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Studies on Histological Grading of Malignancy of Carcinoma of The Uterine Cervix

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Prognosis of carcinoma is variable and can not be predicted from the initial clinical finding. In some cases it recovers permanently while in others it has recurrence, although the clinical findings themselves are quite the same at the beginning of the treatment. In some cases it prognosis rapidly to death in a very short period of time while in others it takes rather a mild course. Thus it is likely that there is a difference in degree of malignancy of carcinoma of the cervix.

Regarding the histological grading of malignancy of cervical carcinoma much has been written up to the present, but it is not clear whether or not this grading will correspond with clinical prognosis.

Under such circumstances it is note worthy that professor IMAI of the Department of Pathology, University of Kyushu, suggested a new classification of carcinoma in 1949.

The present paper deals with the results of the studies on malignancy of carcinoma of the cervix carried out on the basis of that classification.

IMAI's which CPL Classification

IMAI (1949) established CPL classification as it was termed by him, takes not only the growth of parenchymal cells but also the interstitial reactive conditions as well as the expansion of lesions of carcinoma into consideration a new grading of malignancy of carcinoma, and confirmed that it definitely corresponded with clinical prognosis in cases of carcinoma of the tongue, pharynx, breast, uterus and stomach, etc. The CPL classification is based on Imai's assumption that carcinoma causing death without any serious complication should be at top in its malignancy, following carcinoma subjected to surgery, and that, therefore, malignancy of carcinoma should be determined by comparing histological findings

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of cancerous specimen surgically removed with those obtained at the time of autopsy, and then clinical prognosis of cancer could be explained by CPL classification.

1. METHOD OF EXAMINATIONS

One must examine the sections after careful preparation.

1) Preparation of sections: Sections must be cut through the central part of the cancerous mass including its margin and adjacent tissues. Otherwise, cancerous cells often assume networks or globular shapes to make the differentiation as well as the CPL classifications entirely unpractical.

2) Histological specimen must be first examined carefully by a magnifying glass so that a histological orientation can be obtained. Specimen are stained with hematoxylin-eosin or van-Gieson stains and if necessary with argyrophil stain.

2. Basic types of growth of carcinomatous parenchyma

1) Intratissue type (Fig. 1.): According to Imai carcinomatous parenchyma growing within the tissues can basically be classified into the following three types:

a) Expansive type: The type with nests of carcinomatous cells or adenomatous structure, especially increased in thickness or in size.

b) Extensive type: The type with nests of carcinomatous cells or adenomatous structure with thickness beyond a certain degree and with an extensive degree and with an extensive development.

c) Budding type: The type with thin nests of carcinomatous cells showing cell cords with width equivalent to that of 2-3 carcinomatous cells or with carcinomatous cells which grow separately without forming nests.

In the budding type argyrophilic fibrils are often demonstrated among carcinomatous cells.

2) Intracanalicular type: The type of carcinomatous parenchyma which grows in the lymphatic vessels within the tissues.

3. CPL Classification

According to this classification there are three types based on the histological findings of a) marginal growth of carcinomatous mass, b) by with the relationship between parenchyma and stroma, c) grade of intracanalicular expansion.

1) C-form (Cirrhotic form): This type corresponds to the non-budding type or the budding type accompanying the new growth of connective stroma (Fig.2).

Also the intracanalicular type accompanied by the proliferation of adjacent connective tissues is included in this form.

2) P-form (progressive form): This is a carcinomatous mass of the budding type accompanying no new growth of stromal connective tissues in a small or the most part of the margin of carcinomatous tissue, with its parenchyma of a relatively low differentiation increasing the interstices. This form is further classified into three grades according to

its proliferation of cancerous cells. (Fig.3)

3) L-form (Lymphatic and blood vessel permeation form): This is a form showing a proliferation as well as a expansion of carcinomatous cells of low defferentiation within relatively large lymphatic or blood vessels and gland (Fig. 4). It is also classified into three grades.

As in case of tuberculosis IMAI termed the budding accompanied by hyperplasia of stromal connective tissues as "a reactive Schub". P. L form belongs to "non-reactive Schub" with unfavorable prognosis.

According to IMAI P-form of a high degree is small in number in surgical cases of cancer of the cervix. This is the same with the results of the present Studies. The above mentioned discription is the outline of IMAI's theory. The relationship between the degree of budding and the prognosis is different according to the kind of organs concerned. Nemely, in cancer of the tongue and the pharynx, particulary in the former its postoperative prognosis is closely related with the degree of budding of the cancerous parencyma. CPL classification, therefore, is not applicable for cancer of such kind of organs, with the exception of cancer of the stomach in which postoperative prognosis is not influenced with the degree of budding.

MATERIALS AND RESULTS

The present studies are based on 332 specimens of carcinoma of the cervix removed mostly by OKABAYASHI's technic in our clinic during the priod from April 1947, to December 1959, of which specimens were examined at random for each following item.

1. CPL, MARTZLOFF's classification and the parametrial cancerous infiltration

1) CPL classification : Of the 85 cases 37 cases were of C-form, 14 cases of P-from, 44 cases of L-form, and all the cases of P-form were of the combined P-and L-from. Parametrial cancerous infiltration was detected in 14 cases (37.8 per cent) out of the 37 cases in C-from, 29 cases (65.9 per cent) out of the 44 cases in L-form, and 9 cases (64.3 per cent) out of the 14 cases in P-from. It means the

Table I.

CPL Classification and Parametrial Carcinomatous Infiltration

PARAMETRIUM	CPL			P			L		
	C	I	II	III	I	II	III		
Carcinomatous infiltration (+)	14	3	4	2	10	8	11		
Carcinomatous infiltration (-)	23	2	3	0	7	3	5		
Total	37	5	7	2	17	11	16	95	

parametrial cancerous infiltration occurs more frequently in P-and L-forms than in C-form (Table I).

2) MARTZLOFF'S classification : Parametrial cancerous infiltration was observed in 18 cases (60 per cent) out of the 30 cases in spinal cell type and in 20 cases (50 per cent) out of the 40 cases in transitional cell type, whereas in the remaining 11 cases of spindle cell type 4 cases was detected (Table II). Thus there could be found no significant difference between the incidence of the parametrial cancerous infiltration of the spinal cell type and that of the transitional cell type.

Table II.
Martzloff's Classification and Parametrial Carcinomatous Infiltration

MARTZLOFF'S CLASSIFICATION	SPINAL CELLS	TRANSITIONAL CELLS	SPINDLE CELLS	(ADENO CARCINOMA)
PARAMETRIUM				
Carcinomatous infiltration (+)	18	20	4	3
Carcinomatous infiltration (-)	12	20	7	1
Total	30	40	11	4 85

2. CPL, MARTZLOFF'S classifications and the lymph node metastasis.

1) CPL classification with regard to the primary lesion: The lymph node metasasis was confirmed in 24.4 per cent, 33.0 per cent and 52.6 per cent in C-form, P-form and L-form, respectively, apparently the percentage being at the top in L-form (Table III).

Table III.
Correlation Between Lymph Node Metastasis and CPL Classification of Primary Lesion

CPL CLASSIFICATION	METASTASIS			% OF METASTASIS
	CASE NUMBER	NONMETASTATIC	METASTATIC	
C	78	59	19	24.4
P I	7	5	2	28.5 } 33.0
II	8	5	3	
III	0	0	0	
L I	26	13	13	50.0 } 52.6
II	20	6	14	
III	30	17	13	
Total	169	105	64	37.9

2) MARTZLOFF'S classification: No significant difference was observed in the percentage of lymph node metastasis according to this classification.

The permanent cure was in 37.1 per cent in cases with lymph node metastasis, and in 76.4 per cent in cases without it, obviously the percentage being significantly higher in the latter than in the former.

3. CPL, MARTZLOFF's classifications and the expansion of cancerous tissues into the uterine body.

No significant difference was noted in the incidence of the expansion of cancerous tissues into the uterine body.

4. CPL, MARTZLOFF's classifications and the expansion of cancerous tissues into the vaginal wall.

1) CPL classification: The expansion cancerous tissues into the vaginal wall was noted in 23 (30.3 per cent) cases out of 76 cases in C-form, in 7 cases (36.8 per cent) out of 19 cases in P-form and in 39 cases (50.6 per cent) out of 77 cases in L-form, the percentage of L-form being at the top, followed by that of P-form, then C-form, and with significant difference in the percentage between PL-form and C-form, L-form and C-form respectively (Table IV).

Table IV.
CPL Classification and The Expansion of Carcinomatous
Tissues into the Vaginal Wall

CARCINOMATOUS INFILTRATION		(+)		(-)		TOTAL
C form	23	(30.3%)	53	(69.7%)	76	(100%)
P form	7	(36.8%)	12	(63.2%)	19	(100%)
I		9		16		25
		(36.0%)		(64.0%)		(100%)
L form	39	9	38	8	77	17
	(50.6%)	(36.0%)	(49.4%)	(47.1%)	(100%)	(100%)
II		21		14		35
III		(60.0%)		(40.0%)		(100%)
Total	69		103		172	

2) MARTZLOFF's classification: The vaginal expansion was detected in 33.3 per cent, 46.6 per cent and 32.0 per cent in spinal cell type, transitional cell type and spindle cell type, respectively, therefore, no significant difference was noted between each other.

Cases with recurrence in the vaginal stump were seen mostly in typical cases of L-form.

5. CPL, MARTZLOFF's classifications and prognosis five years after surgery.

1) CPL classification: Recurrence was significantly rare in C-form and frequent in L-form, (Table V) as far as OKABAYASH's technic is concerned.

Table V.
CPL Classification and Prognosis Five Years After Operation

PROGNOSIS	METHOD	CPL CLASSIFICATION			
		C-FORM	P-FORM	L-FORM	TOTAL
Operation	Okabayashi's technic	88	11	88	187
	Others	16	6	28	50
Alive	Okabayashi's technic	70	6	38	114
	Others	9	2	7	18
5years after operation	Others	5	0	3	8
Alive with recurrence	Others	0	0	0	0
Primary death	Okabayashi's technic	13	5	47	65
Died of cancer	Okabayashi's technic	7	4	21	32
	Others	0	1	2	
Died of cancer	Okabayashi's technic	1	0	1	
After alive 5 years	Others				

2) MARTIZLOFF's classification : No such difference was noticed.

Conclusions

Since v. HANSEMANN (1890) a large number of studies have been carried out on malignancy of carcinoma, but no definite conclusion has been established.

In the present study, it was confirmed that MARTZLOFF's classification is not practical, whereas IMAI's CPL classification (1949) is valuable to determine the prognosis of carcinoma of the cervix according to its grading. For instance L-form can be compared to "Schub" in tuberculosis and is seen frequently as cervical cancer develops into the adjacent areas and it may have prognostic significance.

Therefore, CPL classification could be regarded as a good histological grading of malignancy of cancer of the cervix suitable for clinical use.

Fig. 1. Intratissue type

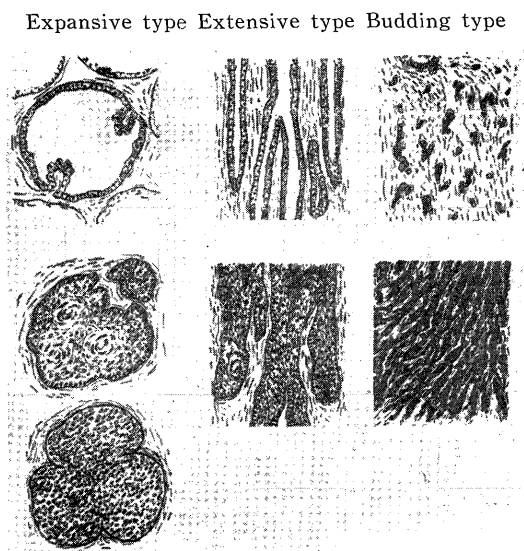


Fig. 2. C-form (Cirrhotic form)



Fig. 3. P-form (Progressive form)

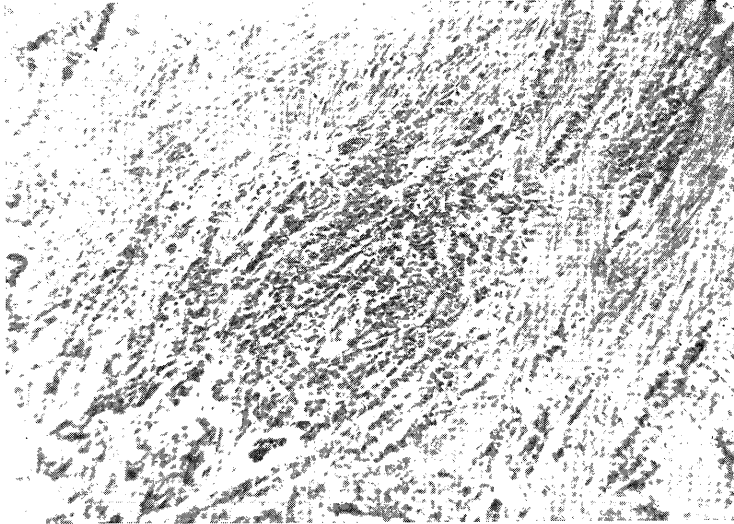


Fig. 4. L-form (Lymphatic and blood vessel permeation form)

