Novel t(15;19)(q15;p13) Chromosome Abnormality in a Thymic Carcinoma

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Abstract

A 22-year-old female with a thymic carcinoma is reported. The tumor was refractory to both chemotherapy and irradiation. The patient died with an aggressive clinical course. Cytogenetic study showed that the tumor cells had a chromosome translocation, t(15;19)(q15;p13), which was not identified previously in human cancer.

Introduction

Specific chromosome translocations have been identified in certain hematopoietic neoplasms and these chromosome abnormalities are thought to play an important pathogenetic role in the disease (1). Improvement in cell culture techniques has made it possible to discover a number of specific chromosome changes in solid tumors; however, we are not aware of any cytogenetic report on thymic carcinoma (2, 3). We report here a case of thymic carcinoma in which a novel t(15;19)(q15;p13) translocation was found.

Case Report

A 22-year-old female presented with chest pain and superior vena cava syndrome on April 19, 1990. A chest X-ray film (Fig. 1) and a computed tomographic scan revealed a large mediastinal tumor which extended to the right hilus and right supravacular region. A right supravacular nodule was biopsied. The excised tumor consisted of monotonous primitive mononuclear cells which contained prominent nucleoli. The formalin-fixed, paraffin-embedded tumor specimens were examined immunohistochemically by the avidin-biotin-immunoperoxidase staining method (4) using the following antibodies: anti-MB-1 (Bio-science, Emmenbrucke, Switzerland), MxPanB (Kyowa, Tokyo, Japan), UCHL-1 (CD45RO), MB-1, MxPanB, LCA (CD45), carcinomaembryonic antigen (Bio-science), glial fibrillary acidic protein (Dakopatts), muscle actin, desmin, myoglobin, S-100 protein, lysozyme (Dakopatts), α1-antichymotrypsin (Dakopatts), α-fetoprotein (Dakopatts), human chorionic gonadotropin (Dakopatts), placental alkaline phosphatase (Dakopatts), neuron-specific enolase (Dakopatts), and Leu-7 (CD57). Electron microscopic study showed that the tumor cells had primitive morphology without displaying differentiation to any cell lineages. Desmosomes were rarely found after an extensive study. Neither tonofilaments nor neurosecretory granules were observed.

Chromosome Analysis

The right supravacular mass biopsied before treatment was teased apart with forceps, and disaggregated cells were passed through a stainless mesh, washed twice with RPMI 1640 medium, and cultured in RPMI 1640 medium supplemented with 20% fetal bovine serum. The 3-day-culture cells were analyzed as described in MATERIALS AND METHODS. The 3-day-culture cells were cultured in RPMI 1640 medium supplemented with 20% fetal bovine serum. The 3-day-culture cells were analyzed as described in MATERIALS AND METHODS.

Discussion

Thymic carcinoma is a thymic epithelial tumor which shows obvious cytological atypia such as large cell size, prominent nucleoli, high nuclear/cytoplasmic ratio, many mitoses, and multifocal necrosis (6–12). The patient's tumor examined at autopsy fulfilled these criteria, although we made a tentative diagnosis of lymphoma initially on a biopsied specimen. Cytologically, thymic carcinoma is subgrouped into squamous cell type, small cell type, clear cell type, and rarely, undifferentiated cell type (6–12). A small population of tumor cells in the present case was positive for EMA and cytokeratin; however, the cells lacked other cell markers. In addition, electron microscopic study showed that the tumor cells were highly anaplastic and displayed no discernible differentiation. These morphological and immunohistochemical features of the tumor were consistent with those of the undifferentiated cell type carcinoma.

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2 The abbreviations used are: LCA, leukocyte common antigen; EMA, epithelial membrane antigen.
Chromosome analysis of the biopsied tumor revealed that the cells had t(15;19)(q15;p13) abnormality. Although Kristoffersson et al. (13) reported chromosome aberrations in thymomas, no cytogenetic studies on thymic carcinoma have been reported (2, 3). Molecular studies of chromosomal translocations have provided important insights into the mechanism of certain hematopoietic malignancies in that chromosome rearrangements result in the expression of oncogenicity of certain cellular genes (1, 14). According to recent reports, E2A and LYL-1 which are associated with pre-B-cell acute lymphoblastic leukemia and T-cell acute lymphoblastic leukemia, respectively, are mapped at chromosome 19p13 (15, 16). Molecular analysis of the breakpoints at t(15;19)(q15;p13) in the present case may lead to the identification of a new cellular oncogene related to the pathogenesis of a solid tumor.

References

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