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Original Article

Analysis of macroscopic difference between adenoma and intramucosal well differented early adenocarcinoma in small colorectal tumors

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Macroscopic analysis was performed in 255 cases of small colorectal polyps, which were almost less than 10 mm in the greatest diameter and had already diagnosed with anti－p53 reagents immunohistochemically. In polyps of I' type, the well differentiated early adenocarcinoma limited in mucosa (m－Adenoca) was clinically found at the size of 6 mm in diameter but could not be differentiated from the adenoma by their size. This mean cancerous diameter examined by p53－immunostaining was corresponded to the boundary diameter of adenoma－carcinoma sequence (ACS) by the morphometric diagnosis, i.e. between 5 and 10 mm. m－Adenoca of II' type was immunohistochemically confirmed at the size of 5 mm or less in the greatest diameter ($p<0.05$), which was, furthermore, completely similar to previous by morphometric multivaliate analyses.

This supported the importance of p53－overexpression in cancer in cancer diagnosis. The p53－immunostaining is very convenient for routine hsitopahtological diagnosis of well differentiated early adenocarcinoma.

Key words : early colon cancer, well differentiated adenocarcinoma, macroscopic findings. p53

Introduction

It was frequently difficult for pathologists to make their diagnosis of m－Adenoca. Carcinoma was usually histologically diagnosed under the subjective basis of each experience of pathologists. (1) This non－scientific approach was corrected by the findings of sm involvement (Morson), linear discriminant function by morphometry (Nakamura), and so on. (2－5, fig. 1) We discussed the differentiation of m－Adenoca with p53－immuno staining in previous report, and this method was proven to be very practical for routine histological diagnsosis. (4)

In this study m－Adenoca diagnosed by p53－immunostaining was macroscopically reanalyzed and their endoscopic findings of polyp configuration was debated. The histogenesis was , furthermore, speculated with a consideration of referrences. (24)

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Materials and Methods

Specimens : 99 cases of adenomas and 156 cases of m－Adenoca were studied. All these specimens had been immunohistochemically diagnosed with anti－p53 reagents because they were difficult to differentiate by hematoxylin－eosin stain. (4) All tumors were superficially protuberant and measured less than 10 mm in the greatest diameter.

Methods : Tumors were endoscopically classified into two groups as followings: (1) protuberant type (typ I') including types Ip', Isp', and Is', and (2) flat elevated type (type II') containing IIa' with/without either typ IIb' or IIc'. The greatest diameter of polyps was separately analyzed with every type of macroscopic configuration.

Results

99 adenomas consisted of 81 polyps of type I' type and 18 ones of type II'. (Fig. 2) Polyps of type I' and type II' were 6.1 mm and 3.6 mm in

the greatest diameter, respectively.

156 m−Adenoca consisted of 124 polyps of type I' and 32 ones of type II'. Polyps of type I' and type II' were 6.0 mm and 4.9 mm in the greatest diameter, respecively. There was a significant difference in the size of polyps between type I' and type II' ($p<0.05$).

Among II' type polyps m−Adenoca was significantly larger than adenoma($p<0.05$).

Discussion

In this study the examined polyps had been immunohistologically diagnosed on the basis of p53−overexpression. In the greatest diameter of polyps of type I', there was no difference between adnoma and m−Adenoca, i.e. both types were 6 mm wide. Adenoma of type I' would be confirmed in the size between 5 and 10 mm. In polyps of type II', m−Adenoca was significantly larger than adenoma, about 5 mm and 3.5 mm in the greatest diameter, respectively. In polyps of m−Adenoca, the greatest diameter of I'−typed polyps was significantly larger than that of II'−type ones($p<0.05$). These meant that I'−typed polyps were found in larger size than that of II'−typed ones. According to previous morphometric diagnoses m−Adenoca of type I' was found in the size of 5−10 mm and m−Adenoca of type II' was identified in the size less than 5 mm(2)(fig. 3). Because the analysis based on morphometric discrimination was completely accordant with our immunohistochemical results, the immunochemical examinations could be substituted for the morphometric studies. Based on the morphometric analyses in Fig. 3, de novo carcinoma would hold a dominant position over adenoma−carcinoma sequence(ACS) in histogenesis of colorectal carcinomas.

Morphometric analysis was very troublesome to apply to routine diagnostic procedures because of time−consuming and expensive equipments, to both caliculate the indexes, i.e. the index of nucleus−gland ratio(ING) and the index of structural atypia(ISA), and discriminate by the linear discriminant function Fca=0.08xING+0.04xISA−6.59. Anti−p53 immunostaining method was, on the contrary, more convenient for routine histological diagnosis because immunostaining procedure was automatically performed and its imunopositivity was easily confirmed at low magnification power view. Immunohistochemical studies should be more applied to discriminate m−Adenoca in clinical diagnosis.

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Fig. 1. Histological diagnosis of cancer: comparison between previous methods and their convenlency

diagnostic basis basis (author)	merits	demerits
classical atypism	very convenient	subjective
sm involvement (Morson)	reflecting the prognosis	Though tumor limited in mucosa without definite atypism, short of malignancy, was diagnosed as benign, the tumor of same atypism invading sm was corrected to carcinoma. Same histology has two diagnoses.
morphometic multivariate (Nakamura)	objective	not convenient (expensive equipment, time-consuming in analysis)
gene	objective	not convenient (expensive equipment, time-consuming in analysis)
immunostain	objective	convenient

Fig. 2. Clinicopathological differences of polypoid colorectal tumors between the adenomas and the mucosal tub1 adenocarcinomas associated with adenoma, discriminated only by p53 protein overexpression.

lesion	macro	cases	age	diameter (mm)
adenoma	I'	81	65 ± 11	6.1 ± 4.5
	II'	18	63 ± 8.5	3.6 ± 1.9 *
	Σ	99	65 ± 11	5.6 ± 4.2
m-Adenoca	I'	124	66 ± 9.5	6.0 ± 4.4 #
	II'	32	64 ± 10	4.9 ± 4.2 *#
	Σ	156	65 ± 9.6	5.8 ± 4.4

*, #: significance, $p<0.05$

Fig. 3 Summary of previous reports between the occurence (%) of adenoma-carcinoma and its diameter

diagnosis	histogenesis		diameter (mm) 3	5	10	20	
classical diagnosis based on experience	ACS 95-100%	adenoma		81%		15%	4%
		with ca.		3%		24%	25%
	de novo ca.: 5%						
morphometric diagnosis	ACS 20-30%	adenoma					
		with ca. 型 (sm%)	0% IIa'	5%	22%	35% I'(7%)	1
	de novo ca. 70-80% 型 (sm%)		100% II'(17%)	95%	78% II'(16%)	65% (38%)	2,3

ACS: adenoma-carcinoma sequence
ca.: carcinoma
sm: submucosal involvement

微小な大腸直腸腫瘍における、粘膜内高分化型腺癌と腺腫の肉眼的相違

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大腸・直腸腺癌の多段階発癌モデルにおいてadenoma－carcioma sequence(ACS)が主張されて以来、早期癌はその肉眼的大きさに比例して異形成を増すことにより、ポリープはその大きさに基づき、小さな腺腫、大きな腺腫、腺腫内腺癌、早期浸潤癌に分類されている。遺伝子による癌の診断が不可能である現状において、このACS理論における癌の組織診断根拠は旧態然とした病理医の主観的経験に基づいている。その為、共通な診断基準が無く、国内のみでなく外国文献との照合が不可能であり、近藤誠の指摘する「放置しておいても死なない癌を一生懸命見つけて治療している」に抗議できないのが現状である。中村恭一らが指摘する異形成の組織計測による判別式が唯一客観的な手法出ある。今回、既報告のp53免疫染色陽性で10mm以下の分化型粘膜内腺癌（m－Adenoca）診断症例156例似ついて、その肉眼的形態を再検討した。その最大径において、II'型は4.9mmと、I'型６mmよりも小型であった(p<0,05)。更に、II'型m－Adenocaは、II'型腺腫3.6mmよりも大型であった。(p<0.05)。この免疫組織学的検討結果は、組織計測による検討結果に著しく類似しており、肉眼所見においても、前者の有効性が再確認された。組織計測による癌の診断は複雑であり日常の病理診断に不向きであり、廉価で容易な免疫組織学的診断手技は有効な手段と判断された。

キーワード：早期大腸癌、高分化型腺癌、肉眼所見、p53

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