28. *The Chromosomal Fragility in Gynecological Cancer*

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A chromosomal study was performed on the patients with gynecological cancer; cervical cancer, ovarian cancer, and endometrial cancer. The aneuploidy and the fragility in the chromosome of 23 patients were investigated for the purpose of the indication of effects and/or side effects on the treatment of malignant tumor.

All the 23 donors of peripheral blood, ranging from 24 to 78 years, were admitted to the Toritsu-Komagome Hospital and the Branch Hospital attached to the Faculty of Medicine, Tokyo University.

Cytological findings. The lymphocytes from the peripheral blood were cultured for 72 hrs in the medium of minimal essential medium without folic acid (MEM-FA) supplemented with 5% calf serum (Sutherland, 1979). Additionally, in order to enhance the fragility, the cells were exposed to 2.2 mM caffeine during the last 6 hrs of the culture (Yunis and Soreng, 1984). The slides were made by means of the flame-drying technique. The chromosome counts were made with 50 well-delineated and not-distributed metaphases for the respective case. The observations of breaks and/or gaps were made by the culture with caffeine.

The details of the cytological findings of all the 23 cases were presented in Table I. Table I shows the distribution of chromosome counts and the chromosome fragility as the frequency of breaks and/or gaps. Out of the total 1150 cells counted, 96 cells had aneuploidies, being 8.3% in incidence. Especially, out of 96 cells having aneuploidies, 73 cells had 45 chromosomes, being 6.3% in incidence. The break points were observed in all 23 cases. The frequencies of break points distributed from 6th in six cells to 196th in 42 cells divided from 50 cells observed. Ten out of 23 cases had the cells with severe break points ranging from one cell to seven cells, in which chromosome counts could not be calculated (Table I).

Remarks and conclusion. Since Dekaban (1965) reported on an heritable fragile site on the human chromosomes, numerous reports have been represented. Recently, the relation on the chromosomal fragility and cancer is a remarkable problem. In this study, the aneuploidy and the fragility in the chromosomes from the peripheral blood were investigated for the purpose of the indication of effects and/or side effects on the treatment of the malignant tumor.

On the aneuploidy, out of 1150 cells, 96 cells had aneuploidies, being 8.3% in incidence. And the frequency of break points was 1.58 per cell (1817/1150), and the frequency of the cells with break points was 53.3% (613/1150). These

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Table I. Distribution of chromosome counts per cell and the frequency of break points, and clinical background of patients

Case no.	Age	Cells obs.	Chromosome count										Cells b. p.	Clinical diagnosis	Clinical stage	Treatment		
			≤44	45	46	47	48	≤	s. b. p.	b. p.	Surgery	CTX				Radiotherapy		
1	36	50	0	0	49	1	0	1	36	98	cervical cancer	0	ATH	(-)	(-)			
2	42	50	0	4	45	1	0	3	37	178	cervical cancer	0	ATH	(-)	(-)			
3	52	50	1	2	46	0	1	0	15	20	cervical cancer	I	ARH+PLA	(-)	WP 50GY			
4	29	50	3	10	36	0	1	4	40	88	cervical cancer	II	ARH+PLA	(-)	WP 30GY			
5	43	50	0	1	49	0	0	2	31	84	cervical cancer	II	ARH+PLA	(-)	WP 50GY, Pa 30GY			
6	45	50	2	6	41	0	1	3	21	39	cervical cancer	II	ARH+PLA	(-)	PVB WP 50GY, RALS 20GY			
7	78	50	0	6	44	0	0	0	12	28	cervical cancer	IV	(-)	(-)	WP 10GY			
8	64	50	0	3	47	0	0	0	29	83	cervical cancer	IV	(-)	(-)	5-FU WP 50GY, RALS 20GY			
9	54	50	0	1	48	1	0	0	14	16	ec	IV	Catheterization	(-)	IA			
10	24	50	0	0	50	0	0	0	10	15	ovarian cancer	I	LSO+Biopsy	(-)	CAP			
11	58	50	0	5	45	0	0	2	42	196	ovarian cancer	I	ATH+BSO+POM	(-)	CAP			
12	57	50	1	6	41	2	0	0	37	88	ovarian cancer	II	ATH+BSO	(-)	CAP			
13	58	50	0	7	42	1	0	2	35	115	ovarian cancer	II	ATH+BSO+POM+PLA	(-)	CAP			
14	49	50	0	1	48	1	0	2	26	80	ovarian cancer	III	ATH+BSO+POM+PaLA	(-)	CAP			
15	62	50	0	1	48	1	0	0	22	50	ovarian cancer	III	ATH+BSO+PLA+POM	(-)	CAP			
16	40	50	0	1	49	0	0	0	20	39	ovarian cancer	III	ATH+BSO+PLA+POM	(-)	CAP			
17	51	50	0	1	48	1	0	0	6	6	ovarian cancer	III	ATH+BSO+PLA,SLL	(-)	CAP			
18	59	50	0	1	49	0	0	0	28	40	ovarian cancer	IV	ATH+BSO+PLA	(-)	CAP			
19	52	50	2	4	44	0	0	6	41	186	ovarian cancer	III	ATH+LSO+PLA+POM,SLL	(-)	CAP WP 50GY			
20	62	50	0	6	43	1	0	0	29	66	ovarian cancer ^{*1}	III	ATH+BSO+POM+PLA,SLL	(-)	CAP			
21	52	50	0	1	49	0	0	0	9	14	ovarian cancer	IV	ATH+BSO+PLA+PaLA	(-)	(-)			
22	59	50	0	5	45	0	0	0	36	151	ovarian cancer	III	ATH+BSO+POM,PLA+PaLA	(-)	CAP			
23	60	50	0	1	48	1	0	7	37	137	double cancer ^{*2}	I	ATH+BSO+POM+PLA	(-)	5-FU			
Total	1150		9	73	1054	11	3	32	613	1817								

Cells s. b. p.: cells with severe break points. Cells b. p.: cells with break points. ^{*1}: Ovarian cancer of low potential malignancy. ^{*2}: Endometrial and ovarian cancer. CTX: Chemotherapy. ATH: Abdominal total hysterectomy. ARH: Abdominal radical hysterectomy. BSO: Bilateral salpingo-oophorectomy. LSO: Left salpingo-oophorectomy. POM: Partial omentectomy. PLA: Pelvic lymphadenectomy. PaLA: Para-aortic lymphadenectomy. SLL: Second-look laparotomy. Catheterization: Catheterization in the bilateral internal iliac arteries. VBM: Combination chemotherapy with vincristine, bleomycin and mitomycin C. PVB: Combination chemotherapy with cisplatin, vincristine and bleomycin. IA: Intra-arterial chemotherapy with adriamycin, cisplatin and 5-fluorouracil. 5-FU: 5-Fluorouracil. CAP: Combination chemotherapy with cyclophosphamide, adriamycin and cisplatin (+5-FU). WP: Whole pelvis. RALS: Remote after loading system, radiation dose at "A" point. GY: Gray. Pa: Para-aortic irradiation.

frequencies were statistically high incidence compared with the frequencies of normal females; 0.72 per cell (466/649) in break points and 29.4% (191/649) in the cells with break points (Kadotani *et al.*, 1989). In this study, it has been not remained still revealed correlation between the effect and/or side effect of the treatment and the chromosomal fragility. The accumulation of the data, it could be useful to elucidate the effect and/or side effect of the treatment for cancer.

The differences of distribution of chromosome counts and of the frequency of chromosome break points between cervical cancer and ovarian cancer have not been recognized.

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