Brief Reports

Combined measurement of serum tumor markers in patients with hepatocellular carcinoma *

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INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most common malignant neoplasms, and its prognosis is very poor if diagnosed late, therefore, early detection is important. As we know not all HCC can secrete AFP, and AFP levels may be normal in as many as 40% of patients with early HCC and 15%-20% of patients with advanced HCC[1]. Therefore, we selected AFP, alpha-L-fucosidase (AFU) and sialic acid (SA) in combination for detecting HCC.

MATERIALS AND METHODS

Subjects were divided into three groups: ① HCC group consisted of 30 patients (26 males and 4 females) with a mean age of 50.4±12.7 years; ② liver cirrhosis group consisted of 30 patients (24 males and 6 females) with a mean age of 45.3±8.4 years; and ③control group consisted of 30 healthy subjects (28 males and 2 females) with a mean age of 33.2±4.8 years whose liver function tests were normal. Diagnosis of HCC was in accordance with the criteria of the National HCC Association of China in 1977[2].

The fasting sera from all subjects were stored at -18℃. AFP was measured by ELISA. The kits were provided by Xiamen Advanced Scientific Institute[3]. AFU was measured according to Troost's method and expressed as nkat/L[3]. The kits were provided by Sanming Lanbo Biological Technique Institute. SA was measured by spectrophotometry. The kits were purchased from Dongou Biological Technical Institute. The data were expressed as $\bar{x}\pm s$ and analyzed statistically by the Student's *t* test.

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RESULTS

The serum levels of AFP, AFU and SA in the three groups are shown in Table 1.

The serum levels of AFP, AFU and SA in patients with HCC were significantly higher than those in patients with cirrhosis ($P<0.01$) and in the control subjects ($P<0.01$). No significant differences were found between the latter two groups.

The cutoff value was defined as $\bar{x}+2s$ (AFP≤30 μg/L, AFU≤180 nkat/L and SA≤630 mg/L).

The positive rates and significance of AFP, AFU and SA in the three groups are shown in Tables 2 and 3.

Results of combined measurement with two positives among the three tumor markers are shown in Table 4.

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate were 86.7%, 98.3%, 93.7%, 96.3% and 94.4%, respectively.

Table 1 The serum levels of AFP, AFU and SA among patients in the three groups (x±s)

Groups	AFP(μg/L)	AFU(nkat/L)	SA(mg/L)
Control	10.2±9.8	106.0±36.5	513.7±57.8
Cirrhosis	14.4±9.0	126.8±52.1	522.7±70.5
HCC	71.7±38.8[bd]	284.5±102.6[bd]	636.7±76.6[bd]

[b]$P<0.01$, compared with controls, [d]$P<0.01$, compared with cirrhosis.

Table 2 Positive rates of AFP, AFU and SA among the three groups

Groups	AFU		AFU		SA	
	n	(%)	*n*	(%)	*n*	(%)
Controls	1	(3.3)	1	(3.3)	2	(6.7)
Cirrhosis	2	(6.7)	4	(13.3)	5	(16.7)
HCC	21	(70.0)	23	(76.7)	21	(70.0)

Table 3 Significance of AFP, AFU and SA (%)

	AFP	AFU	SA
Sensitivity	70.0(21/30)	76.7(23/30)	70.0(21/30)
Specificity	95.0(57/60)	91.7(55/60)	88.3(53/60)
Positive predictive value	87.5(21/24)	82.1(23/28)	75.0(21/28)
Negative predictive value	86.4(57/66)	88.7(55/62)	85.5(53/62)
Accuracy	86.7(78/90)	86.7(78/90)	82.2(74/90)

Table 4 Results of combined measurement of serum AFP, AFU and SA in the three groups

Groups	Postivity	
	n	%
Controls	0	0.0
Cirrhosis	1	3.3
HCC	26	86.7

Patients with HCC showed both positive AFU and AFP in 16/30 patients and negative results in 2/30 patients. Of the remaining patients, 5 were positive in AFP and negative in AFU, and 7 were negative in AFP and positive in AFU (Table 5). No correlation was found between AFP and AFU ($P<0.05$).

Table 5 Comparison between AFP and AFU in patients with HCC

AFP	AFU		
	Positive	Negative	Total
Positive	16	5	21
Negative	7	2	9
Total	23	7	30

DISCUSSION

So far, AFP still remained the most sensitive and specific marker of HCC. Our results showed that the sensitivity of AFP in patients with HCC was 70%, concordant with the reports by many other authors[4,5].

AFU is a lysosomal enzyme involved in the catabolism of the fucose-containing glycoconjugates. In accordance with the study of Deugnier, et al, the serumlevel of AFU activity in patients with HCC was increased[6]. Its positive rate in our study was 76.7% (23/30), similar to other reports (75%-76.7%)[4-7]. This may be related to increased enzyme release by tumor cells[6,7].

Our study showed that serum AFP and AFU activity was independent with no correlations between them as shown in Table 5. Therefore, AFU may be considered as an additional useful marker for detection of HCC.

The SA was considered to be associated with behaviour of malignant tumors. In our studies, its positive rate in patients with HCC was 70% as reported by many other authors[8,9]. The serum level of SA in HCC was also high and was positive in 71.4% when AFP was negative.

The main purpose of using combined measurement of tumor markers is to eliminate the false negative and false positive results as reported by many authors[1,4,5,10]. We used combined measurement of serum AFP, AFU and SA of patients with HCC. With this measurement, any two positives among the three tumor markers as the diagnostic criteria, the sensitivity, specificity, positive predictive value, negative predictive value and rate of accuracy in HCC patients were 86.7%, 98.3%, 93.7%, 96.3% and 94.4%, respectively. Six of 9 patients with HCC who had negative AFP had positive results in both AFU and SA. None of 3 patients with liver cirrhosis and controls who had positive AFP had positive results in AFU and/or SA. Therefore, combined measurement of serum AFP, AFU and SA is of practical significance in diagnosis of HCC.

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