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DNA Ploidy Study in Esophageal Cancers

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ABSTRACT : The values of DNA content in 47 patients with esophageal cancers were evaluated in comparison with clinic o-pathological factors and their prognoses. DNA ploidy profiles were analyzed from paraffin-embedded preparates. The diploid tumors accounted for 41.1% in this series. Aggressive cancer extension was not necessarily seen in the aneuploid tumors as compared with the diploid tumors. One must be aware that some of the diploid tumors indicate worse prognosis.

INTRODUCTION

The relevance of the DNA content of malignant cells to the evalutation of biologically malignant behaviors has become accepted. It is no doubt that in many tumors the presence of an aneuploid population of cells is associated with a poor prognosis. Even in esophageal tumors, it was well clarified that an increase in DNA content was associated with a poor prognosis[1)2)]. In this study, DNA contents are examined to further study as to whether histopathologically prognostic factors correlate with an increased DNA content of esophageal cancer cells in terms of their prognoses or not, and also to clarify the validy of measurement of DNA content is esophageal cancers.

MATERIAL AND METHOD

Forty-seven surgical specimens were eligible for this study. The histopathologic findings were compared with nuclear DNA contents in esophageal cancer cells. Nuclear DNA contents were measured from paraffin-embedded tissuse according to the method reported by Schutte B *at al*[1)].

Table 1 shows a ralationship between macroscopic findings and DNA indices, and the margins of the lesions and DNA indices. There were no close relationship between each other. However, the lesions with unclear margins of the lesions indicated the increase in DNA contents in cells.

Table 2 shows a relationship between the modes of tumor growth and DNA indices and histologic differentiation and DNA indices. There was no close correlation between these factors although poor differentiation of cells tended to indicate an increase in DNA content. **Table 3** shows a relationship between histologic findings and DNA indices.

The nodes of intraepithelial extension did not closely correlate with DNA indices.

However, vascular invasions of vessels and lymphatics were prone to indicate increased DNA contents.

According to the patterns of DNA ploidy, adventitial invasion from a_1 (within the advential layer) to a_3 (outside the adventia) apparently showed an aneuploidy of DNA pattern as shown in **Table 4.** On the other hand, node involvement was seen more often in the demonstration of

Table 1. Comparison between macroscopic findings and DNA index

Mecroscopic classification

	DNA INDEX
protruded	1.54±0.45 (n= 9)
superficial	1.46±0.51 (n= 3)
ulcerative	1.53±0.44 (n=35)

Macroscopic classification

Margins of lesion	DNA INDEX
clear	1.56±0.42 (n=16)
moderately clear	1.55±0.46 (n=24)
unclear	1.39±0.49 (n= 7)

Table 2. Relationships between histologic findings and DNA index

Histologic classification

The modes of growth	DNA INDEX
expansive	1.57±0.31 (n= 8)
intermediate	1.66±0.36 (n=25)
infiltrative	1.44±0.55 (n=14)

Histlogic classification (squamous cell carcioma)

differentiation	DNA INDEX
well	1.50±0.37 (n=15)
moderately	1.63±0.45 (n=27)
poorly	0.33±0.34 (n= 5)

ns.

Table 3. Relationships between histologic findings and DNA index

Histologic classification

epithelial extension	DNA INDEX
ie (−)	1.57±0.38 (n=27)
ie (+)	1.60±0.48 (n=20)

Histologic classification

lymph vessel invasion	DNA INDEX
ly (−)	1.46±0.41 (n=18)
ly (+)	1.62±0.42 (n=29)

Histologic classification

vasclar invasion	DNA INDEX
v (−)	1.49±0.39 (n=25)
v (+)	1.63±0.45 (n=22)

n.s

Table 4. Relationships between histlogic findings and DNA ploidy

Ploidy	a0	a1∼3
diploidy	7	6
aneuploidy	7	27*

*: $p<0.05$

Ploidy	n (−)	n (+)
diploidy	9	5
aneuploidy	8	25*

*: $p<0.05$

Stage

Ploidy	0	I	II	III	IV
diploidy	1	4	1	3	4
aneuploidy	2	3	4	10	15

ns.

aneuploid pattern.

In summary, the more cellular DNA content increases, the more the disease stage advances.

DISCUSSION

In many tumors, the presence of aneuploid population of cells means poor prognsis, indicating a rapid tumor growth with infiltrative extension to the surrounding organs. Recently FCM study extended to the fresh tumors by using flow cytometric study in esophageal cancers[3].

On the other hand, squamous cell carcinoma (SCC) in esophageal cancers is most common. Most of SCC represent a presence of aneuploid population. It is accepted that approximately 92.5% of SCC of the esophagus are non-diploid. Therefore, diploid population imply tumors with a DNA profile similar to normal esophageal tissue including hyperplastic changes.

We must take it into consideration that some tumors show heterogenity for DNA ploidy. Therefore, even if the tumor showes diploid profile in analysis of DNA ploidy, aneuploid population of cells could not be neglected.

Sugimachi[4] reported that factors affecting survival were sex, lymphnode involvement. resection line involvement and macroscopic clearance of tumor. Women were superior to men in survival. However, the frequency of

esophageal cancer in females is relatevely low in occurrerence in comparsion with that in male.

In general, an increase in aneuploid population of cells carries a worse prognosis, but in some SCC a diploid profile has been associated with a worse prognosis[5]. Recently Rutgers[5] reported that a favorable prognosis was shown in the non-diploid, non-tetraploid tumors. Diploid tumors has been distributed with a range of 0%[7] to 40%[8].

In contrast, this study indicated that aneuploid population in esopahgeal cancer cells was less common with a range of 58.9% as compared with other reports[3][7] and also represented aggressive spreading of cancer infiltration with respect to nodal and adventitial involvement.

However, clinically different characteristics of in malignant potential between diploid and aneuploid tumors was not necessarily defined except for nodal and advential involvement in this study.

The reasons for no clear difference in malignant potential between diploid and aneuploid tumors are that diploid population of esophageal cells still behaves the same attitude of aneuploid cells as cited by Hilton *et al.*[8] In fact, diploid tumors account for low incidence in occurrence, although they indicate heterogeneity. Some show worse prognosis and some do not in diploid tumors. The exact role of DNA ploidy status is still unclear in terms of the survival in patients with esophageal cancer. Further study is necessary to clarify the significance of diploid profile.

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