Cytogenetic abnormalities in serous papillary adenocarcinoma of the ovary

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Summary

Purpose of investigation: Epithelial ovarian tumors are usually mucinous or serous type, affecting nearly 1% of women during their lifetime. They may be regarded as benign, borderline or invasive according to pathological examination. Karyotypes of the tumor provide critical information about both the genetic predisposition and the stage of the tumor. We aimed to investigate the correlation between karyotype findings and the stage of the serous papillary tumors of the ovary.

Methods: Tissue cultures were set up from 15 serous papillary adenocarcinoma samples of different stages and examined cytogenetically.

Results: The most common chromosome abnormalities included both numerical and structural abnormalities of chromosomes 1, 3, 6, 7, 8, 11, 21, 22 and X.

Conclusion: Karyotypes became more complex, as expected, with the later stages.

Key words: Serous papillary ovarian cancer; Cytogenetic abnormality.

Introduction

Epithelial ovarian tumors are relatively common when compared to other ovarian tumor types. These tumors are either mucinous or serous type. Histological classifications of tumors are benign, borderline or invasive on the basis of both cytological and architectural features [1].

Carcinogenesis is a multi-step process and this is valid also for ovarian tumors. Most carcinomas arise from the accumulation of multiple cytogenetic abnormalities of different chromosomes. These abnormalities have been reported to be effective in the behavior of ovarian tumors, and important in tumor prognosis [1, 2].

Chromosome abnormalities are more complex in solid tumors when compared to hematological cancers [3].

In this study, we aimed to detect karyotype findings of serous papillary adenocarcinoma samples and determine whether they are related with stages of tumors or not.

Materials and Methods

Patients: Fifteen patients diagnosed with ovarian carcinoma were included in the study. Tumor samples of 0.5 to 1 cm^3 were taken during surgery and put in transport medium under sterile conditions. Histopathological evaluation was also performed and staging was done according to the FIGO classification.

Tissue culture and cytogenetic examination: Mechanically dissected and dissociated tumor tissue was also treated with 0.8 mg/ml collagenase type II solution for 16 hours. Tumor cells were cultured in RPMI 1640 medium containing 10% fetal calf serum, 200 mM L-glutamine, penicillin/streptomycin (10,000 U/ml and 10,000 µg/ml, respectively) five to ten days. Tissue culture medium also contained 10 ng/ml EGF and 5 µg/ml insulin as growth factors. After achieving sufficient mitotic activity, 200 µl colcemide solution (10 µg/ml) was added to the cultures and after 2.5 hours, chromosomes were harvested according to standard protocols [4]. Trypsin-Giemsa (GTG) banding was performed [4]. Chromosome analyses of at least 20 metaphases were performed for each patient.

Results

Karyotypic findings and tumor stage of the 15 patients are summarized in Table 1. Survival periods are also given in the table.

The most striking finding was aneuploidies observed nearly in all patients except the first three (all Stage I tumors). Also marker chromosomes were observed in most of the patients. Trisomy 7, 8, 9 and 19 were observed in three patients (patient no. 6, 13, 14 in Table 1). Also, another striking and most consistent abnormality was loss of X chromosome in three patients (patient no. 5, 13, 14 in Table 1).

In two patients (patient no. 9 and 12 in Table 1) we observed ring structures in chromosome 1. In another patient we observed translocation involving chromosomes 1p and 3q; i(1p) and i(1q) were other structural abnormalities observed in the same patient (patient no. 14 in Table 1). Although numerical abnormalities were seen in Stages II, III and IV, structural abnormalities were seen only in Stages III and IV. Also partial chromosomal gains or losses were seen in Stage IV. In addition to the other findings, we determined fragility in all chromosomes and all metaphases in one patient (patient no. 15 in Table 1).

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Table 1. — *Tumor stages, chromosomal findings and survival of patients.*

Patient No.	Tumor stage	Most prevalent chromosomal finding	Survival
1	1a	Normal karyotype	Alive, 24 months
2	1b	Normal karyotype	Alive, 14 months
3	1c	Normal karyotype	Alive, 12 months
4	IIa	Aneuploidy	Alive, 20 months
5	IIIa	Aneuploidy, marker chromosome and loss of X	Unavailable
6	IIIc	Aneuploidy, marker chromosome and trisomy 7, 8 and 9	Died at 3 months
7	IIIc	Aneuploidy, marker chromosome	Alive, 6 months
8	IIIc	Aneuploidy, marker chromosome	Relapse at 6 months died in 1st year
9	IIIc	r(1) in 3 metaphases, aneuploidy and marker chromosome	Died in 1st year
10	IIIc	Aneuploidy, marker chromosome	Died in 1st year
11	IIIc	Aneuploidy, marker chromosome	Alive, 1 year
12	IV	r(1) in 2 metaphases, aneuploidy and marker chromosome	Died at 9 months
13	IV	Loss of 22 and X, trisomy 19, marker chromosomes and 6q+	Died in 1st year
14	IV	Trisomy 8 and 9, loss of X, t(1p:3q), i(1p), i(1q), 3q-, 6q-, 11p-, and marker chromosomes	Died at 9 months
15	IV	Aneuploidy, fragility in all chromosomes, marker chromosome	Died at 10 months

Discussion

Karyotypic findings in tumors represent the tumor stage and clinical survival of patients. These abnormalities play a key role in tumor pathogenesis and are limited to the tumor tissues of patients. We did not observe any karyotypic abnormality in the peripheral blood samples of patients.

Cytogenetic abnormalities lead clinicians in improving the diagnosis and treatment of tumors [5]. Genetic changes are related to oncogenes and tumor suppressor genes [6].

Complex numeric abnormalities are frequent in tumor materials. These involve the whole chromosome or chromosome segments [3]. Gain of chromosomes 7, 8 and 9 has been reported to be associated with borderline and low-grade tumors as well as normal tissue [3, 6]. However, we observed trisomy 7, 8 and 9 in a Stage IIIc patient and trisomy 8, and 9 in a Stage IV patient. These two patients died in less than one year after diagnosis (patient no. 6 and 14 in Table 1). There were additional chromosome abnormalities in patient 14 such as t(1p;3q) and loss of X.

X chromosome is among the most frequently abnormal chromosome in ovarian carcinoma, which correlates with serous differentiation, advanced stage and the presence of residual disease [2].

Translocations have been reported to be rarely detected in ovarian carcinomas [3]. We observed a t(1p;3q) in a Stage IV patient (patient no. 14 in Table 1). Involvement of chromosome 1 in the translocation is an important finding, since chromosome-1 breakpoints have been reported to be important in the progression or pathogenesis of ovarian cancer. We also observed ring chromosome 1 in two patients (no. 9 and 12 in Table 1). These patients were in Stage IIIc and IV, which supports the above discussion.

We observed marker chromosomes in nearly all patients, except those in Stage I. Marker chromosomes are frequent findings in tumor karyotypes [3]. The marker chromosome is a type of unstable chromosome. Homogeneously staining regions and double-minute chromosomes are also examples of fragility in tumors. We observed obvious fragility in all chromosomes of a Stage IV patient. We concluded that, as the tumor stage became higher, chromosome fragility caused both marker chromosomes and double-minutes.

An interesting point was that although all patients had malign tumors, we did not observe any chromosome 17 abnormalities. Different studies suggest non random structural chromosome rearrangements in solid tumors, but it is difficult to define recurring abnormalities because of complex karyotypes and difficulties in culturing primary solid tumor cells.

Conclusion

Whatever the resulting karyotype, one finding which is important is that, as the tumor stage becomes higher, karyotypes become more complex. Cytogenetic investigation may be helpful for physicians in both the diagnosis and follow-up of patients.

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