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BURKITT'S LYMPHOMA WITH 8;14 AND 2;8 TRANSLOCATIONS SIMULTANEOUSLY

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Burkitt's lymphoma of a ten-year-old boy with specific 8;14 and variant 2;8 translocations is reported. The post mortem diagnosis of Burkitt's lymphoma was based on histological picture and the cytogenetic findings of the tumor biopsy. The child died four days after clinical admission. Because of the rapid progression of the disease immunological and serological investigations could not be performed. Therefore several questions remained unclarified. It is supposed that in the patient's B-lymphocytes multiple transformation events occurred leading to the development of the polyclonal lymphoma, similarly to that described in trasplant-associated lymphoproliferations.

INTRODUCTION

A clinical entity described by Burkitt in 1958 /10/ in East-African children occurs at high frequency in equatorial Africa and New Guinea but has a much lower incidence in the rest of the world. Since 1965, however, there have been several sporadic cases reported from all over the world /2, 3, 17/. Burkitt's lymphoma can be characterized by a specific reciprocal translocation between chromosome 8 and 14. This translocation can be found in 80 % of patients with this disease. In the remaining 20 % two variant translocations: t(2;8) and t(8;22) can be observed /9/.

Hereby we report a case of non-endemic Burkitt's lymphoma in the cell lines of which the typical translocation t(8;14) and variant translocation t(2;8) simultaneously appeared.

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CASE REPORT

The patient, a ten-year-old boy, did not suffer from any serious disease before. His mother has been treated for Hodgkin lymphoma for a year. In the history of the patient abdominal pain and meteorism were mentioned. On clinical admission the extremely thin, dysmorphic patient had enlarged abdomen and serious dyspnoe. In the right part of the abdomen a hard painless tumor of infant's head size filling the pelvis could be presumed. Ultrasonography revealed a high density tumor mass of 12 x 14 cm size. Haemostatus was abnormal. No abnormal cells in peripheral smear and bone marrow were seen. On the third day after his admission laparotomy was performed. A tumor with lobulated surface, in close connection with the surrounding tissues became visible. Metastatic infiltrations of the mesenterium, omentum maius, peritoneum and that of abdominal wall were observed. Biopsy was made without any effort to remove the tumor mass. The child died in two days.

Post mortem histologic diagnosis was lymphoblastic lymphoma of Burkitt's type (Figure 1) with the starry sky pattern. Because of the rapid progress of the disease immunological and serological investigations could not be performed.

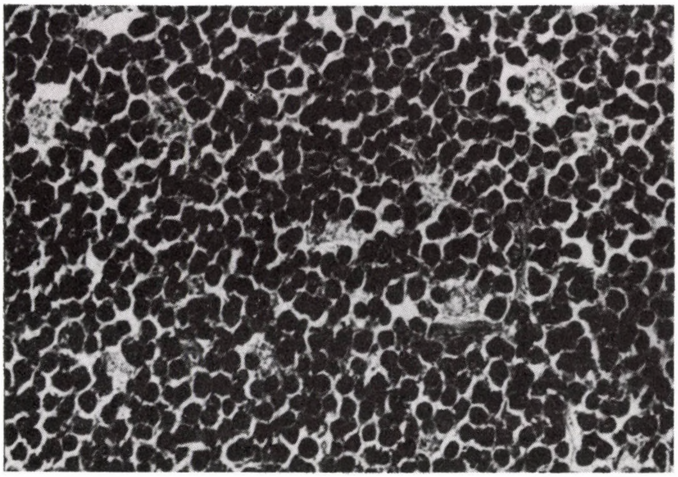


Fig. 1. Burkitt's lymphoma with the starry sky pattern (PAS, 320X)

CYTOGENETIC STUDIES

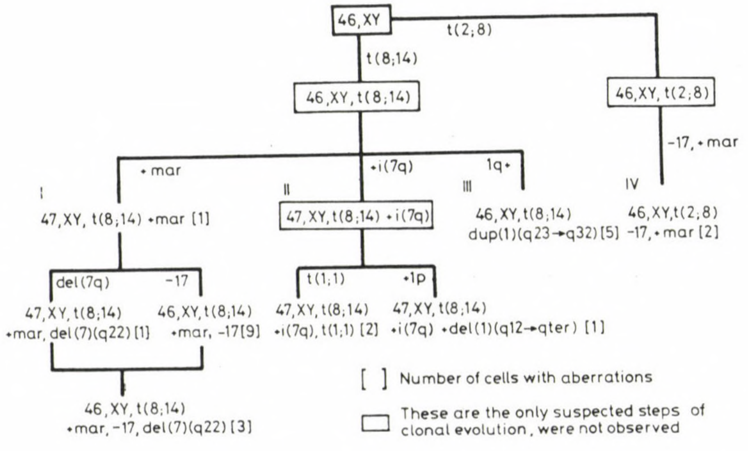
Chromosome analyses were carried out from the tumor tissue. It was cut into small pieces and cells obtained were then suspended in the culture medium (TC 199). Chromosome analyses were performed by direct method. After using modified Giemsa banding technique /28/, karyotypes were described according to the International System for Human Cytogenetic Nomenclature

/18/. We karyotyped as many cells as we could. 24 metaphases were photographed and arranged into karyograms. Each of them was abnormal. Cytogenetic picture proved to be rather complicated.

The modal chromosome number was 46. Four various cell lines were found, in which the steps of clonal evolution could be followed (Table I).

TABLE I

Clonal evolution in cells of Burkitt's lymphoma



In the first cell line of the analysed cells the specific t(8;14) (q24;q32) together with an unidentified marker chromosome was found. In twelve of these cells loss of chromosome 17 occurred. Besides, in three metaphases it was combined with a deletion of the long arm of chromosome 7.

In the second cell line and extranumeral isochromosome of the long arm of chromosome 7 associated with t(8;14). In addition to this, an extra lp (breakpoint ql2), while in two others a tandem translocation of chromosomes 1:t(1;1)(q32;q32) appeared.

Besides t(8;14) the third line was characterized by duplication of one part of the long arm of chromosome 1 (dup 1q)(q23;q32).

The fourth cell line had a t(2;8)(p13;q23) the variant translocation of Burkitt's lymphoma consisted of only two cells. Both of them had monosomy 17 and a marker chromosome.

It is interesting that the marker chromosome appeared in the metaphase with the loss of chromosome 17 only. This implies that chromosome 17 may take part in forming the marker chromosome.

DISCUSSION

It was Manolov and Manolova /21/ who discovered that Burkitt's lymphoma can be characterized by the specific 14q+ marker chromosome Zech et al. /32/ identified the exact translocation between chromosomes 8 and 14. Manolova and Manolov /22/ demonstrated this translocation to be reciprocal. This specific translocation /t(8;14)/ has been described in many cases of both endemic and non-endemic Burkitt's lymphomas and in acute leukemias of Burkitt's type as well /6, 26, 31/. Recognition of the variant translocations: the t(2;8) and the t(8;22) in sporadic cases seemed to help to clarify the etiology /1, 4, 5, 23/. In two years, however, Bernheim et al. /7/ managed to show variant translocations in endemic cases, too, so he concluded that there was no direct connection between the type of translocation and Epstein-Barr Virus (EBV) - association. It was Sandberg and Wake /27/ who suggested that the anomaly of the long arm of chromosome 8 is more specific for Burkitt's lymphoma than the 14q+ marker. Gene mapping studies of these tanslocations have cleared the underlying molecular events. While at breakpoint 8q24 the c-myc protooncogene, at the breakpoints of chromosomes 2, 14 and 22, one of the immunoglobulin genes are located: at 14q32 the heavy chain gene (μ), at 2p12 the light chain (κ) and at 22q11 the λ light chain gene have been assigned /13, 15, 20, 30/. By the rearrangement in the t(8;14) the c-myc is translocated near the μ heavy chain gene. In the other two translocations the immunoglobulin genes are translocated next to the c-myc oncogene /9, 14/. All the three situations result in the deregulation of c-myc oncogene.

The challenging fact in our case is that the two different translocations, the t(8;14) and (2;8) appeared simultaneously in the same sample of the tumor. While the (8;14) was observed in 22 out of 24 cells, the t(2;8) appeared only in two remaining cells. This may indicate a greater proliferative advantage of the cell line with t(8;14) compared to cells with the variant translocation t(2;8). The question arises that, if the disease had not been of so rapid progression, this variant translocation perhaps would not have been visible in a later stage of the disease.

In the additional chromosome changes 1, 7, 17 and marker chromosomes were involved. According to the Fifth Workshop /16/ 14 out of 21 with standard or variant 8q24 translocations had additional chromosome abnormalities. The most common additional change was duplication of part of 1q, always including 1q21-32 which was seen in four patients. One patient had +7 Knuutila et al. /19/ reported chromosome abnormalities in 16 patients with Burkitt's lymphoma or L3 acute lymphocytic leukemia. Trisomy 7 was the most frequent numerical aberration. In addition to one patient had t(1;7) (q21;q32) a gain of a 7q- chromosome and a t(7;?)(7q22;?). They observed structural aberrations of chromosome 1 in five patients. Besides, they wrote -17, 17p+ and appearance of marker chromosomes in patients with Burkitt's lymphoma. Duplications in 1q have been detected in a wide variety of human neoplasms /24, 25/, whereas trisomy 7 is often detected in patients with the t(8;14) /8/.

Cleary et al. /11, 12/ established that most of the patients in transplant-associated lymphoproliferations developing lymphomas have monoclonal tumors, but the disease is multiclonal in biopsy material from different anatomic sites showing different proliferating clones of tumor cells. It is suggested that in these patients multiple independent transformation events occur as a consequence of uncontrolled EBV infection /29/.

In our case it is particularly interesting that cells with various karyotype were obtained from the same part of tumor mass. It is possible that an unknown infection disturbed the immune system's defensive mechanism resulting in an insufficient elimination of the latently EBV-infected B-lymphocytes.

Both primary and secondary immunodeficiencies may induce specific karyotypic abnormalities by the reactivation of a latent EBV-infection /29/. Our data suggest that in the patient's B-lymphocytes multiple transformation events occurred leading to the development of the polyclonal lymphoma.

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