CONCISE REPORT

Specific Translocations Characterize Burkitt’s-Like Lymphoma of Homosexual Men With the Acquired Immunodeficiency Syndrome

By R. S. K. Chaganti, Suresh C. Jhanwar, Benjamin Koziner, Zalmen Arlin, Roland Mertelsmann, and Bayard D. Clarkson

A Burkitt’s-like B-cell lymphoma (BLL) has recently been shown to be associated with the acquired immunodeficiency syndrome (AIDS), which affects homosexual men. We report cytogenetic studies of two BLL tumors in homosexual men. Both tumors had chromosome translocations characteristic of Burkitt’s lymphoma (BL), one the t(8;14) and the other the t(8;22). The pathway of lymphomagenesis in this disorder is discussed in the light of recent data on chromosome change and localization of immunoglobulin genes and oncogenes.

A Burkitt’s-Like B-cell lymphoma (BLL) has recently been described in seven homosexual men with the acquired immunodeficiency syndrome (AIDS), adding this tumor to the already wide list of neoplasms associated with this syndrome. Cytogenetic studies reported on one BLL tumor indicated only normal karyotypes. In contrast, endemic as well as nonendemic Burkitt’s lymphoma (BL) cells are characterized by specific translocations that affect chromosomes 2, 8, 14, and 22. The most frequent of these translocations is t(8;14)(q24;q32), while the variant translocations t(2;8)(p12;q24) and t(8;22)(q24q11) seem to occur less frequently. We have studied the chromosomal complements of tumors from two homosexual men with AIDS who developed BLL. Tumor cells from one exhibited the 8/14 translocation and those from the other exhibited the variant 8/22 translocation. To our knowledge, this is the first report of abnormal karyotypes in any tumors associated with AIDS.

CASE REPORTS

Patient 1

The patient is a 39-yr-old white male who had frequent homosexual contacts. He has had a history of alcoholism and use of recreational drugs. His past medical history included hepatitis, syphilis, gonorrhea, and amebiasis. In July 1982, he noticed a lump on the back of his neck at the level of the hairline. This was followed by development of a right cervical mass. Evaluation at a local clinic revealed right anterior and posterior cervical lymph nodes and shotty bilateral axillary nodes. Further evaluation at another hospital included two lymph node biopsies. The first, of a right cervical node, performed 2 wk prior to admission to Memorial Hospital (MH) on October 3, 1982, gave equivocal results. Repeat biopsy of a right posterior cervical node performed a week later demonstrated a diffuse malignant lymphoma of Burkitt’s type. During this period he was free of fevers, sweats, or chills; his appetite was good, although he lost 5 lb in weight.

Physical examination upon admission to MH revealed a middle-aged man in good state of nourishment and no apparent distress. He was noted to have a purplish macular lesion on the dorsal shaft of his penis, which was diagnosed as probable early Kaposi’s sarcoma by a consulting dermatologist. Results of hematologic examination revealed a white blood cell count of 4,500/cu mm with normal differential counts. Hemoglobin was 14.9 g/dl and the platelet count was 14,700/cu mm. Biochemical values included alkaline phosphate (AP) of 173 U/liter (normal up to 115), lactate dehydrogenase (LDH) of 299 U/liter (normal up to 230), and SGOT of 54 U/liter (normal up to 25). Epstein-Barr virus-viral capsid antigen (EBV-VCA) and cytomegalovirus (CMV) titers were 1:640 and 1:16, respectively. Abdominal and pelvic CT scans and chest x-ray were normal. The liver and spleen scan was abnormal, with a photon-deficient area in the right hepatic lobe. Bone marrow aspiration and biopsy from the left posterior iliac crest revealed infiltration with L3 lymphoblasts. Cerebrospinal fluid (CSF) cytology was negative for lymphoma. The patient was started on MH protocol L17M and is currently responding favorably to this treatment.

Patient 2

The patient is a 29-yr-old white male who began homosexual activity at age 20. He had contacts with approximately one new homosexual partner per week until 4 mo prior to the present illness. He denied use of recreational drugs. His past medical history included syphilis, gonorrhea, and hepatitis, and a single episode of herpes genitalis. He also suffered proctitis and a perirectal abscess. He developed night sweats, weight loss, and generalized bone pain, which he attributed to heavy alcohol consumption (approximately a half gallon of scotch whiskey per week). He entered a detoxification clinic where he developed a right-sided seventh nerve paralysis with dysarthria. A neurologic evaluation led to a tentative diagnosis of Bell’s palsy. His symptoms were not relieved by analgesics and he entered a local hospital where a bone marrow aspiration revealed infiltration with L3 lymphoblasts.

Physical examination upon admission to MH on October 24, 1982 revealed a thin diaphoretic male with right facial nerve paralysis and facial nerve paresis on the left, but otherwise in no apparent distress. Shotty bilateral posterior cervical adenopathy, a 4 x 5 cm left axillary mass infiltrating the skin, a 2 cm right axillary node, and bilateral shotty inguinal adenopathy were noted. Results of hematologic examination revealed a white blood cell count of 12,400/cu mm with 45 polymorphonuclear cells, 3 bands, 8 metamyelocytes, 9 myelocytes, 35 lymphocytes, and 4 nucleated red blood cells. Hemoglobin was 12.4 g/dl and the platelet count was 49,000/cu mm.

From the Laboratory of Cancer Genetics and Cytogenetics, Departments of Pathology and Hematology and Lymphoma Service, Memorial Sloan-Kettering Cancer Center, New York, NY. Supported in part by the NCI Grant CA 15094.

Address reprint requests to Dr. R. S. K. Chaganti, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10021.

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Prothrombin time, partial prothrombin time, blood urea nitrogen, creatinine, and uric acid were normal. Abnormal biochemical values included a phosphate of 5.4 mg/dl (normal up to 4.2), AP of 137 U/liter, LDH of 1,786 U/liter and SGOT of 45 U/liter. EBV-VCA and CMV titers were 1:640 and 1:16, respectively. VDRL and toxoplasma titers as well as HbS antibody, however, was positive. CT scan of the head and chest x-ray were normal. A bone marrow aspiration and biopsy as well as a right axillary node biopsy were performed, and a histologic evaluation of these led to a diagnosis of diffuse undifferentiated lymphoma (Burkitt’s type); CSF cytology was also positive for lymphoma. The patient was started on Memorial Hospital protocol L17M and has entered complete remission.

MATERIALS AND METHODS

For cytogenetic studies, aspirated bone marrow of patient 1 and a cell suspension of a lymph node biopsy of patient 2 were cultured for 24 hr in RPMI 1640 medium supplemented with fetal bovine serum and antibiotics. Chromosome preparations were made following conventional methods using 0.075 M potassium chloride as the hypotonic solution and 3:1 methanol acetic acid as the fixative. Karyotypic analysis was performed on Q-banded preparations. Immunofluorescent staining for surface membrane immunoglobulin fractions was performed on mononuclear cell preparations from peripheral blood and bone marrow following previously described methods.

RESULTS AND DISCUSSION

From each patient, 30 metaphase cells were analyzed. The chromosomal complement of the tumor cells from the first patient was found to be 46,XY, t(8;14)(q24;q32) (Fig. 1), while that of the second patient was found to be 46,XY,del(9)(pter → q22:),t(8;22)(q24;q11) (Fig. 2).

Both patients exhibited B-cell monoclonal proliferation in the bone marrow. However, they differed in expression of surface membrane light chains. The majority of B cells in the marrow of patient 1 expressed κ light chain on their surface, while those of patient 2 expressed mostly λ light chain.

The role of herpes viruses, especially the EB virus, and chromosome rearrangement in the genesis of BL and other B-cell neoplasms in congenital as well as acquired immunodeficiency states is increasingly recognized. Both of our patients exhibited elevated
EBV-VCA titers, indicating exposure to the virus and suggesting a possible role for it in the initiation of their tumors. However, EBV nuclear antigen staining of tumor cells was not performed. A model of lymphomagenesis under these circumstances invokes a virus-initiated polyclonal B-cell proliferation of preneoplastic cells, which are presumably genetically unstable and in which the occurrence of specific translocations promotes development of monoclonal neoplasms such as BL.\(^7\) The translocations in BL, as mentioned above, involve chromosomes 2, 8, 14, and 22. The determinants for immunoglobulin heavy chains, \(\kappa\) light chains, and \(\lambda\) light chains have been mapped to chromosomes 14, 2, and 22, respectively.\(^16\) Furthermore, the positions of the former two are also in the same regions of the chromosomes where breaks occur in the translocations (14q32, 2p12→cen).\(^16\) A direct relationship has recently been established between expression of light chains and type of translocation in BL cells; those with t(8;22) expressed \(\kappa\) chains, while those with t(2;8) expressed \(\lambda\) chains.\(^19\) Tumor of patient 2, as predicted, expressed \(\lambda\) chain.

We have recently shown that the cellular oncogene \(c-myc\) is located on chromosome 8, where its break occurs in the BL translocations (8q24).\(^20\) Activation of \(c-myc\) by insertion upstream of viral promoters in the long terminal repeat sequences (LTR) following infection by avian leukosis virus has previously been shown to be the mechanism for the development of lymphoid leukemia in the chicken,\(^21\) and \(c-myc\) expression has been shown to be elevated in at least one lymphoma cell line with t(8;14).\(^20\) These data lend support to the hypothesis that in the development of BL, the translocations may place a specific oncogene (presumably \(c-myc\)) under the control of genes that are actively transcribing (immunoglobulin determinants), leading to activation of the oncogene and monoclonal proliferation of neoplastic cells. Our cytogenetic observations reported here demonstrate that BLLs in AIDS patients have identical translocations to the ones seen in BL.
Therefore, the pathway leading to BL seems to be common to patients with or without immunodeficiency. Presence of congenital or acquired immunodeficiency presumably renders patients permissive for EBV and other oncogenic viral infections, resulting in increased incidence of associated neoplasms such as BL.

NOTE ADDED IN PROOF

Since this paper was submitted, it has been demonstrated that the c-myc gene becomes translocated to chromosome 14 in the t(8;14) in addition to undergoing transcriptional activation in BL cells.22-24

REFERENCES

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