

ACUTE LEUKEMIA IN KING FAHAD GENERAL HOSPITAL, JEDDAH

Abdul Rahim Gari-Bai, Fachartz; Badr Ali Arab, MBBS;
Mir Asif Ali Khan, MD

The incidence of leukemia is high in Saudi Arabia.¹⁻³ The symptomatology of the disease is nonspecific, demanding a high degree of suspicion among general practitioners and physicians who are primary healthcare providers for the population at large. Delay in diagnosis definitely has an adverse effect on the outcome of this potentially curable malignancy.

The management of leukemia requires a specialized setup, with adequate diagnostic and treatment facilities. From our experience in managing acute leukemia, we have noticed that most patients present late, with associated severe infections, simply because the diagnosis had not been made earlier, even though there had been abnormal hematological parameters on routine blood examination. Secondly, some patients insist on referral to a tertiary center, which too often delays initiation of specific management. We therefore decided to undertake a prospective study of all patients with leukemia attending our hospital. This study was designed to address the modes of presentation of the disease, implications on referral procedures, and more importantly, prospects of management of the disease in our hospital.

Patients and Methods

King Fahd Hospital in Jeddah is the largest Ministry of Health hospital in the Western province of Saudi Arabia, with a 1200-bed capacity. It is the main referral hospital in both the Western and Southern regions. All patients in whom the diagnosis of acute leukemia has been confirmed were included in this prospective study, which spanned a two-year period from March 1992 to March 1994. Common clinical problems, i.e., those symptoms which prompted the patients to seek medical help, were identified. The duration of these symptoms and the number of hospitals visited by the patients before the diagnosis was made was also recorded. Diagnoses were made or confirmed in our hospital by standard hematological

practice. Classification of leukemia was confirmed using morphological and cytochemical studies. Flow cytometry and cytogenetic studies were not performed, since we do not have the required facilities. However, immunophenotyping was done in three patients who posed difficult diagnostic problems, using flow cytometry elsewhere.

The induction regimen for acute myeloid leukemia (AML) consisted of DAT, as follows: daunorubicin 60 mg/m²/d, iv bolus on days 1-3; cytarabine (ARA-C) 100 mg/m²/d, days 1-7 24-hr infusion; and 6-thioguanine 200 mg/m²/d in two divided doses orally. The induction regimens for acute lymphoblastic leukemia (ALL) were the German protocols for children⁴ and for adults.⁵

Results

Thirty-four patients with acute leukemia were seen in the two-year study period. On average, a patient had been to three medical centers (range 1-6), either private or government hospitals, before being referred to us. The duration of symptoms ranged from 14 to 120 days. The

TABLE 1. Characteristics, symptomatology and hematology profile of patients.

Number of patients	34
Saudi/non-Saudi	16/18
Adults/children	28/6
AML/ALL/AL	21/11/2
Treatable/untreatable	21/13
Mean age (range)	36 (2-83)
Symptoms at presentation	
Anemia	27
Febrile illness	17
Bleeding tendency	14
Lymphadenopathy	12
Hepatomegaly	10
Splénomegaly	10
Sepsis	3
Mediastinal mass	2
Gum hypertrophy	2
Hematology profile	
Anemia	31
Thrombocytopenia	30
Anemia and thrombocytopenia	28
Anemia or thrombocytopenia	5
Neither anemia nor thrombocytopenia	1
WBC <2.5x10 ⁹ /L	4
WBC 2.5-15 10 ⁹ /L	3
WBC >15x10 ⁹ /L	27

From the Department of Medicine, King Fahad General Hospital, Jeddah, Saudi Arabia.

Address reprint requests and correspondence to Dr. Gari-Bai: Department of Medicine, King Fahd General Hospital, P.O. Box 10744, Jeddah 21443, Saudi Arabia.

Accepted for publication 7 July 1998. Received 5 August 1997.

most common clinical problem upon presentation was febrile illness (14/34). Three patients had symptoms of anemia and eight had hemorrhagic diathesis as their main clinical problem. Table 1 shows the patient characteristics, the symptoms and hematological profile at the time of presentation. Four non-Saudi patients opted to seek treatment in their native countries. Eleven patients were not considered for intensive treatment. Of these, five had severe infection, four were elderly, one patient was in coma, probably due to cerebral leukostasis, and another had AML-M3 with disseminated intravascular coagulation (DIC).

Nineteen patients were considered for induction chemotherapy. Of these, five demanded referrals to a tertiary center, which were promptly granted, but two of these patients died pending their acceptance.

Induction chemotherapy was started in fourteen patients. One of the patients left against medical advice and induction therapy failed in another with AML-M3 subtype. The remaining 12 patients (6 ALL and 6 AML) completed a planned induction phase of treatment.

Discussion

The spectrum of clinical presentation of our patients with acute leukemia is similar to well-known data in the literature.^{6,7} Although most of our patients had anemia, they probably adapted to it and presented with febrile illness or other complications. As is shown in the study, most of the patients were seen at various hospitals before a definitive diagnosis was made, even though the patients had abnormal hematological parameters. The significance of blood smear examination in demonstrating blasts, which was diagnostic in all our patients, cannot be overemphasized, as has been shown in detecting relapses in AML.⁸ It was because of a delay in diagnosis that 18% (6/34) of patients were not considered for treatment. The patients had serious associated infections, which are a common cause of death among leukemic patients.⁹

Undoubtedly, tertiary centers in Saudi Arabia alone cannot take up the management of all acute leukemia cases because of the high prevalence of the disease and limited bed capacity. Referral from regional hospitals is associated with delays in initiating specific management, which has an adverse effect on a rapidly growing malignancy, such as acute leukemia. We lost two patients who refused to have treatment under our care and who were waiting for a reply from a tertiary center.

To address the issue of prospects of treatment of acute leukemia in our hospital, where certain facilities such as isolation rooms and proper blood bank support are lacking, we defined successful treatment as completion of one induction course for AML, and four weeks of the protocol for ALL. This initial period of treatment is obviously the most demanding phase of treatment. Twelve of the thirteen patients completed this initial induction successfully. This correlates well with general clinical experience.

From this study, which probably reflects the prevailing situation in the management of leukemia in most of the regional hospitals in Saudi Arabia, we conclude that there is a need to increase awareness of the early stage of leukemia among local practitioners. We also recommend that facilities in regional hospitals should be improved and updated, so that patients can be induced into remissions, and when indicated, can later be referred for bone marrow transplant at a tertiary center, such as King Faisal Specialist Hospital and Research Centre in Riyadh. This would ease the burden on the tertiary centers and avoid delays in initiating specific management of this potentially curable malignancy without compromising the overall results.

References

1. Ministry of Health, National Cancer Registry. Cancer incidence in Saudi Arabia 1994. Riyadh May, 1996.
2. Ezzat A, Raja M, Te O, Michels D, Bazarbashi S. Frequency and distribution of 22,836 adult cancer cases referred to King Faisal Specialist Hospital and Research Centre. *Ann Saudi Med* 1996;16:152-8.
3. Al-Bar A, Ibrahim E, Al-Tamimi T, et al. Leukemia in the Eastern Region of Saudi Arabia: a population-based study, 1987-1988. *Ann Saudi Med* 1996;16:521-6.
4. Reiter A, Schrappe M, Ludwig WD, et al. Chemotherapy in 998 unselected childhood acute lymphoblastic leukemia patients. Results and conclusions of the multicenter trial ALL-BFM 86. *Blood* 1994 84:3122-33.
5. Zhang MJ, Hoelzer D, Horowitz MM, et al. Long-term follow-up of adults with acute lymphoblastic leukemia in first remission treated with chemotherapy or bone marrow transplantation. *Ann Intern Med* 1995;123:428-31.
6. Lukens JN. Acute lymphocytic leukemia. In: Lee GR, Bithell TC, Foerster J, et al., editors. *Wintrobe's Clinical Hematology*. 9th edition. Philadelphia: Lea & Febiger, 1993.
7. Greer JP, Kinney MC. Acute non-lymphocytic leukemia. In: Lee GR, Bithell TC, Foerster J, et al., editors. *Wintrobe's Clinical Hematology*. 9th edition. Philadelphia: Lea & Febiger, 1993.
8. Estey E, Pierce S. Routine bone marrow exam during first remission of acute myeloid leukemia. *Blood* 1996;87:3899-902.
9. Schimpff SC. Infection in the leukemia patient: diagnosis, therapy and prevention. In: Henderson ES, Lister TA, editors. *W. Dameshek and F. Gunz's Leukemia*. 5th edition. Philadelphia: W.B. Saunders, 1990.