Translocation (11;16)(q23;p13) Acute Myelogenous Leukemia and Myelodysplastic Syndrome

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Abstract. The purpose of this study is to examine the relationship of t(11;16)(q23;p13) to the type of myeloproliferative disorder noted by hematopathology. Previously, t(11;16) has been reported in fewer than 20 patients, all with the diagnosis of therapy-related (secondary) acute myelogenous leukemia (sAML) or myelodysplastic syndrome (MDS). Putative involved genes are the MLL on 11q23 and CBP at 16p13. Data from The University of Texas M. D. Anderson Cancer Center (UTMDACC) Cytogenetics Laboratory revealed 3 patients with t(11;16) observed during the past 5 years. Two of the patients had a prior diagnosis of non-Hodgkin lymphoma (NHL) and had been treated with chemotherapy, which included cyclophosphamide. The other patient presented with de novo AML and no history of cancer or chemotherapy. Two of the 3 patients had t(11;16) as the sole cytogenetic abnormality. One patient had a t(11;16) clone that included t(9;21) and t(10;21) as additional changes. Translocation (11;16) has previously been reported only as being therapy-related. In this study, the t(11;16) was seen in 2 patients with previous lymphomas treated with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP). A single patient with apparently de novo AML constitutes the first reported instance of non-treatment associated t(11;16) AML.

Keywords: Translocation (11;16)(q23;p13), AML, MDS, secondary AML/MDS

Introduction

Translocation (11;16)(q23;p13) is a rare recurrent translocation associated with myeloproliferative disorders. Less than 20 cases have been reported in the literature; their median age was 14 yr [1]. These translocations have all been associated with previous treatment for cancers of various types. The reported cases had either acute myelogenous leukemia (AML) or myelodysplastic syndrome (MDS). The previous cases had either AML, type M4 myelomonocytic leukemia, or M2 acute myelogenous leukemia with some differentiation. The MDS cases included chronic myelomonocytic leukemia and refractory anemia. Some had excess blasts and some were in transformation [2,3].

The objectives of the present study were:
1. to explore the incidence of t(11;16)(q23;p13) in the patient population of the University of Texas M. D. Anderson Cancer Center; and
2. to determine if the patients had a history of prior cancer and/or treatment for cancer.

Methods

The cytogenetics database from January 1998 to January 2003 was reviewed. All karyotypes that had been reported as t(11;16)(q23;p13) were selected for evaluation.

The karyotypes were all prepared by standard cytogenetics methods and were stained with the Giemsa trypsin G-banding techniques[4]. In some instances, whole chromosome paint fluorescence in situ hybridization (FISH) was used to demonstrate translocation of chromosome 11 or 16. The probes were purchased from Vysis, Inc., and used according to the manufacturer's directions.
Results

Approximately 255 AML cases and 184 MDS cases are seen at UTMDACC per yr. Three patients with t(11;16)(q23;p13) were seen in 5 yr. This resulted in the occurrence of 2 t(11;16)(q23;p13) patients in 1277 new cases of AML seen in 5 yr; ie, an incidence of an approximately 0.2%. The MDS case with the translocation was 1 of 822 new cases; an incidence of approximately 0.1%.

The specific cytogenetic changes observed in each of the 3 patients are listed in Table 1. Two of the patients had AML (one M4 and one M5). The third patient had MDS of the refractory anemia type. The average age was 51 yr; there were two females and one male.

One of the patients had t(11;16) as the sole abnormality (Figs. 1 and 2). One had the t(11;16) and the diploid karyotypes as two distinct clones. One had a complex clone; in addition to t(11;16), this complex clone had t(9;21) and t(10;21) in 11 metaphases as well as 5 metaphases that were diploid female.

Discussion

Abnormalities of 11q23 have been associated with AML. The fusion gene t(11;16)(q23;p13) has been identified in monocytes, granulocytes, and erythroblasts, but not in lymphocytes. Associated disorders have included AML, M2, and M4, CMML, and RAEBT. Chromosome region 11q23 is the site of the MLL gene. MLL has two DNA binding motifs (ie, AT Hook and Zn Finger). It also contains a DNA methyltransferase motif, transcriptional regulatory factors, nuclear localization genes, and a bromodomain [4].

The putative site on 16p13 is the CBF gene, which contains regions for nuclear localization and a transcriptional adaption/deactivator, binds CREB, and has histone acetyltransferase activity. Fusion of the MLL and CBF genes may result in an oncogene that promotes histone acetylation of genes modified by the MLL and reduces CBP cell cycle inhibition. The oncogenic potential may possibly reflect promotion of histone acetylation and/or the altered lack of CBP cell cycle inhibition [5,6].

Translocation (11;16)(q23;p13) is a rare event that occurs in less than 0.2% of patients with AML that have previously been treated for cancers and are referred to our institution. This is the first report of a patient who presented with t(11;16) and AML M4 and no prior history of cancer or cancer chemotherapy.

Acknowledgements

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Table 1. Tabulation of the clinical and karyotypic findings in 3 patients with translocation (11;16)(q23;p13) AML and MDS.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/Sex</th>
<th>Original Cancer/Year</th>
<th>AML/MDS</th>
<th>Karyotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>37/F</td>
<td>NHL Rx *CHOP/2001</td>
<td>Refractory Anemia</td>
<td>46,XX,t(11;16)(q23;p13)[12]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>46,XX[8]</td>
</tr>
<tr>
<td>II</td>
<td>53/F</td>
<td>NHL Rx *CHOP/1997</td>
<td>AML M5</td>
<td>46,XX,t(9;21)(q31;q22), t(10;21)(q22;q22), t(11;16)(q23;p13)[11]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>46,XX[5]</td>
</tr>
<tr>
<td>III</td>
<td>63/M</td>
<td>None</td>
<td>AML M4</td>
<td>46,XY,t(11;16)(q23;p13)[20]</td>
</tr>
</tbody>
</table>

*C = Cyclophosphamide H = Doxorubicin O = Vincristine P = Prednisone
Fig. 1. A karyotype prepared by standard cytogenetics methods and stained by the Giemsa trypsin G-banding technique demonstrates translocation (11;16)(q23;p13) (arrows).
Fig. 2. Whole chromosome paint fluorescence in situ hybridization (FISH) using an 11q23 probe demonstrates a translocation of 11q23 to 16.

**Bibliography**