Acute Monocytic Leukemia with (8;22)(p11;q13) Translocation
Involvement of 8p11 as in Classical t(8;16)(p11;p13)

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ABSTRACT: *A new case of acute monocytic leukemia observed in a 73-year-old male (ANLLM5) with an unusual t(8;22)(p11;q13) is reported. The blasts did not demonstrate erythrophagocytosis, but the presence of both naphtol-ASD-chloro-acetate esterase and butyrate esterase activities was similar to that seen in cases with t(8;16)(p11;p13). Involvement of the 8p11 region in ANLLM4 and M5 is discussed, being the third most frequent rearrangement in acute leukemia with monocytic components seen at our Center.*

INTRODUCTION

Translocation (8;16)(p11;p13) is a recurrent chromosome rearrangement found in acute monocytic leukemias (M5ANLL) [1–8], or acute myelomonocytic leukemias [9–13] and less often in acute myeloblastic leukemia (AML) [14]. Two other translocations, (t(6;8)(q27;p11) and t(8;19)(p11;q13)), also found in ANLLM5 [7] and involving 8q11 band, have been regarded as variants of t(8;16). In many of the reported patients, cytological characteristics of blasts including erythrophagocytosis in bone marrow cells or global increase in enzymatic activities (peroxidase, naphtol-ASD-acetate-esterase, butyrate-esterase) were present. We report a patient with ANLLM5 and t(8;22)(p11;q13), which we suggest represents another variant of t(8;16), also involving 8p11 region.

MATERIALS, METHODS AND RESULTS

Case Report

This male patient, aged 73, had no previous medical history. No organomegaly was found. The blood count showed: hemoglobin, 9.3g/dl; MCV, 93 μ^3; leucocytes, 26.6.109/L (neutrophils 22%, monocytes 6%, blasts 44%); platelets 67.109/L. The bone marrow aspirate was hypocellular with 56% blasts. Serum and urinary lysozyme were not measured.

The patient was treated with a daunorubicin—AraC regimen, followed by G-CSF, and achieved complete remission. He relapsed 5 months later, however, and died 7 months after diagnosis.

Cytogenetic Results

Cytogenetic study was performed at diagnosis after 24-hours of bone marrow culture. Chromosomes were analyzed using R-banding and karyotype was described according to the ISCN.

Chromosome study of bone marrow revealed a clone with a translocation (8;22)(p11;q13) associated with trisomy 8 (28 cells) (Fig. 1). Only one cell had a normal karyotype. The two chromosomes 16 were not involved in structural rearrangements.

Morphology

Blood and bone marrow smears were stained with May-Grünwald-Giemsa. Blasts had large size (25–30 μm) and low N/C ratio (0.6–0.7). Nucleus had either regular or irregular contour, and no visible nucleolus. Cytoplasm was basophilic and contained up to 50 dispersed azurophilic granules. Less than 0.1% blasts showed erythrophagocytosis. Cytochemical tests were performed by conventional methods. Peroxidase was negative. Non-specific (naphtol-ASD-acetate) esterase was strongly positive and inhibited by sodium fluoride. All blasts were positive for naphtylbutyrate esterase, and 13% were positive for both naphtylbutyrate and naphtol-ASD-choloroacetate esterases.

An electron microscopy study of the nucleus showed no heterochromatin and one nucleolus, and showed the cytoplasm to have numerous small monocytic granules. Ultrastructural peroxidase was moderately positive in most but not all granules.

An immunologic study was not performed.

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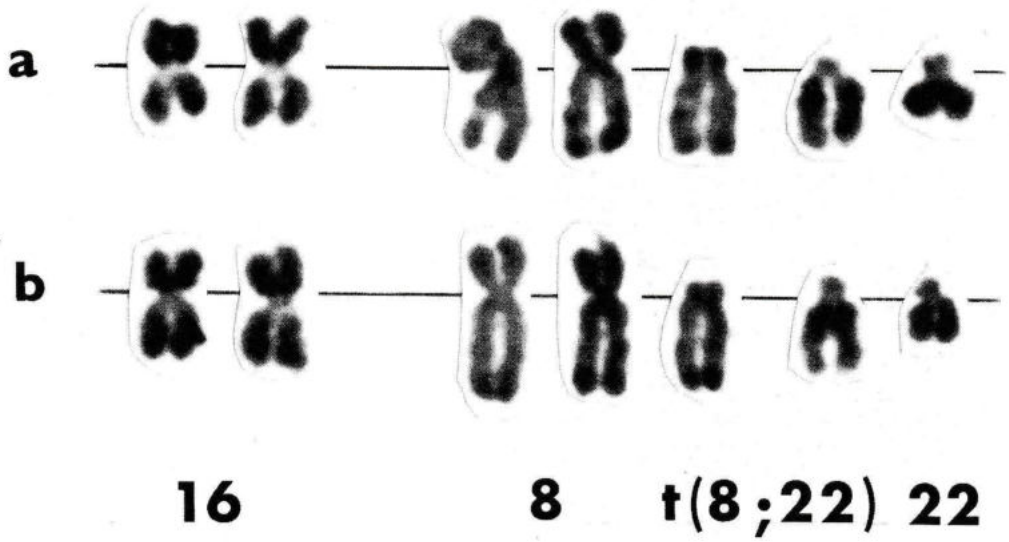

Figure 1 (a, b) Partial karyotypes showing the unusual (8;22)(p11;q13) translocation associated with trisomy 8. Apparently, chromosomes 16 were not involved in this rearrangement.

DISCUSSION

The patient reported here had ANLLM5 displaying some cytologic pictures commonly observed in ANLL with t(8;16). Although blasts in our patient did not demonstrate erythrophagocytosis, they showed the presence of both naphtol ASD-choloroacetate esterase and butyrate esterase activities in the same cell, a feature which has been reported in ANLLM5 with t(8;16)(p11;p13) (for review see [5, 8]). The translocation in our patient involved the 8p11 region, as in the classical t(8;16) and its two variants, t(6;8)(q27;p11) and t(8;19)(p11;q13), observed in ANLLM5 [7]. This new observation adds further argument to the hypothesis that the 8p11 region is important in monocytic differentiation [15] although the gene(s) which may be involved in the role are unknown.

Proto-oncogene c-sis is located on 22q13, the other breakpoint of the translocation we report here. This proto-oncogene is known to be translocated from chromosome 22 to chromosome 9 in chronic myelocytic leukemia [16] but its role in oncogenesis still has to be defined in human leukemias. No further analysis was performed in our patient to study rearrangement or modification of expression of this proto-oncogene.

In our series of 275 karyotypes in de novo ANLL (including 90 cases of ANLLM5 or ANLLM4), 5 cases (3 ANLLM4 and 2 ANLLM5) had a t(8;16)(p11;q13) ([5, 9] and unpublished data). With the addition of the present case, rearrangements involving 8p11 were thus present in 6 patients, i.e., 6.5% of all cases of ANLLM4 and ANLLM5, representing in our Center the third most frequent rearrangement in these FAB subtypes (after rearrangements of regions 16q(22%) and 11q23 (17%)). Further cases of rearrangements involving 8p11 in ANLLM5 and ANLLM4 should be published, in order to confirm the role of the abnormalities of this chromosomal region in leukemogenesis.

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