagnosis of ALL is generally considered in subsequent stages when atypical clinical characteristics of JIA manifest. The atypical presentations of JIA in our patient were severe anaemia, bleeding disorder and lymphadenopathy. Studies[13,14] have shown that important features that predicted a diagnosis of ALL and differentiated it from JIA include a history of night pain, non-articular bony pain and the presence of joint pain out of proportion to physical signs (all of which was seen in our patient). Other distinguishing findings were anemia, leucopenia), lymphocytic predominance and thrombocytopenia. Non-osseous involvement such as hepatosplenomegaly or enlarged lymph nodes occurs in 60% of ALL cases at presentation.[15] Night pain has been observed frequently in children with leukaemia. Children with JRA usually describe achiness, stiffness, and a dull discomfort over the joint(s) that is worse in the mornings. Pain that is excruciating and wakes the child from sleep is not typical for JIA.

A bone marrow aspiration is the confirmatory test in making a diagnosis for ALL, while the diagnosis of JIA is clinical. Rheumatoid factor has 90% sensitivity in diagnosing rheumatoid arthritis in clinically established diseases. It has a limited diagnostic value as it can be positive in 20% of patients with leukaemia[16] and in 4.3% of a healthy population.[17] Secondary hyperuricaemia may rarely be associated with arthritis in patients with acute leukemia.[3,4] The radiographic bone lesions of acute leukaemia are radiolucent metaphyseal bands, generalized osteoporosis, osteolytic bone destruction, periosteal infiltration with new bone formation and osteosclerotic new bone formation.[2,3] The radiographic signs of JIA are periarticular soft-tissue swelling with a fusiform appearance and juxta-articular osteopenia (both of which were seen in our patient). Osteopenia subsequently becomes more generalized as the disease progresses, widening of joint spaces initially then narrowing, joint subluxation and malalignment at a later

stage. In a study[18] carried out among children with musculoskeletal symptoms and a diagnosis of ALL or JIA, it was noted that on plain X-ray, soft tissue swelling and osteopaenia were significantly more common in patients with JIA. On the other hand, radiolucent metaphyseal bands and coarse trabeculations were significantly more common in patients with ALL.

Conclusion

In conclusion, since up to 75% of children presenting with osteo arthritic manifestation of ALL do not have blast in the peripheral blood film, a high index of suspicion is required in order do a bone marrow biopsy to confirm presence of blasts in the marrow. Our patient though had blasts on his peripheral blood film, he had been symptomatic for two months and was transfused on two occasions. We could not establish if he had a blood film done prior to the transfusion and if he had peripheral blasts at onset of his symptoms. We recommend therefore, that any child with severe anaemia necessitating blood transfusion should have blood samples taken out for peripheral blood film prior to transfusion.

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References

1. Tubergen DG, Bleyer A. The leukaemias. In: Behrman RE, Kliegman RM, Jenson HB, Stanton BF editors. Nelson textbook of Paediatrics. 18th Ed. Pennsylvania: Saunders; 2007. p. 2116 – 2120.
2. Resnick D, Niwayama G. Diagnosis of bone and joint disorders. 1st Ed. Philadelphia: W. B. Saunders, 1981. p. 1992-2001.
3. Thomas LB, Forkner CE, Frei E, Besse BE, Stabenau JR. The skeletal lesions of acute leukemia. *Cancer. 1961; 14:608-62I.*
4. Weinberger A, Schumacher HR, Schimmer BM. Arthritis in acute leukaemia: Clinical and histopathological observations. *Arch Intern Med. 1981; 141:1183 – 1187.*
5. Rogalsky RJ, Black GB, Reed MH. Orthopedic manifestations of leukemia in children. *J Bone Joint Surg Am. 1986; 68:494-501.*
6. Clausen N, Gotze H, Pedersen A, Riis-Petersen J, Tjalve E. Skeletal scintigraphy and radiography at onset of acute lymphocytic leukemia in children. *Med Pediatr Oncol. 1983; 11: 291-296.*
7. Edache SO, Ibrahim IA, Isaac EO, Seline NO. Pattern of Childhood Malignancies in Jos, North Central Nigeria. *Journal of Medicine in the Tropics. 2011; 13(2):109-114.*
8. Parkin DM, Ferlay J, Hamdi-Cherif M et al., editors. Cancer in Africa: Epidemiology and Prevention. Lyon, France: IARC Press, 2003.
9. Barbosa CM, Nakamura C, Terreri MT, Lee ML, Petrilli AS, Hilario MO. Musculoskeletal manifestations at the onset of acute leukemias in childhood. *J Pediatr. 2002; 78(6):481–484.*
10. Trapani S, Grisolia F, Simonini G, Calabri GB, Falcini F. Incidence of occult cancer in children presenting with musculoskeletal symptoms: A 10-year survey in a pediatric rheumatology unit. *Semin Arthritis Rheu. 2000; 29(6):348–359.*
11. Parker BR, Marglin S, Castellino RA. Skeletal manifestations of acute leukemia, Hodgkin's disease and non-Hodgkin's lymphoma. *Semin Roentgenol. 1980; 15:302-315.*
12. Miller ML, Cassidy JT. Juvenile Rheumatoid Arthritis. In: Behrman RE, Kliegman RM, Jenson HB, Stanton BF editors. Nelson textbook of Paediatrics. 18th Ed. Pennsylvania: Saunders; 2007. p. 1001 – 1010.
13. Jones OY, Spencer CH, Bowyer SL, Dent PB, Gottlieb BS, Rabinovich CE. A Multicenter Case-Control Study on Predictive Factors Distinguishing Childhood Leukemia From Juvenile Rheumatoid Arthritis. *Pediatrics. 2006;117; 840-884.*
14. Gupta D, Singh S, Suri D, Ahluwalia J, Das R, Varma N. Arthritic presentation of acute leukemia in children: experience from a tertiary care centre in North India. Rheumatol *Int. 2010; 30(6):767-770.*
15. Tuten HR, Gabos PG, Kumar SJ, Harter GD. The limping child: a manifestation of acute leukaemia. *J Pediatr Orthop. 1998; 18; 625 – 629.*
16. Chell J, Fernandes JA, Bell MJ. The orthopaedic presentation of acute leukaemia in childhood. *Ann R Coll Surg Engl. 2001; 83: 186-189.*
17. Nielsen SF, Bojeson SE, Schnohr P, Nordestaarg BG. Elevated rheumatoid factor and long term risk of rheumatoid arthritis: a prospective cohort study. *BMJ. 2012;345:e5244.*
18. Tafaghodi F, Aghighi Y, Yazdi HR, Shakiba M, Adibi A. Predictive plain X-ray findings in distinguishing early stage acute lymphoblastic leukemia from juvenile idiopathic arthritis. *Clin Rheumatol. 2009; 28(11):1253 – 1258.*