CLINICAL RELEVANCE OF ACUTE MIXED-LINEAGE LEUKEMIA

To the Editor:

A recent report by Pui et al.1 focused on the biologic and clinical relevance of acute mixed-lineage leukemia; namely, acute lymphoblastic leukemia expressing myeloid-associated antigens (My+ AML) and acute myeloid antigens expressing lymphoid antigens (Ly+ AML) were analyzed in a pediatric series. In our opinion, a major point in the field of hybrid acute leukemia remaining undetermined is which "ectopic" antigens and what level of ectopic expression significantly affect the clinical outcome. The findings regarding My+ AML are quite controversial.2 On the contrary, T-cell antigens expression in AML seems to characterize a distinct clinical entity in both children and adults.3 From an analysis of 107 AML samples, we demonstrated that CD7 and CD2 simultaneous expression on myeloid blasts is a nonrandom event, recurring in a substantial proportion of patients.4 In our series, CD7+/CD2+ AML patients presented with a higher incidence of adenopathy and meningeal leukemia than did patients with "pure" AML, and were characterized by a poor response to chemotherapy in terms of complete remission (CR) achievement and duration.4 On a clinical ground, our findings were closely in keeping with those reported by Cross et al.5 Also, in the report by Pui et al.1 CD7+/CD2+ AML was the most frequent hybrid pattern in 16 Ly+ AML cases. As in our series, most patients were classifiable as M1 according to the French-American-British classification, and in a consistent number of them a coexistence of large myeloid blasts and small blasts with hand-mirror morphology was found. Notwithstanding, Pui et al.1 stated that "event free survival did not differ between Ly+ AML patients and other AML patients." What would have been the results if only CD7+/CD2+ patients had been analyzed? Furthermore, it is noteworthy that in Pui et al.'s series four Ly+ AML cases who failed AML induction therapy subsequently entered CR with prednisone, vincristine, and L-asparaginase (a quite unusual chemotherapy program for classical AML). The outcome for the CD7+/CD2+ AML cases probably would have been different if this approach had not been used. In our opinion, the analytical subtyping of AML on the basis of T-cell antigen ectopic expression needs further investigating. For example, different combinations of T-cell antigens (eg, CD7, CD2, CD5, CD6) on AML blasts may represent quite distinct biological phenomena, possibly corresponding to different hematopoietic steps. In this respect, we consider CD7+/CD2+ AML to be a distinct clinico-hematologic entity sharing, in an extremely balanced fashion, both myeloid and lymphoid features. We feel that these patients should be allocated to unique clinical trials using combined AML/ALL regimens during the induction as well as the consolidation chemotherapy, with particular emphasis on the prevention of meningeal leukemia, and, whenever possible, included in a bone marrow transplantation program. Finally, further efforts should be addressed toward the classification of promiscuous phenotypes on the basis of their clinical relevance.

FELICETTO FERRARA
Division of Hematology
LUIGI DEL VECCHIO
Blood Transfusion Center
Cardarelli General Hospital
Naples, Italy

REFERENCES


RESPONSE

Ferrara and Del Vecchio's findings are consistent with our observation that cases of acute myeloid leukemia expressing lymphoid-associated antigens (Ly+ AML) are characterized by French-American-British (FAB) M1 or M2 morphology, dual populations of large blasts with myeloperoxidase positivity and small blasts with hand-mirror morphology, and poorer response to myeloid-directed induction therapy.1 When analyses are limited to cases expressing CD7 and CD2, which comprised three-fourths of our Ly+ AML cases, these findings still hold true. However, our Ly+ AML cases, unlike those described by Ferrara and Del Vecchio, did not have a higher frequency of initial central nervous system (CNS) leukemia compared with other AML cases, and none developed CNS relapse.

In our series, event-free survival did not differ between the Ly+ AML and other AML cases. Similarly, no difference was seen in analyses restricted to the CD7+/CD2+ subset (data not shown). Because of the small number of Ly+ AML cases expressing B-lineage-associated antigens, we cannot determine the clinical significance of these cases. However, there was no apparent difference in the presenting features and clinical outcome between the CD7+/CD2+ cases and those expressing B-lineage markers. In this regard, prednisone-vincristine-asparaginase therapy after failure on myeloid-directed therapy induced remission not only in the CD7+/CD2+ AML cases but also in one of the Ly+ cases expressing B-lineage-associated antigens. Although it is conceivable that the CD7+/CD2+ AML cases do represent a distinct
entity, we believe that further study is needed before these cases can be separated from other Ly+ cases.

We are pleased that Ferrara and Del Vecchio concur regarding the need to include lymphoid-directed therapy in Ly+ AML. Whether bone marrow transplantation during first remission is indicated in these cases, in our opinion, will not be clear until intensive lymphoid- and myeloid-directed therapy has been tested. Such therapy, if effective, may alter the prognostic impact of lymphoid antigen expression in AML—as has been found for myeloid-associated antigen expression in childhood acute lymphoblastic leukemia.2,4

We concur with Ferrara and Del Vecchio that additional studies are needed to determine the clinical significance of “ectopic” antigen expression. We would reemphasize, however, that virtually all known “differentiation” surface antigens lack lineage specificity.

CHING-HON PUI
St Jude Children’s Research Hospital
The University of Tennessee, Memphis
College of Medicine
Memphis, TN

REFERENCES


Clinical relevance of acute mixed-lineage leukemia [letter; comment]
F Ferrara and L Del Vecchio