

ALPHA-2 MACROGLOBULIN: AN ADDITIONAL MARKER FOR DIAGNOSIS OF HEPATOCELLULAR CARCINOMA

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SUMMARY

The serum level of α -2 macroglobulin was estimated in normal healthy controls (43) and patients of hepatocellular carcinoma (HCC; 15), cirrhosis of the liver (13) and amoebic liver abscess (ALA; 16). The value of α -2 macroglobulin was significantly raised in HCC as compared to cirrhosis and ALA. Alpha fetoprotein (AFP) estimation was carried out in patients of HCC and the values of α -2 macroglobulin and AFP were found to be inversely related in HCC patients. α -2 macroglobulin is considered another important marker for the diagnosis of HCC in AFP negative patients.

INTRODUCTION

Although alpha fetoprotein (AFP) remains the best known marker for early diagnosis of hepatocellular carcinoma (HCC), new tumour markers are required to be evaluated because one-fifth of all liver cancers in high risk areas do not have an elevation of AFP. Estimation of glutaryl transpeptidase isoenzyme¹, 5-nucleotidase phosphodiesterase isozyme², alpha-1 antitrypsin³, hepatoma associated antigen⁴ and ferritin⁵ have been shown to be of great value in the diagnosis of AFP negative HCC. Our earlier study⁶ had shown that alpha-2 macroglobulin was significantly raised in patients of HCC as compared to controls. The present study was designed to make a comparative evaluation of AFP and alpha-2 macroglobulin as tumour markers for the diagnosis of HCC.

MATERIAL AND METHODS

Alpha-2 macroglobulin was estimated quantitatively⁷ in patients of HCC (15), cirrhosis of the liver (13) and amoebic liver abscess (ALA; 16), and in 43 normal healthy subjects with no evidence of recent or past liver diseases. The diagnosis of HCC and cirrhosis of the liver was based on clinical and histological criteria whereas the diagnosis of ALA was as per WHO recommendations⁸.

Quantitative estimation of AFP was carried out in patients of HCC (15) and healthy controls (20) using a radioimmunoassay kit (Alpha-feto RIA kit) from Diabot Radioisotope Lab, Japan.

RESULTS

The mean \pm SD alpha-2 macroglobulin level was highest in patients with HCC (119 ± 50 IU/ml). In patients with cirrhosis of the liver (79 ± 45 ; $P < 0.05$)

and ALA (77 ± 49 ; $P < 0.05$) and in controls (64 ± 62 ; $P < 0.001$), the levels were significantly lower.

The mean alpha fetoprotein levels in patients of HCC was 119 ± 50 ug/ml. In this group of patients, 8 subjects had AFP levels within the control range of 8 ± 9 ug/ml. However, in these 8 patients, alpha-2 macroglobulin was significantly raised (150 ± 46 IU/ml). But in the 7 patients of HCC where the mean AFP level was 169 ± 66 ug/ml, the alpha-2 macroglobulin levels were within the limits of normal range. The values of r , the coefficient of correlation for linear relationship, was highly significant, showing an inverse correlation between the levels of alpha-2 macroglobulin and AFP in the patients with HCC.

DISCUSSION

Alpha-2 macroglobulin has been to be synthesised by the rat hepatoma cells⁹. It was observed that alpha-2 macroglobulin levels were significantly raised in proved cases of HCC and their levels were higher than those of cirrhotic patients. HCC is a known complication of cirrhosis of the liver, and is often a cause of its sudden decompensation. Various screening tests, like AFP estimation and ultrasound, are used for the detection of this tumour. It is known that AFP may be negative in one fifth of these cases. This study suggests that alpha-2 macroglobulin and AFP have an inverse relationship. Hence, whenever screening tests are to be utilised for the detection of HCC in patients of cirrhosis, both these biochemical parameters should be estimated. The inverse relationship between AFP and alpha-2 macroglobulin may be because some HCC synthesise one marker while some others synthesise the other.

These observations further suggest that alpha-2 macroglobulin estimation may also help to differentiate atypical cases of ALA from HCC.

REFERENCES

1. Sawabu N, Nakagen M, Ozaki K, et al. Gamma-GTP isoenzyme as diagnostic tool for hepatocellular carcinoma. *Ann Acad Med* 1980; 9 : 206-9.

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2. Tsou KC, Lo KW. Serum 5 nucleotidase phosphodiesterase isoenzyme for human liver cancer. *Cancer* 1980; 45 : 209-13.
 3. Oon CJ, Yosi Chio LF, Dixie C, Tan Y. The evaluation of tumour marker proteins in the diagnosis of primary hepatocellular carcinoma. *Ann Acad Med* 1980; 9 : 228-33.
 4. Xu XI, Luo LD, Wan DF, *et al.* Hepatoma associated antigen. *Shanghai Med J* 1979; 2 : 676-81.
 5. Kuneto A, Kubo V, Nagasake Y, *et al.* Clinical evaluation of serum functions in hepatocellular carcinoma and cirrhosis. *Acta Hepatol Jpn* 1980; 21 : 745-53.
 6. Kar P, Chawla YK, Tandon BN, Gandhi BM. Diagnostic significance of alpha 2 macroglobulin in liver diseases. (Communicated).
 7. Mancini G, Carbonara AD, Haremans J. Immunochemical quantitations of antigens by single radial immunodiffusion. *Immunochemistry* 1965; 2 : 235-54.
 8. WHO Expert Committee Tech Rep Ser No 421 Amoebiasis. 1969; 1-52.
 9. Koj A. Comparison of synthesis and secretion of plasma albumin, fibrinogen and alpha 2 macroglobulin by slices of Morris hepatomas and rat liver. *Br J Expt Pathol* 1980; 61 : 332-8.
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