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Comprehensive Review of Adult Acute Myelogenous Leukemia: Cytomorphological, Enzyme Cytochemical, Flow Cytometric Immunophenotypic, and Cytogenetic Findings

Cherie H. Dunphy

Division of Hematopathology, Department of Pathology, St. Louis University Health Sciences Center, St. Louis, Missouri

This study reports findings from a retrospective, comprehensive review of 80 cases of adult AML in regard to cytomorphology, enzyme cytochemistry (EC), flow cytometric immunophenotyping (FCI), and chromosomal analysis. From this review, we conclude that diagnostically challenging cases can only be subtyped by combining the cytomorphology with EC, FCI, and subsequent cytogenetic results. This is particularly true in recognizing the hypogranular variant of AML,M3 (AML, M3m) and distinguishing it from other subtypes. Nonlineage expression of markers (CD1, CD2, CD4, CD5, CD7, and CD56) was nonspecific as to AML subtype. Of interest, CD2 coexpression in acute myelomonocytic leukemia with eosinophilia (M4-Eo) was exclusively associated with inversion of chromosome 16 (inv 16) and was not observed in the other M4-Eo's without inv16. We also recognized a previously undescribed M3m with CD56 coexpression, heightening awareness of this entity which needs to be distinguished from the unique subtype of CD56+ AML with otherwise similar immunophenotypic and morphologic characteristics. In addition, nonlineage expression of CD19 alone was exclusively associated with the cytogenetic finding of *t* (8;21) (q22; q22) and thus may represent a favorable prognostic indicator by FCI. J. Clin. Lab. Anal. 13: 19–26, 1999.

Key Words: AML; flow cytometry; cytogenetics; cytochemistry

INTRODUCTION

Initial diagnosis and subtyping of acute myelogenous leukemia (AML) into AML,M0 through M7 according to the French-American-British (FAB) classification is based primarily on morphologic characteristics augmented by enzyme cytochemical (EC) reactivity patterns and flow cytometric immunophenotyping (FCI) and ultrastructural studies (1). Cytogenetic data are particularly useful in defining acute promyelocytic leukemia (APL) and in identifying prognostic indicators, with translocation (t) (8;21) and deletion (del) or inversion (inv) of chromosome 16 representing favorable indicators.

To our knowledge, there is no comprehensive review in the literature of a large number of adult AMLs with complete cytomorphological findings, EC results, FCI data, and chromosomal findings. Although Khalidi et al. recently published data on 106 adult AMLs, only 74% were FAB subtyped and cytogenetic data were available on only 68 cases (2). In addition, enzyme cytochemical stains did not routinely include myeloperoxidase, Sudan Black B, alpha-naphthyl acetate and butyrate esterases, and chloroacetate esterase. We undertook such a review of 80 adult AMLs in order to evaluate the findings and how the data could best be used in subtyping AMLs, particularly in diagnostically challenging cases. The focus of our review was on the morphologic and immunophenotypic characteristics, not on treatment variables. The emphasis was on how the evaluated parameters could be used in diagnosis. A uniform, reproducible classification of AML subtypes allows for comparisons to be made among various therapeutic regimens from different groups and from program to program within the same institution or cooperative group. Uniform classification allows for the potential identification of different clinical features and laboratory aspects that may be unique to certain subtypes, alone or in association.

MATERIALS AND METHODS

AML Subtypes

Eighty adult bone marrow aspirates/biopsies initially diagnosed as AML and subtyped (M0 through M7) according

Correspondence to: Dr. Cherie Dunphy, Department of Pathology, St. Louis University School of Medicine, 1402 S. Grand, St. Louis, MO 63104.

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to the French-American-British (FAB) classification (3–6) by a comprehensive combination of cytomorphological examination, EC, and FCI in the Division of Hematopathology were retrospectively reviewed by the author. These represented consecutive cases that had complete data available. Of those cases in which the age was available, the age ranged from 27 to 86 years (mean, 63 years). The AML FAB subtypes M0 through M5 and M7 were established by identifying greater than 30% blasts in the bone marrow. For M2 with eosinophilia (M2-Eo), basophilic or eosinophilic differentiation of granulocytic precursors was identified (7). For M3, hypergranular promyelocytes were included in the blast percentage as were promonocytes in M5 and immature megakaryocytes in M7. For M4 with eosinophilia (M4-Eo), greater than 3% eosinophils was identified (8). For M6, greater than 50% erythroid cells were identified and greater than 30% of the nonerythroid cells were myeloblasts. M0 was further established by the presence of < 3% Sudan Black B (SBB) / myeloperoxidase (MPO)-positive blasts in association with myeloid antigen (CD13 or CD33) expression of > 20% of the blasts by FCI; M1, by the presence of ≥ 3% SBB/MPO-positive blasts and < 10% of cells at the promyelocyte stage or beyond; M2, by ≥ 3% SBB/MPO-positive blasts, > 10% of cells at the promyelocyte stage or beyond, and < 20% alpha-naphthyl butyrate esterase (ANBE)- or alpha-naphthyl acetate esterase (ANAE)-positive cells; M4, by > 20% SBB/MPO-positive cells and > 20% ANBE- or ANAE-positive cells; M5, by < 20% SBB/MPO-positive cells and >80% ANBE- or ANAE-positive cells; and M7, by > 30% megakaryocytic elements identified with CD41a and CD42b by FCI. The platelet antigen expression was not considered spurious if the flow cytogram demonstrated intense dual expression of both CD41a and CD42b.

Morphology/Enzyme Cytochemistry

Bone marrow smears had been routinely Wright-Giemsa-stained and stained for the presence of MPO, SBB, ANAE, ANBE, and chloroacetate esterase (CAE) (Sigma Chemical Company, St. Louis, MO) according to kit procedures. MPO-positive staining was interpreted as intense, focal to diffuse, coarsely granular, black staining within the cytoplasm which often, at least partially, covered the nucleus. SBB-positive staining was interpreted as intense, diffuse, coarsely granular, black staining of the cytoplasm which impinged upon the nucleus. ANAE-positive staining was interpreted as moderate to intense, partial to complete, homogenous, reddish-brown cytoplasmic staining. ANBE-positive staining was interpreted as moderate to intense, partial to complete, homogenous, blackish-brown cytoplasmic staining. CAE-positive staining was interpreted as weak to intense, partial to complete, finely to coarsely granular, reddish-pink cytoplasmic staining. Hematoxylin-eosin (HE)-stained sections of the bone marrow core biopsy were reviewed.

Flow Cytometric Immunophenotyping

All of the bone marrow aspirates had been comprehensively analyzed on either an Ortho Cytoronabsolute (Ortho Diagnostic Systems, Raritan, NJ) or FACSCAN (Becton-Dickinson, Mountainview, CA) flow cytometer for antigens using standard techniques and the following commercially available monoclonal antibodies: CD1, CD4, CD5, CD8, CD10, CD15, and HLA-DR (Ortho); CD2, CD13, CD14, CD24, CD33, CD34, CD56, CD117, and TdT (Coulter Clone, Coulter Immunology, Hialeah, FL); CD3, CD7 and CD20 (Becton Dickinson, San Jose, CA); CD1, kappa and lambda (Dako, Carpinteria, CA); and CD45 (Caltag, Burlingame, CA). Bone marrow aspirates had been selectively analyzed with CD41a and CD42b (Dako). Dual staining was routinely performed as follows: CD3/4, 8/56, 19/5, 20/DR, 45/10, 2/24, 14/13, 33/34, 15/117, 41a/42b. Forward and side light scatter properties were used to define the lymphocyte and monocyte (large mononuclear) regions. Expression of a particular marker by essentially all blasts was indicated as +; no expression of a particular marker by the blasts, as – and expression of a particular marker by some (> 20%), but not all, blasts as +/–. "Nonlineage" expression meant the sum of the percentage of cells positive (PCP) for the particular marker plus the PCP for the most reliable lineage marker (i.e., CD13, CD33 or CD14) was ≥ 120%.

Chromosomal Analysis

Results of chromosomal analysis performed on the bone marrow aspirates were available in all cases and all samples were reported as adequate. The chromosomal analyses were performed at three different cytogenetic laboratories in St. Louis, Missouri. Banded chromosomes were analyzed using standard methods and identified using GTG banding. At least 20 metaphases were reported as being examined in each case.

RESULTS

AML Subtypes

The distribution of the AML subtypes is indicated in Table 1.

TABLE 1. Acute Myelogenous Leukemia FAB Subtype Distribution[a]

FAB subtype	Percentage of total AML cases (80)
M0	16.25
M1	10.00
M2 (1 M2-Eo)	45.00
M3 (3 M3m)	7.50
M4 (5 M4-Eo)	11.25
M5 (1 M5a; 4 M5b)	6.25
M6	2.50
M7	1.25

FAB, French-American British; M2-Eo, M2 with eosinophilia; M3m, M3, hypogranular variant; M4-Eo, M4 with eosinophilia; M5a, M5 without maturation; M5b, M5 with maturation.

[a]Numbers in parentheses represent the number of cases in the subtype which represented a particular subtype.

Morphology/Enzyme Cytochemistry

The morphologic findings and enzyme cytochemical staining results generally allowed for the AMLs to be FAB subtyped. However, one of the M2s morphologically resembled an M3m. In this case, CAE revealed weak granular staining of occasional blasts and negativity of the other blasts; MPO and SBB, negative to moderate staining of blasts; and ANBE, staining of a few cells (< 20%) in the marrow. Flow cytometric immunophenotyping revealed a blastic immunophenotype of CD33+, CD13–, CD15–, CD14–, CD34–, CD117+, and HLA-DR +/–. There was no *t*(15;17); instead, monosomy 18 was detected.

One of the M3ms was extremely difficult to recognize morphologically. Some cells had features of hypogranular promyelocytes; however, many did not. Auer rods and faggot cells were not identified in the Wright's-stained smears (Fig. 1A). Morphologically, it was considered likely to be an M2; however, MPO, SBB, and CAE were intensely staining the majority of the leukemic cells and occasional faggot cells were identified with the CAE stain (Figs. 1B and C). FCI revealed the following immunophenotype: CD33+/–, CD13+/–, CD15+/–, CD14–, CD34–, CD117+/– and HLA-DR– (Fig. 2). Chromosomal analysis revealed *t*(15;17) (q22; q11.2). The other five APLs also revealed intense staining of the leukemic cells with MPO, SBB, and CAE.

Flow Cytometric Immunophenotyping

Antigen expression, including CD13, CD14, CD15, CD33, CD34, CD117 and HLA-DR as distributed among the FAB subtypes of the AMLs is outlined in Table 2A. In seven cases, the immature cells (i.e., blasts or atypical promyelocytes) lacked complete expression of both CD34 and HLA-DR. Six of these were the APLs previously discussed. No case of APL had any expression of CD34 or HLA-DR. The seventh case was an M6; the blasts in this case expressed only CD45 and CD117 and revealed intense staining with SBB and CAE. In three cases blasts had no expression of CD34 and variable loss of expression of HLA-DR (HLA-DR+/–). All three cases FAB subtyped as M2 without *t*(15;17). All other cases of AML with CD34– were HLA-DR+.

In regard to the 5 M5s, all were HLA-DR+ with variable expression (+/–) of CD4 and CD56. Of interest, CD14 was present on all the immature cells (monoblasts and promonocytes) in one M5b, was variably expressed in three M5bs, and was not expressed in the M5a. However, in the M5a, 80% and 76% of the blasts were intensely staining with ANBE and ANAE, respectively. CD15 was expressed in three of the cases (1 M5a; 2 M5b) and negative in 2 M5bs. CD34 was negative in all four M5bs and variably expressed in the M5a.

The M7 showed intense dual expression of CD41a and CD42b by the blasts.

Nonlineage antigen expression, including CD1, CD2, CD4, CD5, CD7, CD10, CD19, CD24, and CD56, was present and the distribution among the FAB subtypes of the AMLs is indicated in Table 2B. Fifty-three of the 80 AML cases expressed one or more of the nonlineage antigens indicated. Of interest, nonlineage CD5+ was always associated with CD7+ (1 M0; 1 M2; 1 M4). The M0 was a secondary AML (history of breast carcinoma) with an isochromosome [i(17q)] detected. The blasts were TdT– and had variable CD5+. In the M2, the blasts were HLA-DR+/TdT–. All of the other AML cases with nonlineage expression of T-cell markers (CD1, CD2, CD7) were HLA-DR+ except for 1 (an M3m). Of the 23 cases of AML with CD56+, 22 had expression of either HLA-DR or CD34 or both; the one case with CD56+ and HLA-DR/CD34– was an M3m with *t*(15;17). Of the 4 cases with CD19+ (3 M2; 1 M1), all had a *t*(8;21) (q22; q22). They were CD10/CD20/CD24/ kappa/lambda/and TdT–. Two were CD56+ and all were CD34+.

Chromosomal Analysis

As seen in Table 3, the two cases of M4-Eo which were not associated with inv 16 had multiple, nonspecific chromosomal abnormalities in one; the other case had no chromosomal abnormalities detected. One of the M2s associated with 5q- and one associated with trisomy 8 were also associated with *t*(8;21). The M4-Eos associated with trisomy 8 and monosomy 7 were also associated with inv 16. The M3 associated with trisomy 8 also had *t*(15;17). The M2s associated with monsomy 17 and monsomy 15 were not associated with *t*(8;21).

The CD1+ AML had a normal female chromosome pattern. The CD2+ M4-Eos were associated with inv 16; none of the CD2+ M2s had *t*(8;21). Aberrant CD4 and CD7+ had no association with a specific chromosomal abnormality or pattern. The one case with aberrant CD10+ was an M1 associated with 5q-, 7p-, and 12p-. CD24 coexpression was observed in one case, an M4-Eo with a normal female chromosome pattern. CD56 coexpression was observed in eight M2s, three of which were associated with *t*(8;21); two of these three had CD19+, one of which was also associated with trisomy 22. Of the other 5 M2s without *t*(8;21), three were associated with trisomy 21 and 1 with trisomy 22. Thus, of the eight CD56+ M2s, two had trisomy 22, and three had trisomy 21. Of interest, only three and four cases out of the 80 cases studied had trisomy 22 and trisomy 21, respectively.

Summary

An FAB-based summary table (Table 4) is provided to outline the most important findings and conclusions.

DISCUSSION

Combining histology, cytomorphology, EC, and FCI is essential in FAB subtyping AMLs (M0 through M7). M0 is

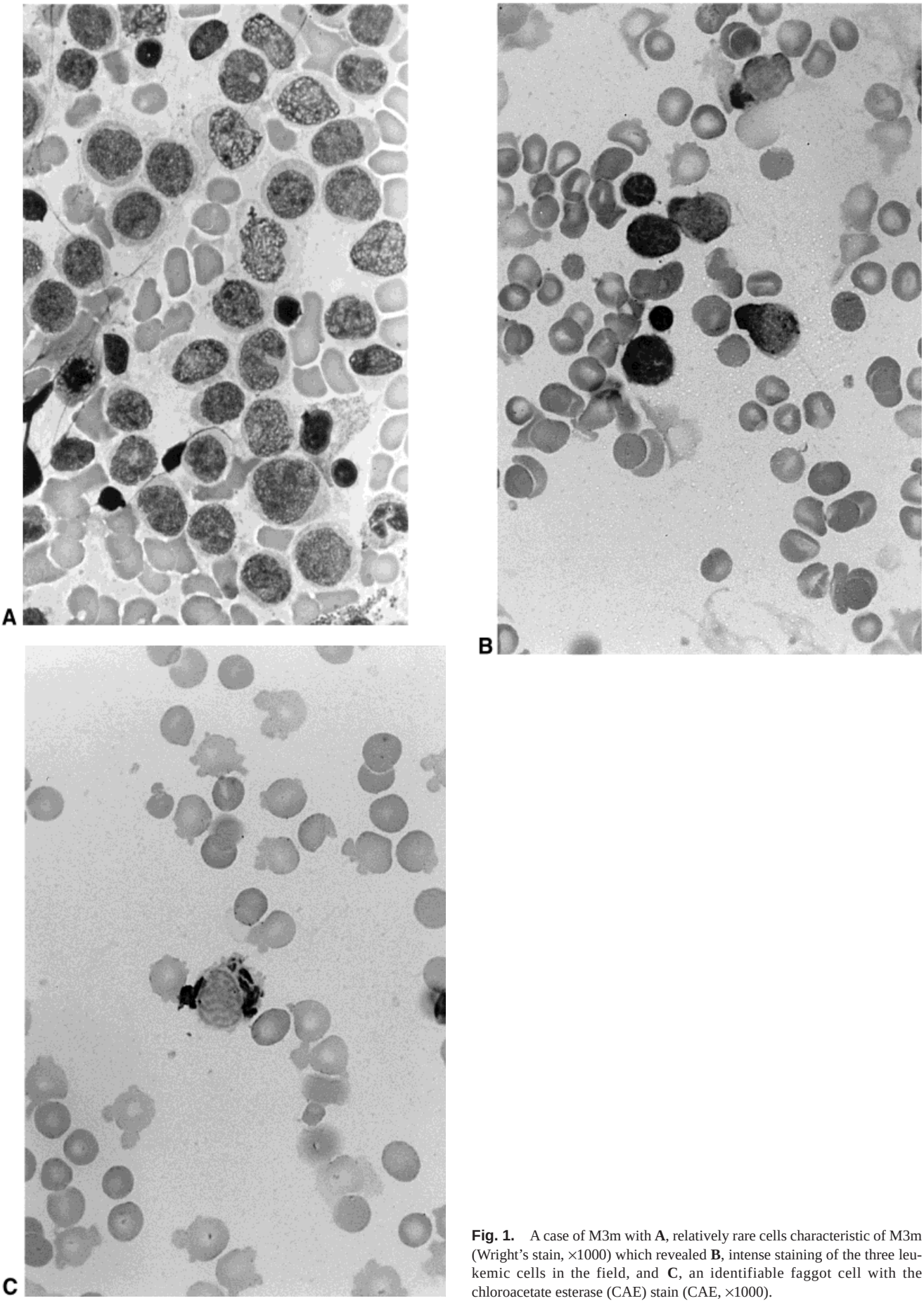

Fig. 1. A case of M3m with **A**, relatively rare cells characteristic of M3m (Wright's stain, ×1000) which revealed **B**, intense staining of the three leukemic cells in the field, and **C**, an identifiable faggot cell with the chloroacetate esterase (CAE) stain (CAE, ×1000).

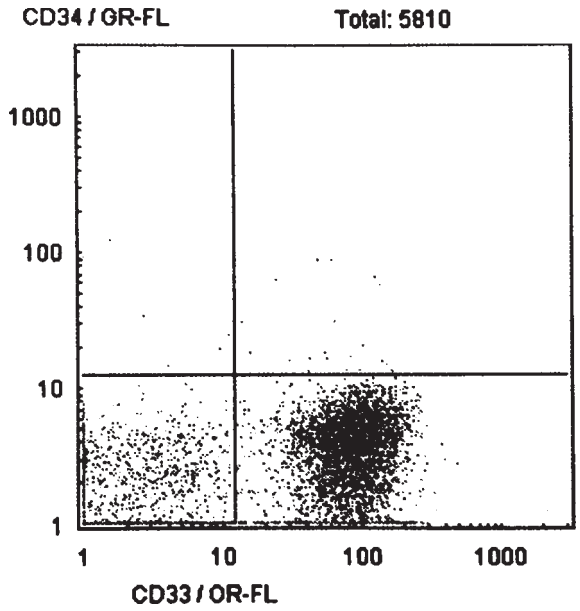

Fig. 2. Flow cytogram of the M3m showing dual plot of CD34 versus CD33. There was intense expression of CD33 with no associated expression of CD34.

important to recognize since the outcome is poor, due to both a failure to achieve complete remission and a high rate of early relapse (9–11). FCI is also particularly useful in diagnosing M7 since these cases frequently are hypocellular aspirates in adults and the clinical impact is significant.

Another clinically important subtype to recognize is APL. Morphologically the hypogranular variant (M3m) may be difficult to recognize and similar to M5. Although, reportedly, there are at least a few cells characteristic of M3 in the M3m (12), one case did not reveal any typical cells of M3, auer rods, or faggot cells on Wright's-stained smears. Only one non-M3 (an M6) lacked complete expression of CD34 and HLA-DR, as the M3s. Only one non-M3 (an M2) morphologically resembled an M3m; it was CD34–, HLA-DR+/–. Of interest, a few cells stained with ANBE, indicating monocytic differentiation and possibly accounting for the morphologic confusion. Occasional cases (27%) of M3 have been reported to be HLA-DR+. In addition, although Drexler et al. (13) reported HLA-DR to be low only in M3 cases, 10% of AMLs, particularly M1 and M2 subtypes, have been reported to be HLA-DR– (14). In our series, HLA-DR– or decreased expression was present in 15% (11/74) of the non-M3s. However, to our knowledge, there

TABLE 2A. Distribution of Antigen Expression Among FAB Subtypes of AML[a]

	FAB subtype of AML								
Antigen	M0 (13)	M1 (8)	M2 (36)	M3 (6)	M4 (9)	M5 (5)	M6 (2)	M7 (1)	Total (80)
CD13	13	6	33	6	7	4	1	1	71
CD14	1	0	1	0	7	4	0	0	13
CD15	4	3	13	4	8	3	0	0	35
CD33	9	6	31	6	8	5	1	1	77
CD34	13	6	28	0	5	1	1	1	55
CD117	11	5	35	4	5	0	2	1	63
HLA-DR	12	6	34	0	9	5	1	1	68

[a]Numbers in parentheses represent the total number of this FAB subtype in the cases studied.

TABLE 2B. Distribution of Aberrant Antigen Expression Among FAB Subtypes of AML[a]

	FAB subtype of AML								
Aberrant antigen	M0 (13)	M1 (8)	M2 (36)	M3 (6)	M4 (9)	M5 (5)	M6 (2)	M7 (1)	Total (80)
CD1					1				1
CD2*	2		3	2	3**				10
CD4	3	4	13	1	8	5	1		35
CD5*	1	1	1					1	4
CD7*	6	1	7		1			1	16
CD10*		1							1
CD19		1	3						4
CD24					1				1
CD56	3		8	1	6	5			23

[a]Numbers in parentheses represent the total number of this FAB subtype in the cases studied.

*Three cases had dual expression of CD2/CD7; 2, dual expression of CD5/CD7; 1, simultaneous expression of CD2/CD7/CD5; and 1, simultaneous expression of CD5/CD7/CD10.

**All 3 cases were of the M4-Eo FAB subtype.

TABLE 3. Cytogenetic Findings in 80 Adult AML Cases

Normal—15 (4 M1, 1 M1, 5 M2, 3 M4, 1 M6, 1 M7) Abnormal—65	
Abnormal (65)	
16 previously recognized non-random abnormality	Other most common abnormalities[a]
t(15;17) (6 APL)	5q– (11) (1 M0, 1 M1, 8 M2, 1 M6)
t(8,21) (1 M1, 4 M2)	trisomy 8 (9) (2 M0, 4 M2, 1 M3, 1 M4, 1 M4-Eo)
inv 16 (3 M4-Eo, 1 M1)	monosomy 7 (8) (1 M01, 1 M1, 5 M2, 1 M4-Eo)
t(9;22) (1 M0)	monosomy 17 (7) (1 M1, 6 M2)
	monosomy 15 (5) (1 M1, 4 M2)
Abnormalities occurring in >1 but < 5 cases*	
12p–(4)	monosomy 21 (2)
monosomy 5 (4)	monosomy 22 (2)
trisomy 21 (4)	monosomy 19 (2)
loss of Y (4)	trisomy 11 (2)
monosomy 3 (3)	7p–(2)
trisomy 4 (3)	monosomy 8 (2)
trisomy 9 (3)	monosomy 20 (2)
monosomy 18 (3)	9q–(2)
trisomy 22 (3)	6q–(2)
loss of X (3)	
Abnormalities occurring together in >1 case*	
5q–, 12p–(3)	9q–, monosomy 17 (2)
5q–, monosomy 7 (3)	monosomy 7, monosomy 17 (3)
5q–, monosomy 15 (3)	monosomy 15, monosomy 17 (3)
5q–, monosomy 17 (2)	monosomy 5, monosomy 18 (2)
	monosomy 17, monosomy 18 (2)
	monosomy 7, monosomy 15 (3)
	monosomy 3, monosomy 7 (2)
	trisomy 4, trisomy 9 (2)

[a]Number of cases in parentheses immediately following abnormality.
*There was no association of a specific subtype with any of these abnormalities.

TABLE 4. Summary Table[a]

FAB subtype	Most important findings/conclusions
M1	CD19+ was exclusively associated with *t*(8;21) (q22;q22) (3 M2, 1 M1);
M2	CD19+ may indicate a good prognosis
M3 (M3m)	M3m must be morphologically differentiated from M5; MPO, SBB, CAE were intensely + M3m usually HLA-DR–/CD34– but may be positive for one or both; EC is useful; must be supported with *t*(15;17) (q22;q11.2)
	One case of M3m CD56+ and one must differentiate from CD56+ AML of ''unique subtype''
M4 (M4-Eo)	60% of the M4-Eos were associated with inv(16), a good prognosis indicator; however not all M4-Eos had this abnormality and vice versa.
	All M4-Eos with CD2+ were associated with inv (16).
M5	M5 may be morphologically similar to M3m as mentioned. In addition, CD14 may be negative and CD34 is often negative with HLA-DR+ in all cases studied. One may distinguish from M3m by EC stains and cytogenetics.

[a]There was no correlation of aberrant expression of T-cell markers or CD56 with FAB subtype.

is only one reported case of M3 with CD34+ (15) and it is unclear if the reported HLA-DR– AMLs were evaluated for CD34+. In these cases, EC may be helpful in distinguishing the subtypes. MPO, SBB, and CAE have been reported to be intensely positive in virtually all leukemic cells in M3 (16). Therefore, if an AML is CD34– and HLA-DR– or HLA-DR+/– but lacks this EC staining pattern, the diagnosis of M3 must be supported by cytogenetic studies. Likewise, if an AML is CD34– or + and HLA-DR+ but shows this EC staining pattern, a diagnosis of M3 should be considered.

In regard to recognizing an M5 subtype, the importance lies in distinguishing this subtype from M3m. Like APL, M5s are generally CD34–. In our series, all M5bs were CD34–/HLA-DR+ and the M5a was CD34+/HLA-DR+; M5a may be CD34+ (17). Although CD14 isconsidered an extremely useful marker in recognizing M5s (2,17), the M5a was CD14–. In addition, although Khalidi et al. report M5a to be CD4–, CD5+, and CD117+, our M5a was CD4+, CD5–, and CD117–. Therefore, a CD14– AML may represent M5 and should be distinguished from APL by correlation with EC, considering that ANAE has been unexpectedly reported in APL (10).

Nonlineage expression of CD1, CD2, CD4, CD5, CD7,

CD10, CD19, CD24, and CD56 was observed. Although CD20 was the most commonly expressed lymphoid antigen in the study of Khalidi et al. (2), this antigen was not expressed. CD7 was most often expressed (46%) in the M0 subtype; however, aberrant expression of the T-cell markers did not specifically correlate with FAB subtype. Of interest, CD2+ M4Eos were all associated with inv 16; this association has not previously been described. There was increased CD2+ in APLs (33%) as has previously been reported (2). Although CD4+ AML has been described as relatively specific for monocytic lineage (14), it was observed in subtypes M0 through M6. The highest incidence of CD4+ occurred in M2 (13 cases), M4 (8 cases), and M5 (5 cases); however, the highest percentage of CD4+ cases included M5 (100%), M4 (90%), M1 (50%), and M6 (50%). Our results differ from those of Larson, et al. (15); 6 CD4+ cases had CD2+; none of Larson's CD4+ cases had CD2+. In addition, the highest percentage of Larson's CD4+ cases included M5, M4, M2, and M6. The clinical significance of the above findings is unclear. Although nonlineage expression of T-cell markers was nonspecific, they are useful in identifying leukemic cells as minimal residual disease or at relapse. In addition, CD7+ AML has been reported to be associated with a worse complete remission rate and overall survival than CD7– AML (18).

CD56+ in AML has been described as a fairly common finding in M0, M2, M4, and M5 (19); it was nonspecifically expressed in our subtypes M0 (15%), M2 (22%), M3 (17%), M4 (67%), and M5 (100%). Thus, overall, 11 of 21 (52%) patients with CD56+ AML demonstrated at least partial monocytic differentiation. Mann et al. described a slightly higher percentage (67%) of monocytic differentiation in CD56+ AML; the other subtypes of CD56+ AML in that series included two M1s, one M2, one hypergranular M3, and one M7 (20). Although CD56+ expression has been described in a unique subtype of AML (CD56+, CD33+, CD13+/–, CD34–, HLA-DR–, CD16–) characterized by a high white blood cell count and marked nuclear folding with variable cytoplasmic granularity resembling M3m (21), this subtype was not observed. In addition, the finding of a CD56+ M3m has not previously been described and, thus, heightens awareness of this entity when considering a diagnosis of this previously described "unique subtype." In addition, the CD56+ cases had the highest incidence of trisomy 22 (67% of cases studied) and trisomy 21 (75% of cases studied).

Although CD24+ in our series was predictive of a monocytic lineage of the AML (an M4), as previously described (22), the sensitivity of CD24 as a monocytic marker was much less. Raife et al. described CD24 having a sensitivity of 79% in M4 or M5; our series revealed a sensitivity of 7% (1/14).

Of interest, CD19+ in four AMLs was exclusively associated with *t*(8;21) (q22;q22); CD19 may thus be a good prognostic indicator and aid in diagnosing AMLs with this translocation. Although CD19+ AML has been associated with *t*(8;21) (q22;q22) (23), this exclusive association has not been previously described in such a large, comprehensive study. In addition, the high frequency of TdT+ and CD56+ previously described in AML with *t*(8;21) (24) was not observed. Brandt et al. described CD19+ in 6 AMLs with a substantial monocytic component (3 M4; 3 M5); recurring chromosomal abnormalities and t(8;21) were not identified (25). This association was not observed in our series. The clinical significance of these findings is uncertain.

The primary role of cytogenetics in AML is as a prognostic indicator and in identifying clinicopathologic entities. Specifically, *t*(8;21) (q22;q22), occurring in 10–20% of M2s and occasionally in M1 or M4, is associated with a high remission rate (26). Another good prognostic indicator is the presence of inv or del (16q22) (27). Although the M4-Eo subtype has indicated this chromosomal abnormality, later reports (23) and our series underscores the importance of cytogenetic studies in such cases, since not all M4-Eos have this abnormality and vice versa. It is interesting that *t*(8;21) (q22;q22) and inv (16) are both good prognostic indicators since they are related at the genetic level. Each involve a gene coding for a subunit of the core binding factor (CBF) transcription factor (28,29). Lastly, unless of the hypergranular type of M3, APLs should be diagnostically supported by the characteristic *t*(15;17) (q22;q12–21). Although there are reported APLs without this translocation (30,31), to this date, there are no reported M3ms without this *t*(15;17) (2,12).

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