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Acute Myeloid Leukemia with Translocation t(8;16) Presents with Features Which Mimic Acute Promyelocytic Leukemia and is Associated With Poor Prognosis

Adi Diab, M.D.^{a,*}, Lynette Zickl, M.S.^d, Omar Abdel-Wahab, M.D.^{a,c}, Suresh Jhanwar, Ph.D.^a, Manjit A Gulam, M.D., Ph.D.^a, Katherine S. Panageas, Ph.D.^e, Jay P. Patel^c, Joseph Jurcic, M.D.^a, Peter Maslak, M.D.^a, Elisabeth Paietta, Ph.D.^f, James K. Mangan, M.D.^h, Martin Carroll, M.D.^h, Hugo F. Fernandez, M.D.^g, Julie Teruya-Feldstein, M.D.^b, Selina M. Luger, M.D.^h, Dan Douer, M.D.^a, Mark R. Litzow, M.D.ⁱ, Hillard M. Lazarus, M.D.^j, Jacob M. Rowe, M.D.^k, Ross L. Levine, M.D.^{a,c}, and Martin S. Tallman, M.D.^a

^aLeukemia Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

^bLeukemia Service, Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

^cHuman Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

^dDepartment of Epidemiology and Biostatistics, Dana-Farber Cancer Institute and ECOG Statistical Center, Brookline, MA, USA

^eDepartment of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

^fDepartment of Oncology, Montefiore Medical Center, Albert Einstein College of Medicine, and ECOG Leukemic Translational Studies Laboratory, Bronx, NY, USA

^gDepartment of Blood and Marrow Transplantation at Moffitt Cancer Center, Tampa, FL, USA

^hDivision of Hematology/Oncology, University of Pennsylvania, PA, USA

ⁱMayo Clinic, Rochester, MN, USA

^jUniversity Hospitals Case Medical Center, Case Western Reserve University, Cleveland, OH, USA

^kDepartment of Hematology, Shaare Zedek Medical Center, Jerusalem, Israel

Abstract

Previous small series have suggested that acute myeloid leukemia with t(8;16) is a distinct morphologic and clinical entity associated with poor prognosis. We describe 18 patients with t(8;16) AML, including their clinical, cytomorphologic, immunophenotypic and cytogenetic

features. Half of the patients had extramedullary disease, most commonly leukemia cutis, which often preceded bone marrow involvement and six had therapy-related AML. Patients with t(8;16) AML commonly present with clinical and pathological features that mimic APL, with promyelocytes and promyeloblast-like cells and coagulopathy in most patients. Several patients also presented with marrow histiocytes with hemophagocytosis and erythrophagocytosis. Comprehensive molecular analysis for co-occurring genetic alterations revealed a somatic mutation in *RUNX1* in 1 of 6 t(8;16) patients with no known AML mutation in the remaining five t(8;16) patients. This suggests that the t(8;16) translocation could be sufficient to induce hematopoietic cell transformation to AML without acquiring other genetic alteration. These data further support classifying t(8;16) AML as a clinically and molecularly defined subtype of AML marked by characteristic clinical and cytomorphologic features that mimic APL, and is associated with very poor survival.

Keywords

leukemia; APL; t(8;16); AML; Therapy-related AML

Introduction

Acute myeloid leukemia (AML) with translocation (8;16) is an uncommon AML subtype that has been characterized as a distinct clinical entity.¹ t(8;16)(p11;p13) results in fusing of MYST histone acetyltransferase 3 (*MYST3*) gene on chromosome 8 with cAMP response element binding protein (*CERBBP*) gene on chromosome 16; both encode proteins with histone acetyltransferase activity. The exact molecular pathogenesis of this AML subtype has not yet been defined, but this fusion protein has been suggested to play a role.²⁻³ The specific molecular alterations in the fused t(8;16) genes as well as how other genetic alterations are involved in the pathogenesis is unclear. Previous case reports have suggested that t(8;16) AML may occur as therapy-related AML (t-AML), often with extramedullary disease and may be associated with a relatively high rate of disseminated intravascular coagulation (DIC).⁴ Morphologically, t(8;16) AML has mostly been described with monocytic features with erythrophagocytosis, and classified by FAB as M4 or M5 subtype.

We report the morphologic and clinical characteristics of 18 patients with t(8;16) AML. In addition, we present the findings from comprehensive candidate gene sequencing of all genes known to be mutated in >5% of AML patients in general, for six patients with t(8;16) in our cohort.

Materials and Methods

Patients

We identified 18 patients who presented with AML and t(8;16) by searching the databases of Memorial Sloan-Kettering Cancer Center (MSKCC) (n=7), University of Pennsylvania (n=4) and through detailed annotation of samples banked on Eastern Cooperative Oncology Group (ECOG) trials (n=7) who presented between 1990 and 2010. We included patients with t-AML without activity of a previous malignancy and had completed treatment. The

diagnosis of AML was established by morphology, immunophenotyping, and molecular genetics of the bone marrow blasts. The specific t(8;16) cytogenetic abnormality was established by karyotyping. Marrow biopsies, aspirates, and cytology smears of 7 MSKCC patients were retrospectively reviewed by one of the authors (JF). Patients from ECOG trials had central morphologic and cytogenetic reviews and underwent central immunophenotyping. The study was approved by the institutional review boards of all participating centers.

Mutational Analysis of t(8;16) samples

DNA was isolated from mononuclear cells after Ficoll purification. All genomic DNA samples were whole genome amplified using Φ 29 polymerase followed by PCR amplification and bidirectional Sanger sequencing of all coding exons of *TET2*, *ASXL1*, *DNMT3A*, *PHF6*, *WT1*, *TP53*, *EZH2*, *RUNX1*, and *PTEN* and of coding exons of *FLT3*, *HRAS*, *KRAS*, *NRAS*, *KIT*, *NPM1*, *CEPBA*, *MLL-PTD*, *IDH1*, and *IDH2* with known somatic mutations. Primer sequences and PCR conditions are provided upon request. All traces were reviewed manually using Mutation Surveyor (Soft Genetics, State College, PA) and validated by repeat PCR amplification and Sanger re-sequencing of unamplified diagnostic DNA. All mutations that were not previously reported to be either somatic or germline were analyzed in matched remission DNA, when available, to determine somatic status. Variants whose somatic status could not be determined were censored with regard to mutational status for the specific gene.

Statistical analysis

Overall survival (OS) was defined from time of diagnosis to death and disease free survival (DFS) was defined as time from achieving complete remission (CR) to time of first relapse. The methods of Kaplan-Meier were used to estimate survival curves and the significance was tested by Log-rank tests, statistical significance was determined with a 2-sided P value <0.05. Correlation analysis and linear regression curve were done using GraphPad software Prism ®.

Results

Patient Characteristics

A total of 18 patients (10 women and 8 men) with t(8;16) AML were diagnosed between 1990 and 2010. Detailed characteristics of each patient are presented in Table 1. The age range at presentation was wide, 2 months to 73 years, (median 52 years); 2 patients were younger than 4 months, and 7 were older than age 60. The median white blood cell count (WBC) at diagnosis was 12.6×10^3 (3.5-86.0)/ μ L. The median of blasts in bone marrow aspirate was 66%. No patient had a clinical antecedent hematologic disorder except one patient with prior chronic myelomonocytic leukemia (CMML). Eight (44%) had documented extramedullary disease: 5 with leukemia cutis (in 2 the diagnosis of leukemia cutis preceded systemic AML by 2-3 months) (supplementary data), 2 had leptomeningeal involvement (documented by cytomorphologic analysis of cerebrospinal fluid (CSF), 1 had a biopsy-confirmed liver involvement, and 2 had leukemic cells in the urine consistent with genitourinary involvement.

Of note, 6 of the 18 patients (33%) had t-AML after a prior malignancy requiring systemic therapy; all had received prior chemotherapy and 2 also radiation therapy. The prior malignancy was breast cancer (3 patients), testicular germ cell tumor (2 patients), and CMML (one patient). The interval between the first treatment of the prior cancer to the diagnosis of t-AML was relatively short, with a median of 10 (range 6 -23) months. Of the patients with breast cancer, 1 was treated with cyclophosphamide as part of cyclophosphamide/methotrexate/5-FU flowed by anthracycline and cyclophosphamide (AC) together with radiation. Both patients with testicular germ cell tumors were treated with bleomycin/etoposide/cisplatin (BEP) (one received 3 cycles and the other received 6 cycles).

Outcome Data

Complete Remission Rate and Overall Survival—Of the 18 patients, 10 (55%) patients achieved a complete remission (CR) with one standard induction cycle of anthracycline and cytarabine. Five patients had primary refractory disease, not responding to other additional therapy. Two patients died within days of diagnosis, and 1 patient (age 2 months) had spontaneous regression.

The median overall survival (OS) of all patients was 8.5 months (Figures 1A), including the two patients who died within days after initial diagnosis. The median OS in the six t(8;16) t-AML was 6 months. This seemed lower than the OS of 8.8 months in *de novo* AML patients; the difference was not statistically significant (Figure 1 B). The median disease-free survival (DFS) of patients in CR was 3.5 (range 1.5-30) months (Figure 1 C). Three patients underwent hematopoietic stem cell transplantation (HSCT), two in first CR and the third patient in second CR. All three patients who underwent HSCT subsequently relapsed and ultimately died of their disease.

Morphology and Immunophenotyping

Of the 18 patients, 11 were classified according to FAB as M5 and three patients as M4; two patients were M1 and one patient each M2 and M0, respectively. Interestingly, 8 of our t(8;16) AML patients were initially referred for suspected APL as their bone marrow and blood had increased number of promyelocytes, and promyeloblasts and the blasts had typical clefted nuclei seen in APL. In addition, histiocytes with hemophagocytosis, mostly erythrophagocytosis, were also seen (Figure 2A). Erythrophagocytosis appeared as degraded red blood cells within histiocytes, seen in the bone marrow, blood, and even urine (Figure 2B). Cytochemical staining was available in 8 patients; all were myeloperoxidase (MPO) positive, but only 3 stained positively for non-specific esterase (NSE).

Immunophenotypic analysis was available for all 18 patients, though detailed immunophenotypic analysis was only available for 8. Monocytic markers CD11b and CD14 were positive in 11/18 and 8/9 patients, respectively. Blasts in most patients expressed the myeloid markers including MPO, CD33, CD13, and CD15. Stem cell surface markers were uncommon as most patients were CD117 (13/16) and CD34 negative (14/17 patients). In 13 of 17 patients, HLA-DR was strongly positive. Table 2 summarizes the other 8 patients with t(8;16) AML with detailed immunophenotyping in comparison to the reported APL immunophenotype. ⁶

Cytogenetics and Mutational Analysis

Cytogenetic studies confirmed the presence of t(8;16) (Figure 2C) in all 18 patients. Ten patients, had t(8;16) as the sole cytogenetic abnormality, and the other 8 patients had more complex karyotypes. The degree of cytogenetic complexity varied amongst patients but was not associated with prior cancer treatment, gender, age, or other clinical characteristics and did not correlate with OS (data not shown).

We performed high-throughput sequencing analysis of 18 candidate genes known to be mutated in 5 of AML patients to identify genetic alterations which might collaborate with t(8;16) to result in leukemia using material from 6 patients for whom pre-treatment material was available. The only t(8;16) patient found to have a co-occurring somatic mutation was found to have a somatic mutation in *RUNX1* predicted to result in a premature stop codon (*RUNX1* c.378het_insTCGTGGCCCTAGGG GATGTCCAGATAC; p. RUNX1 D126fsX3). The remaining 5 patients did not have mutations in any genes known to be recurrently mutated in *de novo* AML.

Disseminated Intravascular Coagulation (DIC)

Given the clinical and morphological similarity of t(8;16) AML to APL, we determined the incidence of DIC at presentation. We defined DIC by low fibrinogen levels, thrombocytopenia, prolonged prothrombin time (PT), and partial thromboplastin time (PTT).⁷ 14 patients had documentation of pretreatment coagulation tests of which 9 patients had DIC and 8 patients had low fibrinogen which correlated significantly with shorter survival ($r^2 = 0.9$; Figure 3).

Discussion

t(8;16) AML is a rare and distinct clinicopathological entity. Only few prior reports described comprehensively the characteristics of these patients.^{8-9,20} Our cohort suggested that t(8;16) AML is characterized by a high frequency of extramedullary involvement, frequent coagulopathy, morphologic features overlapping with APL, can occur after prior cytotoxic chemotherapy, has a poor outcome, and has few known collaborating somatic genetic alterations.

Our patients presented at a relatively younger age (median age of 52 years) compared with higher median of 68 years¹⁰ of the general AML population. The frequency of men and women was similar, in contrast to previous reports where t(8;16) AML was more common in women^{11,20}. Almost one-half (8) of our 18 patients had extramedullary disease, mostly in the skin, which often preceded systemic AML by several months. One pediatric patient, with initial myeloid sarcoma, had spontaneous regression, as previously reported pediatric cases.¹²⁻¹⁵ The CR rate of 55% was not dissimilar from that achieved in AML in general,¹⁶⁻¹⁷ but duration of remission was very short, with a median DFS of 3.5 months. As reported by others¹⁸⁻²⁰ patients with t(8;16) AML had a very unfavorable outcome as evident by a short median OS of 8.5 months. Although allogeneic HSCT may be an effective treatment for patients with unfavorable karyotypes, it is unclear if such an approach will

improve the outcome of patients with t(8;16) as all 3 patients treated with HSCT relapsed after transplantation.^{17,21-24}

Disseminated intravascular coagulation at the time of diagnosis was a prominent clinical feature in the majority of our patients (60%) and those were the patients with the worst outcome. It is unclear if DIC was directly involved in mortality or it was merely a surrogate for more aggressive leukemia. No correlation was found between incidence of DIC and t-AML.

The morphological FAB classification has limited and even confusing role in classifying t(8;16) AML. Most of our patients (14) were classified as FAB M4 and M5. Importantly, in 8 of our patients the blasts also had a striking morphological resemblance to APL cells, in particular, the high percentage of heavily granulated promyelocytic blasts in the bone marrow and peripheral blood. This combined with the DIC in our patients, strongly suggested a presumptive diagnosis of APL. In fact, the treating clinicians and hematopathologists initially suspected APL in these 8 patients, and in 2 patients the suspicion was convincing enough to initiate induction with all-trans retinoic acid (ATRA), before t(15;17) translocation was found negative. The cells from most of these patients stained positive for myeloperoxidase, of them 3 also stained positive for NSE. Despite the morphological similarities between APL and t(8;16) AML, their immunophenotypic characteristics were different. Though our study is underpowered to draw statistically significant conclusions, given the rarity of this entity, our observations are important in the management of t(8;16) AML. Biologically, the morphological promyelocytic appearing blasts in t(8;16) patients and lack of CD34 expression (albeit in a small number of patients studied) suggest that the leukemic cells have a relatively mature granulocytic phenotype.

t-AML usually has worse prognosis than de novo AML.²⁵⁻²⁸ In this cohort, we found a relatively high rate of patients with t-AML (34%). Four of the 6 t-AML patients had t(8;16) as a sole abnormality, suggesting a role in the leukemogenesis; the remaining 2 patients had complex karyotype. t-AML with t(8;16) was reported after prior treatment with both alkylating agents or topoisomerase II inhibitors that included anthracyclines and epipodophyllotoxins with and without radiation.^{19, 29} The short latency, absence of a known preceding MDS, and the reciprocal translocation, suggests that t(8;16) t-AML is more likely related to prior exposure to topoisomerase II inhibitors, which all had received.

Another intriguing observation is our finding of spontaneous remission in one t(8;16) AML infant patient which has been reported in a few other pediatric patients. Transient pediatric AML with t(8;16) possibly suggests a mechanism that involves a molecule or process that is specific to early normal hematopoiesis, which is different from all other t(8;16) AML patients.

Our study is the first to report an extensive mutational analysis in t(8;16) AML. With the exception of a somatic *RUNX1* mutation in a single patient, we did not identify mutations in known leukemogenic disease alleles in all others. This finding suggests that the abnormality induced by t(8;16), occurring in the histone acetyltransferase gene, may be sufficient to induce hematopoietic transformation and result in AML without acquiring additional genetic

alterations. Nevertheless, further genetic analysis using exome- or whole-genome sequencing approaches could identify in t(8;16) AML patients novel collaborating genetic alterations and co-occurring lesions which could affect therapeutic response.

In summary t(8;16) is a distinct AML entity, in which the transforming properties of its leukemogenic fusion gene needs to be better understood, which might define novel and effective therapies, specific to this subtype of AML.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

1. Mitelman, F. Johansson, B., Mertens, F., editors. Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer. 2011. available at <http://cgap.nci.nih.gov/Chromosomes/Mitelman>
2. Borrow J, Stanton PV Jr, Andresen JM, Becher R, Behm FG, Chaganti RS, et al. The translocation t(8;16)(p11;p13) of acute myeloid leukaemia fuses a putative acetyltransferase to the CREB-binding protein. *Nature Genetics*. 1996; 14:33–41. [PubMed: 8782817]
3. Champagne N, Pelletier N, Yang XJ. The monocytic leukemia zinc finger protein MOZ is a histone acetyltransferase. *Oncogene*. 2001; 20(3):404–409. [PubMed: 11313971]
4. Huret, J., Senon, S. MYST3 (MYST histone acetyltransferase (monocytic leukemia) 3. *Atlas Genet Cytogenet Oncol Haematol*. 2005. <http://AtlasGeneticsOncology.org/Genes/MYST3ID25ch8p11.html>
5. Patel JP, Gonen M, Figueroa, Fernandez Hugo, Sun Zhuoxin, Racevskis Janis, et al. Prognostic and Therapeutic Relevance of Integrated Genetic Profiling in Acute Myeloid Leukemia. *N Engl J Med*. 2012; 366:1079–1089. [PubMed: 22417203]
6. Paietta E, Goloubeva O, Neuberg D, Bennett JM, Gallagher R, Racevskis J, et al. A surrogate marker profile for PML/RAR alpha expressing acute promyelocytic leukemia and the association of immunophenotypic markers with morphologic and molecular subtypes *Cytometry B*. 2004; 59:1–9.
7. Kwann CH. The Pathophysiology of Coagulopathy in APL. *Clinical Advances in Hematology & Oncology*. 2011; 9(2):7–9.
8. Stark B, Resnitzky P, Jeison M, Luria D, Blau O, Avigad S, et al. A distinct subtype of M4/M5 acute myeloblastic leukemia (AML) associated with t(8;16)(p11;p13), in a patient with the variant t(8;19)(p11;q13)--case report and review of the literature. *Leukemia research*. 1995; 19(6):367–379. [PubMed: 7596149]
9. Rozman M, Camos M, Colomer D, Villamor N, Esteve J, Costa D, et al. Type I MOZ/CBP (MYST3/CREBBP) is the most common chimeric transcript in acute myeloid leukemia with t(8;16)(p11;p13) translocation. *Genes Chromosomes Cancer*. 2004; 40:140–145. [PubMed: 15101047]
10. [Accessed on 10-2-2011] SEER Research. <http://seer.cancer.gov/faststats>
11. Gervais C, Murati A, Helias C, Struski S, Eischen A, Lippert E, et al. Acute myeloid leukaemia with 8p11 (MYST3) rearrangement: an integrated cytologic, cytogenetic and molecular study by the groupe francophone de cytogenetique hematologique. *Leukemia*. 2008; 22:1567–1575. [PubMed: 18528428]
12. Sainati L, Bolcato S, Cocito MG, Zanesco L, Basso G, Montaldi A, et al. Transient acute monoblastic leukemia with reciprocal (8;16)(p11;p13) translocation. *Pediatr Hematol Oncol*. 1996; 13:151–157. [PubMed: 8721029]
13. Dinulos JG, Hawkins DS, Clark BS, Francis JS. Spontaneous remission of congenital leukemia. *The Journal of pediatrics*. 1997; 131(2):300–303. [PubMed: 9290620]
14. Classen CF, Behnisch W, Reinhardt D, Koenig M, Möller P, Debatin KM. Spontaneous complete and sustained remission of a rearrangement CBP (16p13)-positive disseminated congenital myelosarcoma. *Ann Hematol*. 2005; 84:274–275. [PubMed: 15605245]

15. Weintraub M, Kaplinsky C, Amariglio N, Rosner E, Brok-Simoni F, Rechavi G. Spontaneous regression of congenital leukaemia with an 8;16 translocation. *Br J Haematol.* 2000; 111:641–643. [PubMed: 11122113]
16. Rowe JM, Tallman MS. Intensifying induction therapy in acute myeloid leukemia: Has a new standard of care emerged? *Blood.* 1997; 90:2121–2126. [PubMed: 9310463]
17. Dohner H, Estey EH, Amadori S, et al. Diagnosis and treatment of acute myeloid leukemia in adults: recommendations from an international expert panel, on behalf of the European leukemiaNet. *Blood.* 2010; 115:453–474. [PubMed: 19880497]
18. Tasaka T, Matsushashi Y, Uehara E, Tamura T, Kakazu N, Abe T, Nagai M. Secondary acute monocytic leukemia with a translocation t(8;16)(p11;p13): case report and review of the literature. *Leuk Lymphoma.* 2004; 45:621–625. [PubMed: 15160929]
19. Quesnel B, Kantarjian H, Bjergaard JP, Brault P, Estey E, Lai JL, et al. Therapy-related acute myeloid leukemia with t(8;21), inv(16), and t(8;16): a report on 25 cases and review of the literature. *J Clin Oncol.* 1993; 11(12):2370–2379.
20. Haferlach T, Kohlmann A, Klein HU, Ruckert C, Dugas M, Williams PM, et al. Cytogenetics and Molecular Genetics AML with translocation t(8;16)(p11;p13) demonstrates unique cytomorphological, cytogenetic, molecular and prognostic features. *Leukemia.* 2009; 23:934–943. [PubMed: 19194466]
21. Rowe JM, Tallman MS. How I treat acute myeloid leukemia. *Blood.* 2010; 116(17):3147–56. [PubMed: 20558611]
22. Lekakis L, Giral S, Couriel D, Shpall EJ, Hosing C, Khouri IF, et al. Phase II study of unrelated cord blood transplantation for adults with high-risk hematologic malignancies. *Bone Marrow Transplant.* 2006; 38:421–6. [PubMed: 16892072]
23. Craddock CF. Full-intensity and reduced-intensity allogeneic stem cell transplantation in AML. *Bone Marrow Transplantation.* 2008; 41:415–423. [PubMed: 18209726]
24. Schmid C, Schleuning M, Ledderose G, Tischer J, Kolb HJ. Sequential regimen of chemotherapy, reduced-intensity conditioning for allogeneic stem-cell transplantation, and prophylactic donor lymphocyte transfusion in high-risk acute myeloid leukemia and myelodysplastic syndrome. *J Clin Oncol.* 2005; 23:5675–5687. [PubMed: 16110027]
25. Goldstone AH, Burnett AK, Avivi I, et al. Secondary acute myeloid leukemia has a worse outcome than de novo AML, even taking into account cytogenetics and age: AML 10, 11, 12 MRC Trials. *Blood.* 2002; 100(88a) abstr 322.
26. Kern W, Haferlach T, Schnittger S, Hiddemann W, Schoch C. Prognosis in therapy-related acute myeloid leukemia and impact of karyotype. *J Clin Oncol.* 2004; 22:2510–2511. [PubMed: 15197216]
27. Pulsoni A, Pagano L. Treatment of Secondary Acute Myeloid Leukemia. *J Clin Oncol.* 2005; 23:926–927. [PubMed: 15681547]
28. Rowe JM. Therapy of secondary leukemia. *Leukemia.* 2002; 16:748–750. [PubMed: 11960361]
29. Bernasconi P, Orlandi E, Cavigliano PM. Translocation (8;16) in a patient with acute myelomonocytic leukemia, occurring after treatment with fludarabine for a low-grade non-Hodgkin's lymphoma. *Haematologica.* 2000; 85:1087–1091. [PubMed: 11025602]

Fig. 1.

Overall survival in patients with t(8;16) AML. Overall survival (OS) in the entire study population (2 patients still alive at 30 months, and one patient alive at 16 months) (A), according to t-AML *versus de novo* AML (B), disease free survival (DFS) of all patients (C).

Fig. 2. Cytopathological features of t(8;16) AML overlap with that of APL and include prominent histiocytes and erythrophagocytosis. BM-blasts with clefts, Pac-man-like (long arrows), and histiocyte with erythrophagocytosis (short arrows)-600× magnification, H&E stain (A). Histiocytes with degraded red blood cells, suggestive of erythrophagocytosis (600× magnification, voided urine cytology, Papanicolaou stain) (B). Abnormal karyotype of one patient (small arrows demonstrate breakpoints) (C).

Fig. 3.

Disseminated intravascular coagulation (DIC) is common in patients with t(8;16) AML. Overall survival correlates with the degree of presenting fibrinogen levels ($r^2 = 0.90$; data plotted for 8 patients only with available presenting fibrinogen level) (A) (all patients with DIC died, no censored patients).

Table 1

Summary of clinical information, cytomorphological features, laboratory findings and survival data in patients with t(8;16) AML.

No.	Gender	Age at diagnosis (years)	AML subtype (FAB)	Prior treated malignancy	WBC at diagnosis ($\times 1000\mu\text{L}$)	% of blasts (BM aspirate)	Erythrophagocytosis	DIC	Current survival status
1	Male	32	M5	Yes-NSGCT	35.4	20	Yes	Yes	Deceased
2	Male	49	M4	NR	10.2	70	Yes	Yes	Deceased
3	Female	58	M5	Yes-breast Ca	5.1	43	Yes		Alive
4	Male	4 months	M5	NR	72.7	71	Yes	Yes	Deceased
5	Female	2 months	M5	NR	7.5	56	Yes		Alive
6	Male	43	M5	NR	11.1	89	Yes	Yes	Deceased
7	Male	61	M5	Yes-seminoma	59.2	38	Yes	Yes	Deceased
8	Female	38	M2	NR	5.2	56	N/A		Deceased
9	Female	52	M4	NR	12.5	62	Yes	Yes	Deceased
10	Female	53	M1	NR	3.5	82	N/A		Deceased
11	Female	44	NOS	NR	4.2	87	N/A		Alive
12	Female	73	M5	NR	4.2	3	N/A		Deceased
13	Female	66	M1	Yes-breast Ca	47.8	90	N/A	Yes	Deceased
14	Male	68	M5	Yes-CMML	61	90	N/A		Deceased
15	Male	21	M5	NR	12.7	90	No	Yes	Deceased
16	Female	63	M4	Yes-breast Ca	34.8	80	No		Deceased
17	Female	66	M5	NR	86	78	No	Yes	Deceased
18	Male	65	M5	NR	55	57	Yes		Deceased

Abbreviations: AML: acute myeloid leukemia; BM: bone marrow; FAB: French-American-British; DIC: disseminated intravascular coagulation; N/A: not available; NOS: not otherwise specified; NSGCT: non-seminoma germ cell tumor.

Table 2

Summary description for immunophenotype markers in 8 patients with 8;16 AML versus APL.

Antigenic marker	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8	APL
HLA-DR	+	+	+	+	+	+	+	+	-
CD11b	+	+	+	+/-	+/-	+	+	+/-	-
CD13	+	+	-	+	+	na	-	+/-	+
CD14	+	+	+	+	na	na	+/-	+/-	-
CD15	+	+	+	+	+	+	+	+	-
CD33	+	+	+	+	+	+	+	+	+
CD34	-	-	-	-	-	-	-	-	-
CD45	+	+	+	+	+	na	-	-	-
CD56	+	-	na	-	+	na	na	+/-	-
CD117	-	-	-	-	-	na	na	-	+
CD133	-	na	na	na	na	na	na	na	-

Abbreviations: +, positive/high expression; -, negative/low expression; +/-, partial expression; na, not available; APL, acute promyelocytic leukemia; Pt, patient.