



# Chromosome Abnormalities in Primary Endometrioid Ovarian Carcinoma

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**ABSTRACT:** *Specific and recurrent chromosome abnormalities may occur in regions of the genome that are involved in the conversion of normal cells to those with tumorigenic potential. Ovarian cancer is the primary cause of death among patients with gynecologic malignancies. We performed cytogenetic analysis in a subgroup of epithelial ovarian tumors, the endometrioid tumors, which are histologically indistinguishable from endometrial carcinoma of the uterus. We studied 10 endometrioid tumors to determine the degree of cytogenetic similarity between these two carcinomas. Six of 10 endometrioid tumors showed a near-triploid modal number, and one had a tetraploid modal number. Eight of the 10 contained structural chromosome abnormalities, of which the most frequent were 1p- (5 tumors), 6q- (4 tumors), 19q+ (4 tumors), and chromosome 3 rearrangements (4 tumors). These cytogenetic results resemble those reported for papillary ovarian tumors and differ from those of endometrial carcinoma of the uterus. We conclude that despite the histologic similarities between the endometrioid and endometrial carcinomas, the genetic abnormalities in the genesis of these tumors differ significantly.*

## INTRODUCTION

Ovarian cancer has the highest fatality rate of all gynecologic tumors. In the U.S. female population, cancer of the ovary accounts for 4% of all cancers and is responsible for 6% of all cancer deaths [1]. The high mortality rate is due to the advanced stage of disease at diagnosis. Ovarian cancers affect primarily postmenopausal women, with only 10–15% of cases diagnosed in premenopausal patients [1].

We describe the cytogenetic findings in 10 ovarian endometrioid tumors. The endometrioid tumors constitute a type of epithelial ovarian cancer so named because of the histologic resemblance to the typical carcinomas of the endometrium. They account for 15–20% of ovarian cancers [2]. In well-differentiated tumors, the histologic pattern is identical to that of uterine endometrial carcinoma, as shown in Fig. 1, whereas in less differentiated lesions the endometrioid pattern appears to be restricted to focal areas. We examined the degree of genetic similarity between the endometrioid tumors of the ovary and those of the endometrium.

## MATERIALS AND METHODS

Ovarian tumor samples were obtained from surgical pathology immediately after surgery. The carcinomas were classified histologically by the department of pathology. Specimens for cytogenetic analysis were mechanically triturated and enzymatically disaggregated; the cell suspension was cultured by standard techniques [3]. Primary cultures were monitored for mitotic activity and harvested in 7 days. The prepared slides were trypsinized and stained with Leishman's stain. At least 20 metaphases were analyzed from G-banded slides, and 4 karyotypes were prepared whenever possible. Results of the cytogenetic analysis were described according to the guidelines of the International System for Human Cytogenetic Nomenclature [4, 5].

## RESULTS

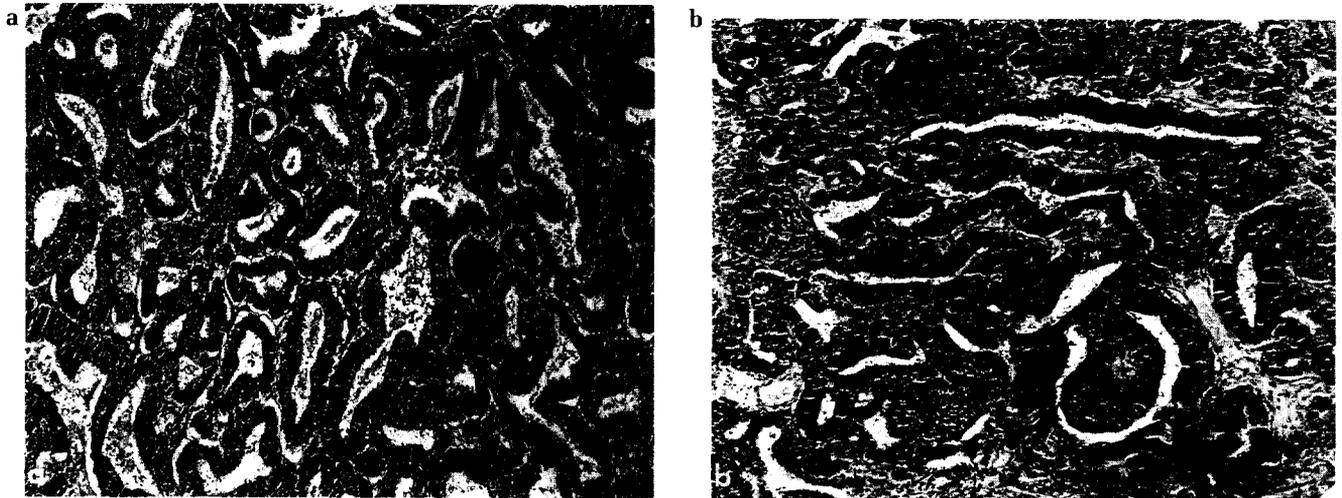
We performed cytogenetic analysis of 10 ovarian tumors, identified histologically as endometrioid adenocarcinomas. Six of the carcinomas showed a near-triploid modal number, and one showed a near-tetraploid modal number. The most frequent numerical aberration was loss of chromosome X, ascertained in six tumors, including four of the near-triploid tumors. One tumor had a normal karyotype; in another, clonality could not be established because of the limited number of analyzable metaphases. The remaining eight tumors contained clonal structural abnormalities of chromosomes 1, 3, 6, and/or 19, as shown in Figs. 2–4. Five tumors showed aberrations of the long arm. Addition

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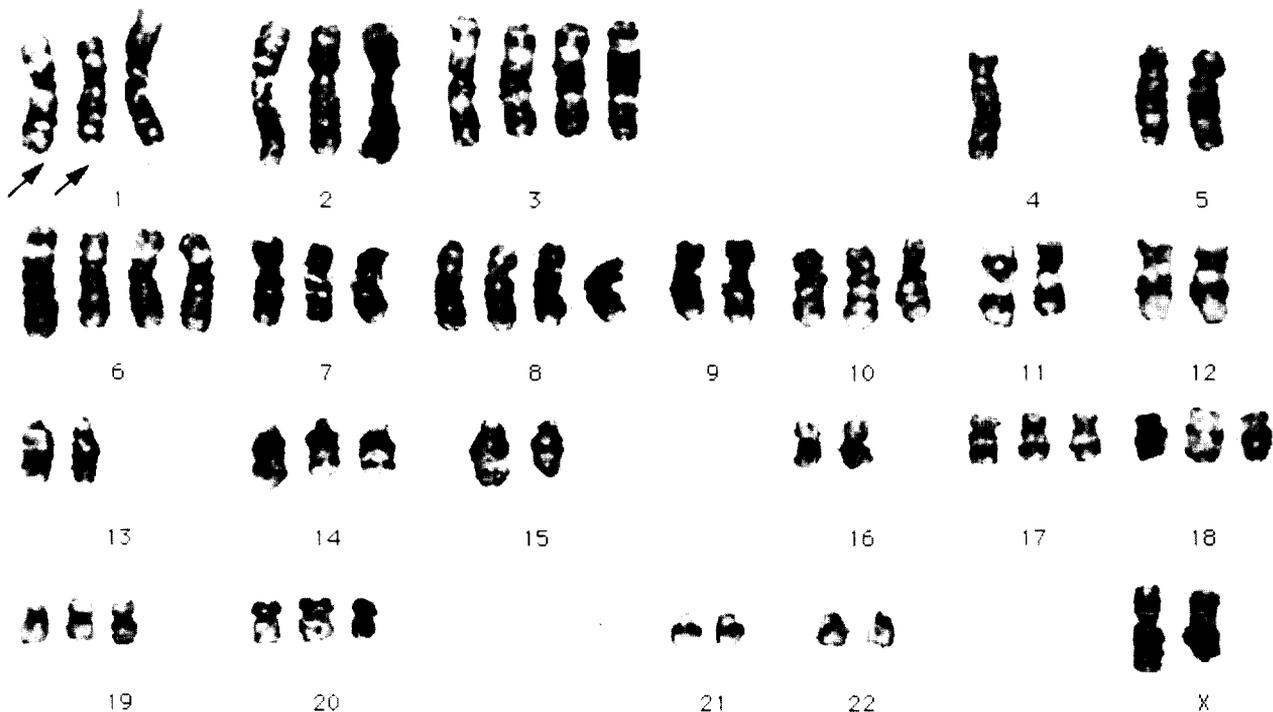
**Figure 1** Histologic appearance of endometrioid adenocarcinoma of the ovary; case 91-019 (a) is similar to that of uterine endometrial adenocarcinoma, case number 3 in [3] (b).

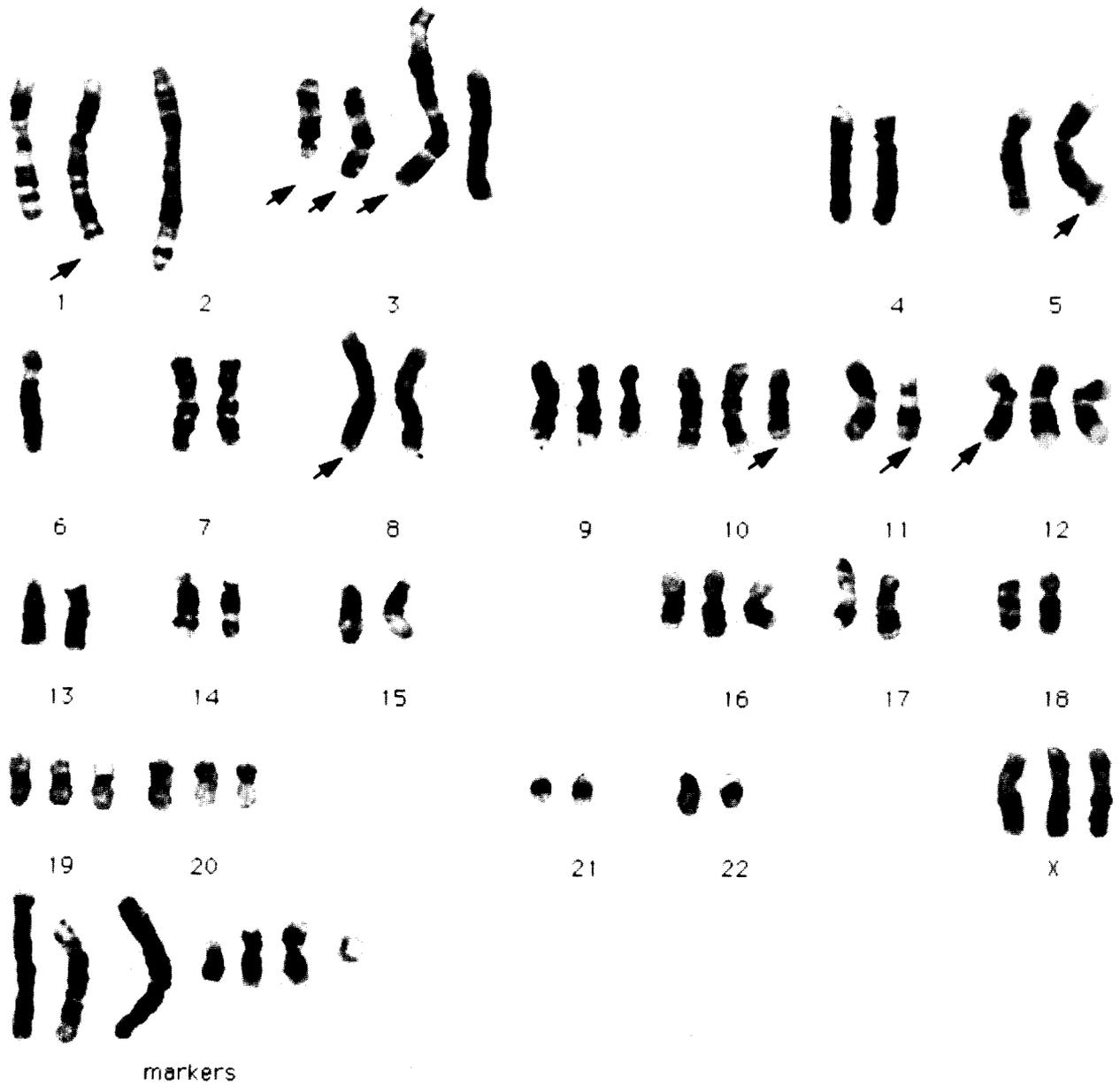
of unidentified material to chromosome 19q13.2–13.4 was a finding in four tumors. The long arm of chromosome 6 was involved in deletions or rearrangements in four specimens with breakpoints clustered at 6q22 (three tumors). Structural abnormalities of 3p or 3q were noted in two tumors each. The karyotypic results of the cytogenetic analyses are summarized in Table 1. Figure 5 summarizes the chromosome breakpoints observed.

**DISCUSSION**

Recurrent structural aberrations in chromosome 1, 3, 6, 11, and 19 have been recognized in ovarian cancer [6]. Addition of material of unknown origin to the short arm of chromosome 1 is the most common alteration in ovarian cancer [7], followed by deletions of the long arm. Our findings are consistent in that for the 10 ovarian tumors with endometrioid differentiation, structural alterations of chro-

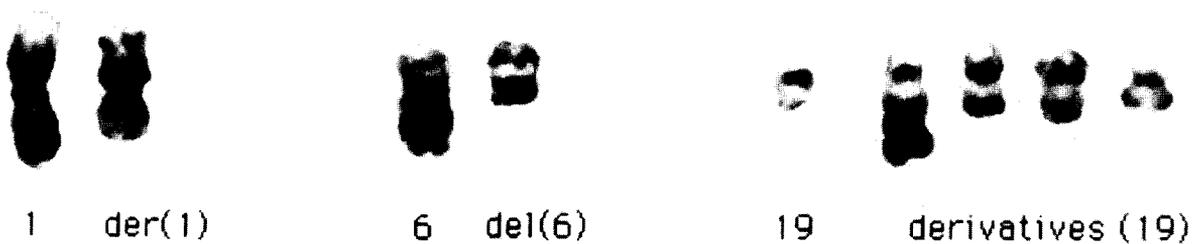
**Figure 2** Karyotype of a G-banded metaphase from case 90-044 showing 60,XX,-X,der(1;6)(q10;p10)x2,+3,-4,-4,-5,+6,+8,-9,-11,-12,-13,-15,-16,-21,-22. Clonal structural aberrations are indicated by arrows.





**Figure 3** Karyotype of a G-banded metaphase from case 90-173 showing 60,XXX,-1, der(1)del(1)(p.36.1)add(1)(q24),-2,-2,add(2)(q32),del(3)(q12),add(3)(q11.2),add(3)(p26),-4,-5,add(5)(p15.3),-6,-6,-7,-8,add(8)(p22),del(10)(q22q24),-11,t(11;12)(p11.2;q24.1),-13,-14,-15,-17,add(17)(p13),-18,-21,-22,+7mar. Clonal structural abnormalities are indicated by arrows.

**Figure 4** Partial karyotype from case 91-010 showing structural abnormalities for chromosomes 1, 6, and 19.



**Table 1** Summary of karyotypic results for 10 ovarian endometrioid carcinomas

Case	Age (yr)	Karyotype
90-173	76	57-60,XXX,-1,der(1)del(1)(p36.1)add(1)(q24),-2,-2,add(3)(p26),add(3)(q11.2),del(3)(q12),-5,add(5)(p15.3),-6,-7,-8,add(8)(p22),del(10)(q22q24),-11,der(12)t(11;12)(p11.2;q24.1),-13,-14,-17,-18,+6-7mar[cp3]
89-257	63	61-69,X,-X,-X,del(1)(p35),+add(1)(p22),add(2)(p11.1),add(3)(p12),-4,-4,-5,der(6;?19)(p10;q10),add(6)(q22),add(7)(p21),add(7)(q34),der(9)t(6;9)(p12;q12)×2,-10,add(11)(23),hst(11)(q12),+der(12)t(2;12)(p11.1;q22),+del(12)(q12)×2,-13,add(15)(p11.2),add(16)(p13.3),-17,-19,add(19)(q13.4),der(19)t(1;19)(q12;p12),-20,-21,-22,+3mar[cp5]
90-098	71	74-88<4n>,X,-X,-X,-X,-2,del(3)(p14),add(3)(p14),-4,-4,-5,add(6)(q22),-8,-9,del(10)(q22q25),-11,-11,-14,-15,-16,-16,-16,-17,-17,-18,-18,add(19)(q13.4),inc[cp6]
90-044	58	60-62,XX,-X,-1,+der(1;6)(q10;p10)×2,+3,-4,-5,+6,+8,-9,-11,-12,-13,-15,-16,-21,-22,+mar[cp6]
91-010	56	62-70,XX,del(X)(q22),-1,der(1)add(1)(p33)del(1)(q23),der(2)t(2;9)(q35;q12),-4,-4,-5,add(5)(q12),add(6)(q13),add(6)(q12),+del(6)(q12),del(7)(q22q35)×2,-8,-8,-8,-9,-10,-10,-11,del(11)(q23)×2,-12,-14,-14,-15,-16,add(16)(p13.2),-17,i(17q),-18,-19,add(19)(q13.2),add(19)(q13.2),+add(19)(q13.2),+add(19)(q13.2),-22,add(22)(q11.2),+14mar[cp5]
90-227	64	62-74,XX,-X,+der(1)add(1)(p33)add(1)(q32),add(8)(q23),del(11)(q23),add(17)(p13),add(19)(q13.2),+add(20)(q13.2),inc[cp4]/46,XX[2]
90-192	64	46-58<2n>,X,-X,del(1)(q31),del(3)(q12),del(6)(q22),del(11)(q12q14.1),+3mar,inc[cp6]
91-019	31	46,XX,+add(4)(q28),+5,+8,+10,-14,-16,-17,-19,-21,+mar[1]/46,XX[3]
91-077	43	38-42,X,-X,add(1)(p32),dic(1;8)(p21;q24.3),der(2)add(2)(p22)add(2)(q32),del(12)(q11),add(14)(q31),+3mar,inc[cp6]
91-030	59	46,XX[6]

mosome 1 were the most common. On the other hand, chromosome 1 aberrations are those most common in all human carcinomas and in many hematopoietic malignancies [8]. The frequent involvement of this chromosome in human neoplasms has led to the hypothesis that this chromosome has a role in tumor progression rather than initiation [8].

In a cytogenetic study of ovarian cancer by Whang-Peng et al. [7], chromosome 3 was the second most frequently involved chromosome in structural abnormalities with variable breakpoints noted in the p and q arms. Similarly, we observed alterations in chromosome 3 in four tumors. Pejovic et al. [6] observed a translocation between chromosomes 3 and 11 in one endometrioid tumor.

Although often detected in ovarian cancer, alterations of chromosome 6q may be specific only for a subgroup in the ovarian tumors [8]. Deletions of the long arm of chromosome 6 have been reported in endometrioid tumors from two patients in a study of ovarian tumors by Roberts and Tattersall [9]. In three tumors we noted that additions and deletions were clustered at 6q22, providing support for the proposal that genes located in 3p and 6q are likely candidates for participation in ovarian tumorigenesis [10].

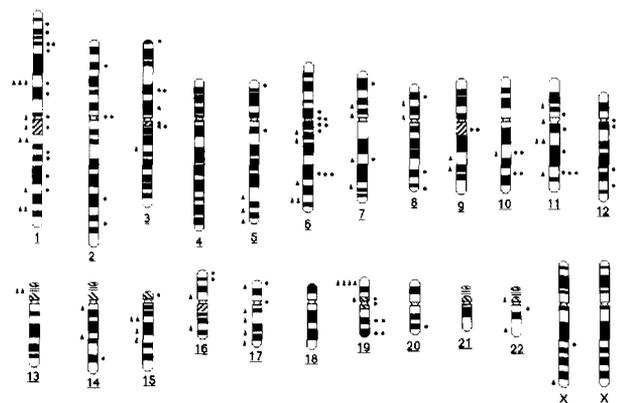
For chromosome 11, the most frequent structural abnormality we detected was a deletion in the q arm (three cases) and, in one case, a homogeneously stained region was present in 11q. In contrast, Jenkins et al. [11] described only numerical abnormalities of chromosome 11 in their study of six endometrioid tumors.

Published reports [6, 7, 11] have described alterations of both the short and the long arms of chromosome 19 in ovarian malignancies, and the involvement of chromosome 19 has been suggested to be associated with early tumor progression [12]. We too observed a clustering of additions at chromosome 19q13.2-13.4.

A simple chromosome rearrangement as the sole change in an endometrioid carcinoma, as described by Pejovic et al. [6] and Roberts and Tattersall [9], did not characterize any of our tumors. The loss of chromosome X, although

linked to tumor progression [13], is not specific to ovarian carcinomas and is frequently described in normal tissue from older individuals [14].

We report the cytogenetic data for a subset of epithelial tumors of the ovary, the endometrioid tumors. Recognized as a separate histologic entity in the early 1960s, the endometrioid carcinomas are the second most common type of epithelial ovarian tumor [15]. The epithelial origins of this tumor are believed to vary with the clinicopathologic setting. Endometrioid carcinomas most frequently arise in the fifth and sixth decade, as did those we report, and are believed to derive from the surface epithelium of the ovary. In contrast, endometrioid ovarian carcinomas that develop in an endometrioid cyst usually occur in women at least 10 years younger. The ultrastructural resemblance between endometrioid carcinomas and well-differentiated carcinomas of the endometrium raised the question of genetic similarity between the two tumors.



**Figure 5** Distribution of clonal chromosome breakpoints in our ovarian endometrioid carcinomas (circles) and in other published cases (triangles).

Our work [16] and that of other investigators [17–20] suggests that trisomy 1q, 10, 2, 7, and 12 are the most frequent aberrations in uterine endometrial adenocarcinoma. Our data indicate that karyotypic changes in endometrioid tumors resemble those reported for papillary ovarian tumors more closely than those of endometrioid carcinoma of the endometrium. We conclude that despite the histologic similarities between these two tumors, the underlying genetic changes may differ significantly in endometrioid ovarian carcinoma and uterine endometrial carcinomas.

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