Bone Pain In Children Caused By Acute Lymphoblastic Leukemia

Bidasari Lubis
Bagian Ilmu Kesehatan Anak
Fakultas Kedokteran
Universitas Sumatera Utara

Introduction

Acute Lymphoblastic leukemia (ALL) is the most common malignancy in children,\textsuperscript{1-3} accounting for almost one quarter of newly diagnosed pediatric cancer cases.\textsuperscript{1} It is the commonest type of leukemia in childhood with a peak incidence between 3 and 5 years of age,\textsuperscript{1,2,3,4,5,8} and slightly more frequently in boys than girls.\textsuperscript{1,2,8}

The causes is not known, but environmental agent including irradiation, chemical carcinogens, retroviral infections have been implicated. Cytogenic abnormalities also have been found.\textsuperscript{1,2,4}

In the majority of patients with ALL there is pallor, tiredness, irritability, often accompanied by fever, bone pain, bruising, petchiae, purpura and bleeding, increasing over a period of weeks, sometimes even months. Anorexia and generalized malaise are common, but significant weight loss is rare at presentation.\textsuperscript{1-8}

Bone pain due to periosteal elevation occurs in one quarter of children usually younger children, and causes them to limp or refuse to walk.\textsuperscript{1} As many as 40\% of patient with childhood leukemia initially present with a limp or painful bone or joints.\textsuperscript{8} These symptoms may be the result of direct leukemic infiltration of the periost, bone infarction, or expansion of the marrow by the leukemic cells.\textsuperscript{5,8}

Lymphadenopathy is occasionally prominent, and splenomegaly is found in about 66\% of cases. Hepatomegaly is less common. Rarely, signs of increased intracranial pressure, such as headache and vomiting indicate leukemic meningeal involvement.\textsuperscript{1,5,6}

Haematologic abnormalities includes elevated leukocyte count (>10,000/mm\textsuperscript{3}) occur in approximately one half of patients, with ALL; in approximately 20\% of patients, the initial leukocyte count is greater than 50,000/mm\textsuperscript{3}. Neutropenia ( , 500 granulocytes/mm\textsuperscript{3}) is a frequent phenomenon. Anemia (haemoglobin < 10 g/dl) exist in approximately 80\% of patients at at diagnosis. Thrombocytopenia occurs in most patients; 75\% have fewer than 100,000 platelets/mm\textsuperscript{3}.\textsuperscript{2,6,6,8} Cerebrospinal fluid should be examined for leukemic cells.\textsuperscript{5} Morphologic assesment of abone marrow aspirate is sufficient to establish the diagnosis af ALL in more than 95\% of cases.\textsuperscript{1}

A chest radiograph is necessary to determine whether there is a mediastinal mass or hilar lymph node enlargement or infection, but routine skeletal surveys and nuclear bone scan add little to the initial evaluation.\textsuperscript{4,6} The radiologic changes are most easily seen in the long bone, especially around the areas of rapid growth and include 1) subperosteeal new bone information, 2) transvers metaphyseal radiolucent bands, 3) osteolytic lesions involving the medullary cavity and cortex, 4) diffuse demineralization, and 5) transver metaphyseal lines of increase density.\textsuperscript{8}
ALL can usually be diagnosed from 1) the presence of blast cell in the peripheral blood, 2) a bone marrow aspiration, 3) cytochemical staining characteristics, 4) immunophenotype, and 5) cytogenetic features.

The differential diagnosis of ALL includes:
1) Infectious mononucleosus, 2) Idiopathic thrombocytopenic purpura, 3) Juvenile rheumatoid arthritis, 4) Kala azar, 5) Aplastic anemia, 6) Metastatic neuroblastoma, 7) myeloproliferatifs syndromes. 

Contemporary treatment of ALL is based on clinical risk feature. The treatment program for standard-risk patients includes administration of induction chemotherapy, "Prophylactic" treatment of CNS, and continuation chemotherapy. A combination of prednisone, vincristine, and asparaginase should produce remission in about 98% of children with standard risk ALL. Systemic continuation therapy, usually consisting of the antimetabolites methotrexate and 6 mercaptopurine should be given for 2,5-3 years.

Various clinical and laboratory finding at the time of diagnosis such as white blood count, organ infiltration, lymphoblast morphology, sex, age, race and immunophenotype have been correlated with prognosis. It must not, of course, be forgotten that prognostic factors vary considerably with the treatment given and that the single most important factor is the therapeutic schedule employed.

The aim of this paper is to report a case with bone pain in children caused by acute lymphoblastic leukemia in H.Adam Malik Hospital.

Case

F, 12 years 10 months, Indonesian boy, was referred to H.Adam Malik Hospital by Paediatrician in Kisaran Hospital on August 7th, 1997 with the suspicion of leukemia. The main complaint of this patient were bone and joint paint that was present since 2 weeks before admitted to the hospital. The pain was migrated over the joint at the upper and lower extremity, and also accompanied by swelling of the joint. He could not walked for about one week. He was suffered from fever about two weeks before admitted to the hospital. There was no history of bleeding and bruising.

He was born spontaneously at home on September 24th 1984, by midwife as the third of three siblings. His two siblings were healthy. Birth weight was 3000 g and body length was not measured.

His father was 42 years old, employee and his mother was 38 years old, housewife; both apparently healthy.

On physical examination, consciousness was clear, general condition was good, disease status was moderate and nutritional status was good.

Body weight was 32 kg, height was 149 cm. Temperature was 37°C. There were no dyspnea, cyanosis, iderma and pallor.

Head: eye; light reflex was positive, pupil isocoric nose and mouth were normal

Chest: Symetrically and no retraction.

HR: 98 x1min, regularly, no murmur
RR: 24x1min, regularly, no rales
Abdomen: Soft and flexible, peristaltic was normal
liver was palpable 3 cm below rib margin; sharp, flat and smooth.
Spleen was palpable-SII

Extremities:
Upper extremity: swelling of right arm and wrist joint lower extremity:
no abnormality. There were no enlargement of lymphonode.

Laboratory finding:
Blood: Hb. 10.4 g%
WBC: 56,000/mm³
Diff.count: 0/0/0/4/96/0
Ht: 32%
BSR: 110 mm/hr
Thrombocyte: 86,000/mm³
Urine: Uric acid crystal (+)
Stool: no abnormality

Morphology:
erthrocyte: normocytair normochromic
leukocyte: lymphoblast 96 %
thrombocyte: normal

Differential Diagnosis:
1. Acute lymphoblastic leukemia (ALL)
2. Junevile rheumatoid arthritis

Treatment:
- IVFD Dextrose 5 % NaCl 0,45 % gtt/ml, macrodrips
- Inj. Kalpicillin 1 g/6 hr/IV
- Inj. Gentamycin 80 mg/12 hr/IV
- Cavital Syr 2 x 1 tsp
Diet: 1800 calories with 60 g protein

Suggestion:
- Bone marrow punction (BMP)
- ECG
- Chest X-ray
- Bone survey

Follow up
On August 9 h, 1997
Liver function test (LFT):
- Total bilirubin: 0,34 mg/dl (<1)
- Direct bilirubin: 0,18 mg/dl (<0,25)
- Alkaline Phosphatase: 255 U/L (60-170)
- SGOT: 18 U/L (2-18)
- SGPT: 11 U/L (<22)

Electrolyte:
Na: 134 meq/l (136-144)
K: 3.82 meq/l (4-5)
Uric Acid 8.6 mg/dl (2.5-7.0) Cl : 108 meq/l (97-137)

On August 11\textsuperscript{th}
Bone marrow puction (BMP):
Diff.count: - Lymphoblast : 98 %

\begin{itemize}
  \item Large cell, nucleus polymorphic, moderate abundant cytoplasma, loose chromatin
  \item Segmen neutrophil: 1 %
  \item erythrocyte: 1 %
  \item granulopoiesis was depressed
  \item erythropoiesis was depressed
  \item M:Eratio was difficulted to evaluate
  \item lymphopoiesis was hyperactive
  \item reticuloendothelial system was depressed
  \item megakaryocyte was depressed
\end{itemize}

Conclusion: ALL - FAB L2

Working Diagnosis: Acute lymphoblastic leukemia

On August 12\textsuperscript{th}, 1997
ECG; Conclusion: ECG within normal limit.

Chest X-ray: No abnormality

On August 14\textsuperscript{th}, 1997
Cytostatic treatment was given according to the national leukemic protocol for high risk ALL

Treatment:
- IVFD Dextrose 5 % NaCL 0,45% 22 gtt/min,macrodrips
- Inj. Kalpicillin 1 g/6 hrN
- F armitrexate 1 mg/IT
- Dexamethason 1 mg/IT
- Cytarabin 20 mg/IT
- Daunorubicin 30 mg/drip
- Vincristin 1,5 mg/IV
- Allupurinol 2 x 1 00 mg (oral)
- Cotrimoxazol 2 x 960 mg (oral)
- Dexamethason 1, 5mg-1, 5mg-1 mg
- Cavital Syr 2x1 tsp

On August 25\textsuperscript{th}, 1997
Pallor (+), bone and joint pain (+)/fever (-)

Physical examination:
Head: Eye; conjuctival palpebra: pallor (+)

\begin{itemize}
  \item Cheast : HR : 96x1min,regularty, no murmur
  \item RR : 24x1min,regularty, no rates
\end{itemize}

Abdomen: soft and flexible

\begin{itemize}
  \item liver: Palpable 3 cm below rib margin, sharp, flat and smooth
  \item Spleen: palpable –SII
\end{itemize}
Extremities: swelling of wrist joint was decreased

Laboratory finding:
- Hb : 7.4 g%; WBC : 11400/mm3; Diff.count:0/0/1127n2/0
- Treatment: Transfusion of PRC 250 CC
  Other medicinee were continued

On August 28th, 1997
Bone survey: Osteolytic lesion with periosteal reaction 0 distal of the right ulna
  The other bones were normal
  Conclusion: leukemic appearance in bone

On September 25th, 1997
Edema(+), Pallor (+), bone and joint pain (-)

**Physical Examination:**
- Abdomen: liver: palpable 1 cm below rib margin, sharp, flat, and smooth
  - Spleen: palpable-SI
- Extremities: edema (+)
- Laboratory finding:
  - HB: 6.9g%; WBC: 2200/mm³
  - Total Protein: 3.5 g/dl (6.3-8.8)
  - SPE: Albumine: 2.1 g/dl (3.2-5.2)
    - globuline: 0.38 g/dl (0.1-0.3)
    - globuline: 0.25 g/dl (0.6-1.0)
    - globuline: 0.32 g/dl (0.7-1.1)
    - globullns: 0.9 g/dl (0.8-1.1)
- Treatment: Albumine 20, % 48 g (5Occ) was given in 3 days
  - Transfusion of PRC 250 cc

On September 29th, 1997
- Pallor (-), bone and joint pain (-), fever(-), edema(-)

  Physical examination:
  - chest: HR : 80x1min, regularly, no murmur
    - RR: 24x1min, regularly, no rales
  - Abdomen: Soft and flexible
    - Liver & spleen were nor palpable
  - Extremities: edema (-)
  - Laboratory finding:
    - Hb: 9.8 g/dl; weC: 2600/m3 ; Diff.count:OJO/5/46/49/0
    - Thrombocyte: 123,000/mm3

On October 6th, 1997
- Edema (+)
Laboratory finding:
HB : 9,8g/dl ;WBC: 3000/mm³
Total protein: 3,8 g/dl
Albumine: 1,9 g/dl
Treatment: Albumine 20% 48 g (50 cc)

On October 10th, 1997
Pallor (-), fever(-), edema (-), bone and joint pain (-)
Patient could walked normally, and he was discharged from the hospital and continued therapy as ambulatory patient.

Discussion
This case was differential diagnosed with leukemia and juvenile rheumatoid arthritis because were found bone and joint pain without pallor or history of bleeding.
According to literature pain and swelling of the joint are less frequent but may be presenting manifestations of disease and can initially cause confusion in diagnosis. Migratory joint pain accompanied by swelling and tenderness can be misdiagnosed as juvenile rheumatoid arthritis or as rheumatic fever.

In this case, bone survey showed osteolytic process and periosteal reaction only in the right ulna where as the other bones were normal.
Anemia is common in B-progenitor cell ALL and uncommon in rapidly progressive T-Cell ALL and adolescent have fared poorly in many studies because of their higher incidence of T-Cell. 1
Therefore the possible immunophenotype of leukemia cell in our case is T-Cell ALL.

The management of the patient began with the establishment of the diagnosis. We have given cytostatic according to the leukemic protocol for high risk ALL based on some criteria were found in this case, such as:
1. Age greater than 10 years
2. Leukocyte count > 50,000/mm³
3. Haemoglobin >/10g/dl

The prognosis of this case is poor because of some criteria above that also represent a prognostic factors.
Improvement was found after about 2 months of chemotherapy and the patient could walked normally.
Until now, cytostatic chemotherapy was still continued and he was controlled to Paediatric Haematology and oncology H. Adam Malik Hospital as an ambulatory patient.

Resume
We have reported a case with bone pain in a 12 year 10 month old boy caused by ALL. Diagnosis was based on clinical manifestation, laboratory finding and radiologic examination.
After about 2 months treatment with cytostatic, improvement was present
References.