



A retrospective evaluation of infant patients with acute lymphoblastic leukemia treated at a single institution

Sir,

We report a retrospective evaluation of 10 infants with acute lymphoblastic leukemia (ALL), diagnosed and treated at a single institution, who achieved a 10-year actuarial event free survival of 50%.

Infant acute leukemia (AL) is a distinct leukemic subset with an extremely poor prognosis, having a 25% event free survival (EFS) at 4 years.¹⁻⁶

Rearrangements of the ALL1/MLL gene at 11q23 cytogenetic band^{7,8} have been demonstrated in 70% of infants. Recently, this molecular alteration has been associated with an adverse clinical outcome.^{7,9}

Biological and clinical features, treatments, and outcome of 10 ALL infants, observed and treated at the Children's Hospital "Bambino Gesù" of Vatican City State between August 1986 and September 1996, are summarized in Table 1.

The genomic ALL1/MLL configuration was investigated in 4 patients for whom stored material was available. Three of them showed an ALL1 rearrangement, while the fourth had a t(4;11)(q21;q23) translocation.

Patients were treated according to the then current treatment protocols of the Italiana Association of Pediatric Oncology and Hematology (AIEOP).¹⁰

Two of 4 patients treated with LA84 INF, which includes high dose methotrexate (6 g/m²), are in first complete remission (CR) at 84 and 108 months from diagnosis; the remaining two cases are in second CR after extra-hematologic relapses (testis, CNS) which occurred at 110 and 70 months from diagnosis.

All 5 patients treated with the AIEOP 9102, 9103, 9502 protocols (BFM like) achieved CR. Three out of 5 patients are still in first CR at 17, 17 and 26 months; the fourth patient had a CNS relapse after

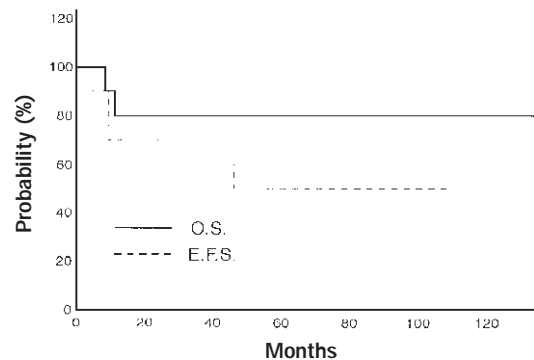


Figure 1.

8 months of CR, and is now in second CR 24 months after an allogeneic bone marrow transplantation; the fifth patient had a hematologic relapse and died of his disease 11 months after diagnosis. Finally, the case with t(4;11) failed to respond to an induction treatment which included adriamycin, cytarabine and prednisone. As shown in Figure 1, the 9-year EFS and OS were 50% and 80%, respectively.

Casual selection of infants with less aggressive disease is probably the most plausible explanation of our observed favorable results. In fact, we detected a low incidence of pre-B and hybrid immunophenotypes. Six patients had a normal karyotype, while a 11q23 cytogenetic alteration and/or ALL1/MLL rearrangements were demonstrated in only four cases. This hypothesis is further supported by the observation that our ALL1/11q23 rearranged cases did less well than the other patients. In contrast, the fact that patient #3, who presented at diagnosis with 660x10⁹/L white blood cells but had an ALL1 germline configuration, is actually cured of his disease, indirectly confirms that ALL-1/MLL rearrangement is the most important adverse prognostic factor in infant ALL.

Table 1. Clinical and biological features as well as type of treatment and therapeutic response in 10 infants with ALL.

Pat.	Age (months)	Sex	WBC (10 ⁹ /L)	Immuno-phenotype	Cytogenetic analysis	DNA analysis	Therapy	1 st CR	Relapse	2 nd CR	Follow-up (months)
1	8	F	28	T-ALL	46 XY	ND	LA 84, INF	yes	yes (CNS)	yes	135 +
2	4	M	85	ND	46XY	ND	LA 84, INF	yes	yes (testis)	yes	112+
3	10	M	660	T-ALL	46XY	ND	LA 84, INF	yes	-	-	108+
4	7	M	15	Common	+8	ND	LA 84, INF	yes	-	-	84+
5	2 days	F	68	Common	t(4;11)	ND	ARA-c, ADM, PDN	no	-	-	8
6	4	F	21	Common	46XX	ND	AIEOP 9102	yes	yes (CNS)	yes	36+
7	3	F	17	Hybrid	t(4;11)	ALL1 rearr.	AIEOP 9103	yes	yes (BM)	-	11
8	1 day	F	90	Common	del (10 p)	ALL1 rearr.	AIEOP 9502	yes	-	-	26+
9	10	M	150	Pre-B	46 XY	ALL1rearr.	AIEOP 9502	yes	-	-	17+
10	10	M	23	Pre-B	46 XY	ALL1 g l	AIEOP 9502	yes	-	-	17+

As to toxicity, only one patient, who received a total anthracycline dose of 240 mg/m², developed a severe dilated myocardiopathy.

In conclusion our results confirm that some infants with ALL can be cured by conventional chemotherapy. Thus, we believe that careful stratification for prognosis is needed to treat these patients with adequate risk-adapted therapeutic strategies.

Matteo Luciani,* Giuseppe Cimino,# Adriano Angioni,°
Lidia Angiolina Russo,* Teresa Sprovieri,# Giulio De Rossi*

*Divisione di Ematologia, °Laboratorio di Citogenetica e di Tipizzazione cellulare, Ospedale Pediatrico "Bambino Gesù", Città del Vaticano; #Dipartimento di Biotecnologie Cellulari ed Ematologia, Divisione di Ematologia, Università "La Sapienza" di Roma, Italy

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Correspondence

Matteo Luciani, MD, Divisione di Ematologia, Ospedale Pediatrico "Bambino Gesù", Città del Vaticano, piazza Sant'Onofrio 4, 00165 Rome, Italy.

Phone: international +39-06-68592129 – Fax: international +39-06-68592392.

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Three cases of Kikuchi-Fujimoto disease

Sir,

Kikuchi-Fujimoto disease (KFD) is a benign form of necrotizing lymphadenitis of unknown cause, usually affecting young women^{1,2} and characterized by lymphadenopathy often associated with fever and leukopenia. Cervical nodes are usually involved, while generalized lymphadenopathy, hepato-splenomegaly and extranodal involvement are uncommon. Laboratory tests show only a raised ESR.³ The diagnosis is based on distinctive lymph node histologic features:^{4,5} focal necrosis in cortical and paracortical areas; karyorrhectic nuclear debris mixed with a polymorphous cell population including immunoblasts and histiocytoid cells. Polymorphonuclear leukocytes and B cells are characteristically absent. In early phases T-suppressor lymphocytes are predominant. Lesions in different stages of development may coexist; focally, the histologic pattern might be mistaken for lymphoma or other diseases.^{4,6} The disease resolves spontaneously within 2-3 months; relapse is not common. For unknown reasons, this disease is more frequent in Japan, where it was first described.

In a five-year period, we have observed three patients with KFD.

Case #1. A 36-year-old woman presented in January 1993 with fever and cervical lymphadenopathy, unresponsive to antibiotics and low dose prednisone. The ESR was 70 mm, all other laboratory tests were negative. Bone marrow examination was normal. Lymph node histology was typical of KFD (Figure 1). The patient recovered in three weeks with no other treatment.

Case #2. A diabetic 53-year-old man was observed in December 1996 with a four-month history of fatigue, fever, and moderate cervical and axillary lymph node enlargement. His ESR was 88 mm, all other tests were normal. Bone marrow examination showed a normocellular marrow. Lymph node biopsy demonstrated KFD. He received antibiotic therapy after biopsy, and the disease resolved over four weeks.

Case #3. A 31-year-old woman was admitted in March 1997 because of fatigue, fever, night sweats, cough and cervical lymph node enlargement. Laboratory tests were all normal, including ESR. Lymph node biopsy showed necrotizing lymphadenitis of the KFD type. She recovered in six weeks with no treatment (Table 1).

The etiopathogenesis of KFD is still obscure. Some clinical and histologic features suggest a possible infectious etiology, particularly viral.^{3,7} It has also been supposed that KFD may have different etiologies, all provoking an abnormal cell-mediated immune response. This hypothesis is supported by the finding of cytoplasmic tubuloreticular structures; similar structures are observed in other diseases, particularly systemic lupus erythematosus (SLE).³ KFD and SLE may be associated and KFD may precede the onset of