Original Article

Presenting Clinical and Laboratory Data of Childhood Acute Lymphoblastic Leukemia

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Abstract

Background

Leukemia is the most prevalent childhood cancer and Acute Lymphoblastic Leukemia (ALL) constitutes 75% of all cases. The most frequent presenting symptoms are fever, weight loss and pallor. Early detection of clinical symptoms positively affects timely diagnosis. The objectives of the present study were to assess frequency of presenting symptoms, laboratory data, immune phenotypes and prognostic factors in children with diagnosis of ALL.

Materials and Methods

We performed a prospective follow-up study of 100 patients aged 1-16 years diagnosed with ALL, admitted to Shahid Sadoughi hospital pediatrics ward from March 2006 to February 2010. Demographic and biochemical data were obtained from their medical record. Data were analyzed using SAS 9.1.3 software.

Results

The mean of patients' ages was 9 years. Complete blood cell count was abnormal in all of the patients, and pancytopenia was detected in 27% of the patients. Of all the patients, 25% had abnormal white blood cell (WBC) count at presentation, 37% had leucopenia and 38% had leukocytosis. WBC count was above 50,000/mm^3 in 22% of cases. Anemia was detected in 85% of the patients. There was no significant sex difference, but a significant age difference existed among patients ($p < .05$).

According to flowcytometry results, 61% of patients had T-cell and 39% had B-cell immune phenotype. The frequency of undesirable prognostic factors was more in T-cell than the B-cell group, but this difference was only significant for male patients ($p<0.05$).

The most common presenting symptoms were systemic symptoms, which comprised of lethargy and malaise in 81%, anorexia in 72%, pallor in 69% and fever in 59% of cases. Musculoskeletal system was the most common system involved.

Conclusion

In our study, T-cell immune phenotypes comprised the most frequent form of ALL in children. The presence of male sex and high WBC count could make its outcome worse. However, on time chemotherapy could alter the outcome of these patients.

Keywords

Leukemia, ALL, Lymphoblastic leukemia, symptoms

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Introduction

Leukemia is a heterogenous group of disorders, caused by neoplastic transformation in blood cell precursors during their differentiation in bone marrow. Acute lymphoblastic leukemia is the most prevalent leukemic cancer; comprising 75% of all leukemia cases. It could be suspected through a wide range of clinical and laboratory findings. Eventually it is diagnosed via complete cell count and histopathology (1).

Leukemia is the most prevalent childhood cancer and constitutes 31% of childhood malignancies in children under 15 years old and 25% of childhood cancers in children less than 20 years of age (1). About 3250 new cases are diagnosed annually in the United States (2,3). Acute Lymphoblastic leukemia (ALL) constitutes 75% of cases and acute and chronic myelogenous leukemia (AML and CML) constitute 20% and 5% of all cases respectively (1).

The prevalence of all forms of leukemia is more in children under 5 years of age and decreases significantly with advancing age (4-6). The disease is a little more prevalent in boys than girls with a male-female ratio of 1.3-1.4:1 (2, 4). ALL prognostic factors include patient's age at diagnosis, WBC count, cytogenetic findings, response to therapy and immune phenotypes. Leukemic cells express specific antigents called CD markers on their cell surfaces and in their cytoplasms. They can be detected with flowcytometry method and patients categorized as B-cell and T-cell groups and 6 subgroups.

ALL could present clinically with a wide range of symptoms, which the most frequent is systemic symptoms such as fever, loss of appetite and pallor. Neurologic symptoms such as nausea, headache and lethargy, facial nerve palsy, excessive weight gain and behavior change can be seen at the time of diagnosis (7). About 40% of cases have been reported to present with bone pain and limp (8). The most frequent laboratory findings have been reported to be low platelet count, high WBC count and anemia (8).

The aim of this prospective study was to determine the frequency of presenting symptoms, laboratory data, immune phenotypes, prognostic factors and their correlation with patient sex in children admitted to Shahid Sadoughi hospital, pediatrics ward with diagnosis of ALL.

Materials and Methods

We performed a prospective follow-up study of 100 patients aged 1-16 years diagnosed with ALL, admitted to Shahid Sadoughi hospital pediatrics ward from March 2006 to February 2010. ALL was diagnosed histopathologically reported by a clinical pathologist or a pediatric hematologist-oncologist (the corresponding author herself).

Bone marrow aspiration samples were assessed by flowcytometry department of Yazd Transfusion Organization. Using PAS III device (www.partec.de), CD markers including CD34, CD33, CD13, HLA-DR, CD19, CD20, CD10, CD7, CD5, CD3, CD2) were identified. According to CD markers, patients were categorized as B-cell, T-cell groups, also immature T-cell, intermediate T-cell, mature T-cell, Pro.B-cell, Pre.B-cell, mature B-cell subtypes. Demographic and prognostic data were also obtained elaborately.

For comparison of variables among groups, univariate analysis was performed. The Means of the values extracted and compared by Student's *t* test for continuous variables and $\chi 2$ test for discrete variables using SAS 9.1.3 software. P-value less than 0.05 was considered significant.

Results

Out of the 100 children diagnosed with acute leukemia, 62 were boys and 38 were girls (male: female ratio: 1.6:1). The ages of 23% of patients were between 1-4 years old; 32% were between 5-9 years old and 45% were between 10-16 years old. The mean age of the studied population was 9 years old (1-16 years).

Due to unavailability of immune phenotype data of 5 patients, they were excluded from the results. The frequency of ALL groups and subgroups according to immune phenotypes in our study is presented in Table 1.

Table 1. Frequency of ALL groups and subgroups according to immune phenotypes

Subtype	Frequency	Percent
Immature T-cell	9	9.4%
Intermediate T-cell	7	7.3%
Mature T-cell	47	49.5%
Pro.B-cell	12	12.6%
Pre.B-cell	13	13.6%
Mature B-cell	7	7.3%
Total	95	100%

There was no difference in its sex distribution, but a significant age distribution difference was detected.

Table 2. Frequency of clinical symptoms at presentation

Symptom	Frequency	Percent
Lethargy & Malaise	81	81%
Anorexia	72	72%
Musculoskeletal	48	48%
Fever	59	59%
Cough	31	31%
Epistaxis	24	24%
Gum Bleeding	12	12%

The most frequent presenting symptoms were systemic symptoms including lethargy and malaise (81%), anorexia (72%), pallor (69%) and fever (59%).
Musculoskeletal system was the most commonly involved, and the most common manifestation was bone pain, present in 48% of patients (Table 2). Gastrointestinal manifestations were the second most common, which about 30% of patients had nausea and vomiting and abdominal pain at the time of diagnosis.
Coughing was seen in 31%, lung infections and upper respiratory tract infections in 25% of them, epistaxis in 24% and petechia in 18% of patients (Table 3).

Table 3. Frequency of significant clinical signs at presentation

Sign & Lab. data	Frequency	Percent
Hepatomegaly	34	34%
Splenomegaly	36	36%
Lymphadenopathy	25	25%
Petechia & Echymosis	18	18%
CNS involvement	12	12%
Weight loss	56	56%

Ocular and genito-urinary manifestations were the least common and no cases of photophobia, proptosis, ataxia, cranial nerve palsy and hoarseness were reported in our patients. The most frequent presenting complaint of the nervous system was headache (12%).
Of the symptoms related to low platelet counts, epistaxis was the most frequent one (26%), petechia and echymosis, each one in 18% of cases and gum bleeding in 12% (Table 2).
Complete blood cell count was abnormal in all of the patients, and pancytopenia was detected in 27% of the patients. Of all the patients, 25% had abnormal WBC count at presentation, 37% had leucopenia and 38% had leukocytosis. WBC count was above 50,000/mm3 in 22% of cases.
Anemia was detected in 85% of the patients. There was moderate degree of anemia in 56% (Hb: 7-11 g/dl), and 29% had severe anemia (Hb<7 g/dl).
Thirty four percent of 1-9 years old patients had hemoglobin below 7 g/dl, but it was seen only in 22% of 10-16 years old patients.
Platelet count was more than 100,000mm3 in 27% of patients, 54% had count between 20,000-100,000/mm3 and 19% had count below 20,000/mm3 (Table 4).

Table 4. Frequency of laboratory indices in leukemic patients

Laboratory index	Frequency	Percent
WBC > 22000/mm^3	22	22%
WBC < 22000/mm^3	78	78%
Hemoglobin 7-11 g/dl	56	56%
Hemoglobin <7 g/dl	29	29%
Platelets >100,000/mm^3	27	27%
Plt 20,000-100,000/mm^3	54	54%
Platelets <20,000/mm^3	19	19%

The distribution of poor prognostic factors according to immune phenotypes is noted in table 5.

Table 5. Distribution of poor prognostic factors according to immune phenotypes

Prognostic factors	B-Cell	T-Cell	p-value
Age<1y or >10y	40%(13)	60%(37)	0.05
Male sex	31%(10)	69%(44)	0.02
Hepatomegaly	21%(7)	34%(22)	0.09
Splenomegaly	27%(9)	36%(23)	0.08
Lymphadenopathy	19%(6)	25%(16)	0.07
WBC>50.000/mm^3	6%(2)	15%(10)	0.03
Plt<100.000/mm^3	51%(16)	63%(40)	0.09

No significant sex or age distribution differences were detected. Anemic changes were more frequent in 1-9 years olds than 10-16 years olds (94% vs 72%), (p-value<0.05).
The distribution of clinical symptoms were almost the same in 1-9 and 10-16 year olds, but fever, perspiration, weight loss and headache were more common in children 1-9 years old (71%, 24%, 42%, 20%) than children between 10-16 year old (44%, 0%, 14%, 5.5% respectively).
Distribution of symptoms in both sexes were also similar, but bone pain, limp and UTI were more common in girls than boys (63%, 24%, 8% in girls and 39%, 6% and 0% in boys respectively).
Gum bleeding and anorexia were more common in boys than girls (18%, 79% vs 2%, 60% respectively).

Discussion

In this prospective study we analyzed leukemic children's immune phenotypes, 66.2% of our patients had T-Cell and33.8% had B-cell leukemia. The major leukemic groups of T and B-cell in other studies were reported as 18.4% T-cell in Thailand, 28% in Bulgaria, 22% in Malaysia and 9.4% in Mexico compared to the 66.2% in our study. This difference in frequencies may be due to impact of environmental carcinogenic factors in our area.
Acute leukemia is the most common bone marrow malignancy that can present with pancytopenia due to bone marrow infiltration. In one study of 936 children with untreated, newly diagnosed ALL, 51% presented with hemoglobin concentration less than 7.5 g/dL, 73% with platelet count less than 150,000/microL, and 30% with a total peripheral WBC count less than 5000/microL(9), but in the present study pancytopenia was detected in 27% of cases.
There was a male preponderance in our study with a male: female ratio of 1.6:1. This higher ratio was reported in other studies as well (2, 4).
The frequency of most common presenting clinical findings, like musculoskeletal symptoms, was similar to previous studies (10, 12).
The occurrence of bone pain was more in our study in comparison to previous studies (14).
The frequency of constitutional symptoms conforms to other studies, as approximately two-thirds of children with leukemia are reported to have fever at the time of presentation in other studies (8).

Bone pain, particularly affecting the long bones, which caused by periosteum involvement, is reported to be a dominant presenting symptom in 21 to 38 percent of cases of acute leukemia in other studies as well (10-13).
Fever and chills occurred more frequently in 1-9 years olds compared to 10-16 years olds. It was found by Rogalsky et al. That persistent fever also might be the only complaint in children with leukemia (14). In the other hand, in a French study, having more than three infections per year before age years was associated with a significantly reduced risk of childhood acute leukemia, as was surgical operation for ear-nose- throat infections before age 2 years (15). In another French study, having more than three infections during infancy was linked to a reduced risk of ALL (16).
Most of the children diagnosed with ALL in the present study were 5-10 year old age, but it was 1-5 years in the studies by Svendsen, Swensen and McNally (4-6).
In our study, T-cell immune phenotypes comprised the most frequent form of ALL in children. Although the presence of poor prognostic factors like male sex and high WBC count can make its outcome even worse; prompt institution of chemotherapy can alter the outcome of these patients. On the other hand investigations have to be made to determine the influencing factors that increase the prevalence of T-cell ALL in our community.
We emphasized again the value of screening laboratory data obtained when diagnosis of leukemia is highly suspected, based on patient's history and presenting clinical manifestations.

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