

## Significance of Serum Laminin and type IV Collagen Content Change Between Liver Benign Lesions and Malignant Tumor

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**Abstract Objective** To investigate the change of serum LN, CIV content in the patients with liver benign lesions and malignant tumor and explore their significance in liver malignant tumor. **Methods** 36 patients, including 22 males and 14 females, were divided into two groups, malignant tumor group (10 cases) and benign tumor group (26 cases). 15 cases of non-hepatic patients act as control group. Radioimmunoassay kits were used to measure serum LN, CIV content before and after treatment. **Results** in patients with liver malignant tumor, LN, CIV are significantly higher (LN  $225 \pm 55.1 \text{ ng/ml}$ , CIV  $118.7 \pm 26.8 \text{ ng/ml}$ ) than that in the patients with liver benign tumor or non-hepatic disease and increase gradually as the disease progressing ( $P < 0.05$ ). LN, CIV content would increase again when liver malignant tumor metastasize or recurrence. There are no significant difference between liver benign lesions group and control group ( $P > 0.05$ ). **Conclusion** the examination of serum LN, CIV is useful for distinguishing liver benign lesions and malignant tumor, deciding liver malignant tumor metastasis or recurrence and monitoring curative effect.

**Key Words** laminin; type IV collagen; benign lesion; malignant tumor; liver

Recently immunohistochemistry research indicated that the binding of laminin (LN), collagen IV (CIV) to endothelial and epithelial may regulate the movement, development and differentiation of cell, and related closely to the invasion and metastasis of tumor. In this research, we investigated the content change of LN and CIV in patients with benign and malignant liver tumor and its clinical significance.

### MATERIALS AND METHODS

#### Clinical data

36 patients come from our hospital in-patients, including 22 males and 14 females, aging from 22 to 72 (mean, 48.7) years old. Among these cases, 10 cases with liver cancer (4 cases with late metastasis), 14 cases hepatic cyst, 10 cases hepatic angiosarcoma, 2 cases liver tuberos degeneration. All patients were examined by liver B ultrasonic wave, Computer Tomography (CT) and/or Magnetic

Resonance Imaging (MRI) to identify the benign and malignant lesion, the laboratory marker of AFP, AKP, AFU, GGT were also examined. Two patients with liver tuberos degeneration were biopsied by liver paracentesis, 10 patients with liver cancer were operated or interventional therapeutics and have the pathological evidence, 15 cases non-hepatic patients act as control, which includes 9 males and 5 females, aging from 25 to 66 years old, mean age is 42.5 years old.

#### Methods

2.0 ml venous blood of patients were collected at empty stomach and pour into the dry tube, then centrifugated and collected the supernatant, stored at  $-20^\circ\text{C}$  for later determination. LN and collagen IV levels were determined by RIA which were provided by military medical institute in shanghai. Unit: ng/ml. We conducted the experiment according to logit-log regression and calculated the sample results.

#### Statistical method

The results are presented as  $\bar{X} \pm \text{SD}$  (standard deviation), applying the SPSS software bags, The results are presented as with  $t$  examination and  $X^2$  examination.

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## RESULTS

Content of the laminin and collagenIV in serum of patients with benign and malignant tumor see table 1.

The serum level of LN and CIV in the 10 patients with malignant tumor after therapy was (168.55±22.4) ng/ml and (53.8±18.8) ng/ml respectively, which were significant lower than that before therapy [(225±55.1) ng/ml, (118.5±26.8) ng/ml] ( $p < 0.05$ ). 4 cases of them appeared recurrence or metastasis of the tumor, the levels of LN and CIV in them increased again and were (298.3±68.4) ng/ml and (126.8±19.6) ng/ml respectively, and the difference was significance in statistics ( $X^2=4.12$ ,  $p < 0.05$ ).

### Relationship between the LN , CIV and AFP, AKP, AFU, GGT

The levels of AFP, AKP, AFU and GGT were all increased in the patients with malignant tumor, and they had a positive correlation with LN and CIV ( $r=0.7612\sim 0.9108$ ). However, they have no significant correlation in patients with benign tumor (see table 2)

## DISCUSSION

As the main component of basement membrane in cellular interstitial, LN and CIV regulate the movement, development and differentiation of cell. In addition, immunohistochemistry research shows

that they are closely related to the tumor's invasion, development, and metastasis in recent years<sup>[1]</sup>. Laminin is a non-collagen constitutive glycoprotein in extracellular interstitial, which was mainly synthesized in the liver by endothelial cell and fat-storing cell. It was the main component in basement membrane, and distributed widely in vessel basement membrane hyaline layer in normal tissue, binding to type IV collagen constitute the skeleton component of basement membrane<sup>[2]</sup>. The invasion and metastasis of tumor is a considerable complex process. There are dual actions of LN in infiltration and metastasis of tumor. when LN and CIV constitute the basement membrane, it might be a barrier and arrange the sinus-like to form the basement membrane of neocapillary network in tumor tissue. In addition, LN in tissue produce the chemotaxis to endothelial and promote its differentiation. As well as, it stimulate the cellular to secrete the vascular growth factor, facilitate the neovascularization. All this accelerate the metastasis of tumor cell, matrix degradation, formation of tumor vessels, which cause the increasing of LN in vivo. So, to examine the serum content of LN may well understand the level in vivo<sup>[3]</sup>. Adhesiveness play an important role in the invasion and metastasis of tumor. At the same time, adhesiveness act as a double effect on incursion tumor cell. On one hand, homotype tumor cell adhesive ability reduced, which cause them detach from the primary neoplasia to metastasis; on the other hand, it is necessary to adhere to the distant matrix, thus tumor cell continuous adhesiveness and obtain the

**Tab. 1** Content of the laminin and collagenIV in serum in patients with benign and malignant tumor (ng/ml)( $\bar{x}\pm s$ )

group	case	LN	CIV
malignant tumor	10	225±55.1 <sup>△</sup>	118.7±26.8
benign tumor	26	80.3±20.1*	34.6±18.6*
control	15	76.8±18.8	32.4±13.2

<sup>△</sup> compared with benign tumor:  $t=3.97$ ,  $p < 0.01$

\* compared with control :  $t=0.82$ ,  $p > 0.05$

**Table 2** correlation assay between the LN, CIV and AFP, AKP, AFU, GGT

groupe	AFP	AKP	AFU	GGT	P
malignant tumor	0.9108	0.7612	0.8011	0.8816	<0.01
	0.9016	0.7822	0.7651	0.8715	<0.05
benign tumor	0.001	0.031	0.086	0.028	>0.05
	0.013	0.026	0.032	0.078	>0.05

mobile tensile strength. The process of invasion is the alternation between the adhesion and de-adhesion. LN is the main agent involved the adhesiveness and degradation<sup>[4]</sup>. Type IV collagen is the skeleton component of functional basement membrane between the epithelial and liver cell, which may degraded by type IV collagenase secreted from tumor cell. Matrix metalloproteinase inhibitors in tissue inhibit the activity of type IV collagenase, thereby inhibit the invasion and metastasis of tumor cell<sup>[5,6]</sup>. Liver cancer cells become cancer embolus, when entering portal vein or hepatic veins, they must penetrate blood sinusoid where there are many reticulum structures composed by collagenous fibers. At the same time liver cancer cells release CIV enzyme to destroy the structures and become metastasis<sup>[7]</sup>, and result in CIV level reduce in tissue basement membrane and increase in blood.

In this research, we observed the serum level of LN and CIV in patients with benign and malignant tumor, and the results showed that the increased levels of LN and CIV in serum were closely related to the malignant tumor, suggesting that they might be one of early markers in the diagnosis of malignant liver tumor. Therefore the serum level of LN and CIV have very important significance in identification of benign and malignant tumor and curative effect judgement.

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