A Unique Pattern of Central Nervous System Leukemia in Acute Myelomonocytic Leukemia Associated With inv(16)(p13q22)

By Romayne Holmes, Michael J. Keating, Ann Cork, Yvonne Broach, Jose Trujillo, Willard T. Dalton, Jr, Kenneth B. McCredie, and Emil J Freireich

Twenty-six patients with inv(16)(p13q22) or del(16)(q22) in association with acute myelomonocytic leukemia (AMML-M4, FAB classification), and abnormal marrow eosinophils have been treated at this institute. Initial bone marrow eosinophilia (≥4%) was observed in 22 of 26 patients (85%), and abnormal eosinophil morphology, characterized by immature cells with some interspersed basophilic granules, was evident in 26 of 26 (100%). Giemsa-banded chromosome analysis performed in all patients revealed 16 cases with inv(16)(p13q22) alone, and ten cases with additional chromosome changes. Twenty-five patients received combination induction chemotherapy, and 23 (92%) achieved complete remission (CR). The median duration of remission was 18 months (range, six to 72+ months), and the median duration of survival was 34 months (range, 0.5 to 133 months). Nine patients (35%) relapsed in the CNS at a median time of 19 months (range, six to 133 months) from first marrow CR. All patients had leptomeningeal disease, and in addition, six of nine (66%) demonstrated two or more enhancing lesions on computed tomography brain scan, consistent with intracerebral myeloblastomas. Review of 384 Giemsa-banded patients with acute myeloid leukemia revealed no other morphologic or cytogenetic subgroup with either an equivalent incidence of CNS leukemia or documented intracerebral myeloblastomas. This series of inv(16)(p13q22)/del(16)(q22) AMML reports a favorable prognosis for such patients and associates a specific clonal cytogenetic subgroup of acute leukemia with a distinct propensity for CNS relapse, manifesting as leptomeningeal disease and intracerebral myeloblastomas.

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OVER RECENT YEARS, knowledge of the intrinsic biology of acute leukemia has been rapidly expanding; in particular, high-resolution banding techniques used in chromosome analysis now indicate that many patients with acute myelogenous leukemia (AML) have an associated clonal cytogenetic abnormality.1,2 These chromosome changes are emerging as dominant determinants for the expressed morphology, treatment response, and subsequent outcome of AML. Recently, Arthur and Bloomfield described structural rearrangements of chromosome 16 in association with AML. The changes in chromosome 16 involved the fragile site q22, and were expressed as either a partial deletion, del(16)(q22), or as a pericentric inversion of chromosome 16 at q22, inv(16)(p13q22). Patients showed initial bone marrow eosinophilia (≥4%) and acute myelomonocytic leukemia (AMML-M4, French-American-British [FAB] classification).3,4 Others have subsequently reviewed patients with inv(16)(p13q22) and AMML, emphasizing atypical morphology in the eosinophil population, and suggesting a favorable prognosis for this group.5,7

Involvement of the CNS in AML is well recognized but uncommon.7,11 Certain hematological parameters carry an increased risk for CNS leukemia (CNSL), and include high presenting WBC counts, elevated serum lactic dehydrogenase (LDH) and morphological subgroups AMML (M4) and acute monocytic leukemia (AMoL-M5).12,14 In addition, the incidence of CNSL is reported higher with extended survival, and in patients who are seen before age 50.12,15 To date a specific cytogenetic subgroup of AML has not been associated with CNSL. However, in this clinical and cytogenetic review of 26 patients with chromosome 16 abnormalities and AMML, we report a high incidence of CNSL, manifesting as leptomeningeal disease and intracerebral myeloblastomas.

PATIENTS AND METHODS

Three hundred eighty-four patients with AML and Giemsa banding chromosome analysis were treated at the University of Texas M.D. Anderson Hospital and Tumor Institute at Houston between 1976 and 1983. The karyotype of all patients was reviewed by coauthors A. Cork, Y. Broach, and J. Trujillo. Twenty-six patients who had inv(16)(p13q22) or del(16)(q22) formed the basis of this report. Chromosome analysis used trypsin-Giemsa banding (G-banding) techniques, and abnormalities were described according to the International Society for Human Cytogenetic Nomenclature criteria.16,17 Twenty-five metaphases or more were available for analysis in 24 of 26 cases (92%).

Morphological classification of leukemia was performed by conventional criteria according to the FAB cooperative criteria.8 All initial marrow specimens were reviewed for leukemia cell and eosinophil morphology. The diagnosis of AMML required the presence of more than 30% blast forms in the marrow and more than 20% monocytic cells in the marrow or blood, or both. All patients received induction regimens of cytosine arabinoside vincristine, and prednisone (OAP) in combination with Adriamycin (ADOAP), rubidazone (ROAP), or m-AMSA (AMSA-OAP). At achievement of remission, at the discontinuation of therapy, and if symptoms suggested CNS involvement, spinal taps were performed.
and were submitted for cell count, cytology, biochemistry analysis (protein, glucose, chloride), and bacteriologic screening. With each spinal tap, 100 mg of cytosine arabinoside was injected intrathecally. CNSL was said to be present when two or more spinal taps revealed pleocytosis, abnormal cytology, or elevated protein (>45 mg/dL) separately or in combination. CNS remission was defined as normalization of all cerebrospinal fluid parameters and computed tomography (CT) brain scan for a minimum of two months from CNS induction treatment.

RESULTS

Clinical and Hematologic Data (Table 1)

Of 384 Giemsa-banded patients with AML, 26 (7%) with either inv(16)(p13q22) or del(16)(q22) have been seen at this institute. The median age of the 26 patients was 43 years (range, 20 to 78 years), with 14 men and 12 women. No patient had previous exposure to chemotherapy, irradiation, or industrial carcinogens. One patient (No. 23) had a myelodysplastic syndrome for ten months before development of acute leukemia.

Fourteen of the 26 (54%) patients had extramedullary disease at diagnosis. The presenting hemoglobin levels and platelet counts were similar to other patients with AML; however, initial white cell counts were generally high (median, 67 × 10^9/L; range, 3 to 320 × 10^9/L). Serum LDH was >600 in 17 of 26 (65%) cases, and no abnormality in renal function, uric acid

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Clinical, Hematologic, and Cytogenetic Features of 26 Patients With Acute Myelomonocytic Leukemia (AMML) and Chromosome 16 Abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 1</td>
<td>tDec 1972 38/M 0 34 47 Jan 1983 (relapse) 13 cells 46 XY, 2q-, 7q-, inv(16)(p13q22) Feb 1976 (relapse) 5% 47,XX, +3, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 2</td>
<td>Dec 1974 56/F 0 7 13 95%,46,XX, inv(16)(p13q22) 5% 47,XX, +3, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 3</td>
<td>†Jan 1975 24/M Liver, spleen, nodes 63 45 139,100%,46,XY, inv(16)(p13q22) 15% 46,XY, 18q-, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 4</td>
<td>March 1975 41/F Liver 5 2 2 0 100,46,XX, inv(16)(p13q22) 15% 46,XY, 18q-, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 5</td>
<td>Sept 1975 65/M Liver, spleen 2 139 100%,46,XY, inv(16)(p13q22) 15% 46,XY, 18q-, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 6</td>
<td>May 1976 42/F Liver 2 87 100%,46,XX, inv(16)(p13q22) 15% 46,XY, 18q-, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 7</td>
<td>Nov 1976 20/M 0 35 71 100%,46,XY, inv(16)(p13q22) 15% 46,XY, 18q-, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 8</td>
<td>Feb 1977 56/F 0 12 5 100%,46,XX, inv(16)(p13q22) 15% 46,XY, 18q-, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 9</td>
<td>Feb 1977 42/M Liver, spleen 18 (d 14) 320 100%,46,XY, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 10</td>
<td>Dec 1977 27/F 0 20 4 100%,46,XX, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 11</td>
<td>Jan 1978 28/F Liver 2 2 100%,46,XX, inv(16)(p13q22)</td>
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<tr>
<td>No. 12</td>
<td>Feb 1979 28/M 0 14 7 100%,46,XX, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 13</td>
<td>†May 1979 60/M 0 10 29 85%,46,XY, inv(16)(p13q22)</td>
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<tr>
<td>No. 14</td>
<td>March 1980 33/F Gum 11 147 100%,46,XX, inv(16)(p13q22)</td>
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<tr>
<td>No. 15</td>
<td>†May 1980 53/F 0 14 (d 14) 150 100%,46,XX, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 16</td>
<td>†July 1980 62/M Spleen 5 280 100%,46,XY, inv(16)(p13q22)</td>
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<tr>
<td>No. 17</td>
<td>Aug 1980 53/M 0 8 10 100%,46,XY, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 18</td>
<td>Sept 1980 63/M Spleen 4 320 90%,46,XY, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 19</td>
<td>†Dec 1980 44/M 0 23 86 100%,46,XY, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 20</td>
<td>April 1981 22/M Liver/nodes 5 186 100%,46,XY, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 21</td>
<td>†Dec 1981 45/F Nodes 7 126 100%,46,XY, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 22</td>
<td>†March 1982 40/M Scalp mass 6 63 100%,46,XY, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 23</td>
<td>Dec 1982 78/F 0 6 3 6 cells 46XX, del(16)(p22)</td>
</tr>
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<td>No. 24</td>
<td>†Jan 1983 35/M 0 28 100 75%,46,XY, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 25</td>
<td>Jan 1983 46/F Nodes 16 50 100%,46,XY, inv(16)(p13q22)</td>
</tr>
<tr>
<td>No. 26</td>
<td>Feb 1983 34/M Liver, spleen 15 83 100%,46,XY, inv(16)(p13q22)</td>
</tr>
</tbody>
</table>

*Marrow cytogenetic data correlates with date of diagnosis, unless otherwise stated.
†Patients relapsing in the CNS.
CNS LEUKEMIA IN AMML WITH inv(16)(p13q22)

level, or coagulation profile was observed for the group.

All patients presented with AMML-M4, commonly associated with an increased percentage (>4%) of marrow eosinophils (22 of 26 [85%]). In two patients who did not show bone marrow eosinophilia at presentation (No. 9 and 15), the eosinophilia became evident after induction chemotherapy was started. In both cases, initial marrow blast percentages were close to 100%, and presenting white cell counts were high, possibly masking the eosinophil population before treatment.

The dysplastic eosinophils demonstrated a range of maturity. At one end of the spectrum very immature, large eosinophil blast cells were observed. More mature eosinophils, with interspersed basophilic cytoplasmic granules were readily recognized in all patients with inv(16)(p13q22)/del(16)(q22) AMML. On review of the 384 G-banded patients, we observed 47 (12%) exhibiting initial bone marrow eosinophilia of more than 4% (Table 2). Such eosinophilia occurred in most cytogenetic groups, but was particularly evident in inv(16)(p13q22)/del(16)(q22) patients. In addition, morphologically abnormal eosinophils were not generally observed in the other cytogenetic groups (Fig 1).

Cytogenetic Findings

Twenty-five patients, at diagnosis (23 patients) or at subsequent relapse, showed inv(16)(p13q22), and one patient showed del(16)(q22). The chromosome 16 abnormalities were present in at least 90% of analyzed metaphases in all but one patient (No. 3). Sixteen patients had inv(16)(p13q22) as their sole karyotypic abnormality (Fig 2), and the remainder had additional chromosome changes, with trisomy 8 evident in four of these patients. Phytohemagglutinin-stimulated lymphocytes revealed a diploid karyotype in all patients with evaluable peripheral blood metaphases.

Response to Treatment and Survival

Twenty-five patients received induction chemotherapy. Patient 23 received a low-dose cytosine arabinoside regimen during his preleukemic phase, with no response, and died when not a patient of the institute. Twenty-three patients (92%) achieved complete remission (CR), the majority after one course (20 of 23, 87%). Patients 11 and 18 died during remission induction therapy of sepsis and of an uncontrolled ventricular arrhythmia, respectively. Both had hypoplastic marrows at the time of death. The median duration for first remission was 18 months (range, six to 72+ months), and median duration of survival was 34 months (range, 0.5 to 133 months). High second and third remission rates were observed with reinduction chemotherapy (nine of 16 [56%], and four of five [80%], respectively) (Table 3). No significant differences in remission duration or survival were seen between patients with inv(16)(p13q22)/del(16)(q22) alone and those with additional chromosome changes.

CNS Leukemia

Nine of the 26 patients (35%) relapsed in the CNS. In no case was CNSL evident at achievement of first marrow CR. The median time to develop CNSL from first CR was 19 months (range, six to 133 months), with patients 1 and 3 having gained second marrow remissions before developing CNSL. There were seven men and two women. The nine patients, when compared with those 17 who did not develop CNSL, tended to have higher presenting white cell counts (median, 86 x 10^9/L vs 50 x 10^9/L) and marrow eosinophil percentages (median 14% vs 8%) (P > .10). No marked difference in the incidence of markedly elevated serum LDH (>600) was observed between the two groups (four of nine [44%] vs ten of 17 [59%]). Of patients relapsing in the CNS, six of nine (66%) had inv(16)(p13q22) as their only karyotypic abnormality, and three of nine (33%) had additional chromosome changes. CNSL was not observed in the one patient with del(16)(q22). At the time CNSL was diagnosed, five patients were in marrow relapse, and four were in remission. Subsequently, these latter four patients all relapsed in the bone marrow.

Eight of the nine patients developing CNSL presented with abrupt onset of neurologic symptoms involving headache, nausea and vomiting, tinnitus, diplopia, and/or gait disturbance. CNSL was diagnosed only at autopsy in patient 13. Neurologic examination was abnormal in five patients revealing papilloedema, third, fifth, or seventh cranial nerve palsies, and cerebellar dysfunction.

All patients had leptomeningeal leukemia with cerebrospinal fluid (CSF) pleocytosis, abnormal cytology, and elevated protein levels (median, 75 mg/dL; range, 58 to 110 mg/dL). In addition, abnormal eosinophils, identical to the initial marrow population, were present.
Fig 1. (A) Bone marrow smear from case 24, showing acute myelomonocytic leukemia (AMML-M4) and large eosinophils with inter-
spersed basophilic granules (heavy arrows). (B) Bone marrow smear from a patient with acute myelogenous leukemia (AML-M2),
t(8q;21q) and marrow eosinophilia. Eosinophils are left-shifted, but otherwise unremarkable (light arrows). Wright-Giemsa stain. Magnification x600.

Fig 2. G-banded karyotype of a metaphase from the bone marrow sample obtained from a patient with acute myelomonocytic leukemia (AMML-M4). The arrow designates the chromosome number 16 with the pericentric inversion [inv(16) (p13q22)].

Fig 3. Centrifuge preparations of cerebrospinal fluid from cases No. 24 (A), 22 (B), and 21 (C), each showing immature cells with abnormal eosinophil granules (arrows). Wright stain. Magnification x600.
in the CSF of six of nine (66%) of the group (Fig 3). Six of the nine CNS patients (66%) demonstrated two or more enhancing lesions on CT brain scan, consistent with intracerebral myeloblastomas (Fig 4). Open-brain biopsy performed in two cases confirmed the diagnosis of leukemia. Treatment modalities used for CNSL included cranial irradiation, high-dose cytosine arabinoside, and intrathecal therapy. Four of the six patients achieved CNS remission. The median survival of patients with inv(16)(p13q22) AMML developing CNSL v those 16 patients who did not was not significantly different (median, 27 months v 31 months).

We reviewed the incidence of CNSL in the 384 G-banded patients with AML to compare the rate of CNSL within various cytogenetic and morphologic groups and to ascertain the incidence of intracerebral myeloblastomas in AML (Table 4). The overall incidence of CNSL was 26 of 384 (7%), and no other cytogenetic group had an equivalent incidence of CNSL relative to inv(16)(p13q22) patients. Extended survival is reported to increase the risk of CNSL; however, in the two cytogenetic groups at this institute [t(8q;21q) and t(15q;17q)] with equivalent survival to inv(16)(p13q22) patients, this was not observed.

Neither did the morphological subgroups of AML show a high incidence of CNSL. Both AMoL (M5) and AMML (M4) have been reported to have an increased incidence of CNSL. We observed a slightly higher occurrence of CNS disease in the M5 group (one of 13, 8%); however, the M4 patients not associated with chromosome 16 abnormalities had a low incidence (five of 91, 5%). In addition, G-banded patients who had bone marrow eosinophilia (≥4%) and patients with high initial white cell counts developed CNSL rarely when inv(16)(p13q22) cases were excluded from analysis. Last, the six cases of intracerebral myeloblastomas appeared unique to the inv(16)(p13q22) AMML patients, and were not observed in any other cytogenetic or morphologic subgroup of AML.

**Eosinophilia in Other Cytogenetic Groups**

Twenty-five patients without abnormalities in chromosome number 16 had bone marrow eosinophilia of

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**Table 3. Remission Rate, Remission Duration, and Survival for 26 Patients With inv(16)(p13q22)**

<table>
<thead>
<tr>
<th>Remission No.</th>
<th>Patient No. (%</th>
<th>Median Duration CR (mo)</th>
<th>Range (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td>23/25 (92)</td>
<td>18</td>
<td>(9-72)</td>
</tr>
<tr>
<td>Second</td>
<td>9/16 (56)</td>
<td>9</td>
<td>(2-93)</td>
</tr>
<tr>
<td>Third</td>
<td>4/5 (80)</td>
<td>6</td>
<td>(2-12)</td>
</tr>
</tbody>
</table>

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**Fig 4. Examples of intracerebral myeloblastomas.**
more than 4%. Nine patients had a diploid karyotype (one had a constitutional chromosomal defect), four had a translocation (8q:21q), and 12 had a variety of other abnormalities. The complete remission rates were 56%, 75%, and 33%, and median survivals were 37 weeks, 135 weeks, and 4 weeks, respectively, in these three groups. The eosinophils in these cases demonstrated a left shift and mild dysplasia (Fig 1B), but none of the blast cells had dysplastic eosinophil granules. None of these patients developed CNSL.

**Occurrence of AMML and Bone Marrow Eosinophilia Before Banded Chromosome Studies**

On review of adult patients with AML treated at this institute between 1965 and 1973, we observed 13 patients with AMML, bone marrow eosinophilia, and abnormal eosinophils, characteristic of the inv(16)(p13q22) group. Chromosome analysis using air-dried direct preparation was performed in nine of these patients with seven of nine (78%) having a diploid complement, and two of nine (22%) showing 47 chromosomes, with an additional C and B, respectively. Ten of 13 patients (77%) achieved CR, with a median survival of 21 months (range, one to 47+ months). CNS relapse occurred in three of 13 patients (23%), with abnormal eosinophils present on CSF analysis in one case and intracerebral myeloblastomas documented in two patients.

**DISCUSSION**

The 1984 Fourth International Workshop on Chromosomes in Leukemia included inv(16)(p13q22) and del(16)(q22) as a specific cytogenetic group within AML. In this review of 26 patients with chromosome abnormalities, we confirm the clinicopathologic associations of AMML (M4), initial bone marrow eosinophilia, and abnormal eosinophil morphology. In addition, our long follow-up period and consistency in induction chemotherapy regimens has led to further clinical observations with regard to this cytogenetic subgroup of AML.

Although increased numbers of bone marrow eosinophils may be observed in most chromosomal categories of AML, only patients with inv(16)(p13q22)/del(16)(q22) characteristically demonstrate this association (Table 1). All our patients demonstrated abnormal marrow eosinophils, typified either by intensely staining basophilic granules, or by marked immaturity, approaching blastoid cells. These eosinophils appear to be morphologically malignant. Patients who have AMML and such marrow eosinophils should have banded chromosome studies performed because of the favorable prognosis of this group. Although patients with translocation (8q:21q) with eosinophilia share the same good prognosis with the inv(16)(p13q22)/del(16)(q22) patients, CNSL was not seen in the t(8q:21q). The patient with diploid karyotypes or cytogenetic abnormalities other than inv(16)(p13q22)/del(16)(q22) or t(8q:21q) had low response rates, short survival, and no cases of CNSL. The eosinophil morphology differed in these patients from the inv(16)(p13q22)/del(16)(q22) patients in that, while the eosinophils demonstrated a left shift, minimal dysplasia was seen and no blast cells had dysplastic eosinophilic granules.

The median duration of survival for the 26 patients treated at this institute was 34 months. Seven patients remain in first remission (11+, 12+, 14+, 39+, 42+, 52+, and 72+ months), emphasizing the potential for long-term survival and possible cure. In addition, the high second and third remission rates observed contribute substantially to the encouraging survival. No significant difference in remission duration and survival was seen between patients who had chromosome 16 abnormalities alone, and those with additional cytogenetic changes. In particular, trisomy 8, which was the most consistent additional abnormality in the group, has a poor prognosis in this series, with a CR rate of five of 17 (29%) and a median survival of 17 weeks. This similarity in prognosis for both groups suggests that inv(16)(p13q22)/del(16)(q22) is the dominant cytogenetic determinant for survival. Leptomeningeal leukemia developed in nine of 26 patients (35%), with concurrent intracerebral myeloblastomas present in six of nine (66%). An equivalent incidence of CNSL was not seen in any other morphologic or cytogenetic subgroup of AML treated at the institute during the same period. Acute leukemias with monocytoid features (AMML[M4] and AMoL[M5]) are reported to
CNS LEUKEMIA IN AMML WITH inv(16)(p13q22)

15. Evans AE, Gilbert ES, Zandstra R: The increasing incidence

Develop CNSL more frequently than other morphologic subgroups with AML. In this study, only patients with inv(16)(p13q22) AMML demonstrated a high incidence of CNSL, suggesting it is some characteristic other than morphology that predisposes patients with the inv(16) abnormality to the development of CNSL.

The pathogenesis of leptomeningeal leukemia in these patients is unknown. Targeting of leukemia cells to the CNS probably occurs early in the disease. In animal model systems, sublines of malignant cells capable of colonizing in specific organs have been established. The steps involved in specific organ targeting are complex, and incorporate interaction between the metastasizing cell surface glycoproteins and the host endothelial cells. Cell lines with inv(16)(p13q22)/del(16)(q22) have not been developed, and their surface properties are not explored. However, the work in animal experiments on metastatic processes provides challenging areas of investigation in this cytogenetic subgroup of acute leukemia.

The occurrence of intracerebral myeloblastomas in six of nine (66%) of patients relapsing in the CNS is a unique clinical finding for this cytogenetic group. Again, on review of all morphologic and chromosomal subgroups of AML treated in the same period, such intracerebral myeloblastomas were observed exclusively in inv(16)(p13q22) AMML patients. Extramedullary myeloblastomas are rare in acute and chronic leukemia, whereas intracerebral myeloblastomas in AML form the basis of case reports only. In the six patients with abnormal CT brain scans, the lesions were adjacent to the leptomeninges, implying direct invasion of the CNS parenchyma from the subarachnoid space. Such direct spread was established in one patient (No. 19) who underwent open-brain biopsy. In this case, a histologically confirmed tract of leukemia extended from the leptomeninges to a circumscribed intracerebellar lesion. The pathogenesis of parenchymal invasion may involve the abnormal eosinophils observed in the CSF. In vitro, certain peptides contained within eosinophil granules (eosinophilic major basic protein and eosinophilic cationic protein) can generate marked endothelial damage and profound disturbances in coagulation. Such destructive peptides released from the observed CSF eosinophils could facilitate infiltration of leukemia cells and the subsequent formation of intracerebral myeloblastomas.

In conclusion, this review of 26 patients with inv(16)(p13q22)/del(16)(q22) confirms the associations of AMML (M4), initial bone marrow eosinophilia, and abnormal eosinophil morphology previously reported. In addition, our patients had excellent remission rates and a favorable survival. The development of CNSL in nine patients (35%), with concurrent intracerebral myeloblastomas in six cases, is a new clinical association for inv(16)(p13q22)/del(16)(q22) AMML. This high incidence of CNS relapse and unusual pattern of involvement was unique to the cytogenetic group. Considerable morbidity was suffered by patients relapsing in the CNS, and in the future, consideration for incorporation of a CNS prophylaxis program is warranted in such cases.
A unique pattern of central nervous system leukemia in acute myelomonocytic leukemia associated with inv(16)(p13q22)

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