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A STUDY OF SERUM α-FETOPROTEIN AND PLASMA DES-Y- CARBOXY PROTHROMBIN IN HEPATOCELLULAR CARCINOMA

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ABSTRACT

Introduction: The importance of α-fetoprotein (AFP) and des-Y-carboxy prothrombin (DCP) in the clinical treatment of hepatocellular carcinoma (HCC) has been studied extensively, the authors examined the clinical picture of HCC with regard to the state of these two tumor markers. The cutoff values were set at 100 ng/mL for AFP and 0.0625 AU/mL for DCP. Forty-eight patients (20.7%) had high levels of AFP and low levels of DCP, 22 (9.3%) had high DCP levels and low levels of AFP, 12 (4.6%) had high levels of both AFP and DCP, and 155 (65.4%) had low levels of both DCP and AFP. Patients with high levels of DCP but low levels of AFP were predominantly male and had large lesions but few nodules. Patients with high levels of both tumor markers had the most discouraging outcome observed in this study (death within 3 years).

Conclusions of the study is a patients with high levels of DCP and low levels of AFP exhibited the unique clinical characteristic of large HCC nodules that were few in number. In addition, it was observed that measurement of both AFP and DCP can predict the survival of patients.

INTRODUCTION

Hepatocellular carcinoma (HCC), one of the most common cancers in the world, is especially prevalent in Asian countries, where cirrhosis that develops from viral hepatitis is endemic. Although the prognosis is relatively favorable in comparison with other cancers of the alimentary system, it is still unsatisfactory in that its overall 5-year survival rate is no more than 50%[1]

The most potent diagnostic tools for HCC are imaging studies, including ultrasonography, computed tomography (CT), magnetic resonance imaging, and celiac angiography. Tumor markers are also an indispensable way of diagnosing the disease. Y-Fetoprotein (AFP) has served as a representative tumor marker of HCC for more than 30 years, and des- -carboxy prothrombin (DCP) has been found to be another useful marker.[2] Although 50–80% of HCC patients show elevated AFP levels, these levels are also found in cirrhotic patients without HCC, suggesting that AFP elevation is not specific to HCC.[3]

In contrast, DCP is a less sensitive but more specific marker for HCC. DCP is abnormal prothrombin that lacks Y-carboxylation of its glutamin residue. It is unable to bind the calcium ion that is essential for conformational transition and functional activity. Because the Y-carboxylation is vitamin K dependent, this protein appears when a patient is in a vitamin K deficient state[.4]The HCC-related elevation of this protein was initially reported in 91% of HCC patients with elevated levels.[5] Recent studies showed that elevated levels of DCP were found in less than 50% of patients, because HCC is diagnosed at earlier stages. In contrast to the low positivity rate, the specificity of this marker is higher than that of AFP, with most reports indicating more than 95% specificity.[6,][7] This prompted us to reconsider the relation between the profiles of tumor markers and the clinical features of HCC in this study.

MATERIALS AND METHODS

Our study examined 366 patients with HCC who underwent surgical or medical treatment at our institute between years 2015 to 2016. Among these patients, DCP and AFP were measured in 237 cases, 179 males and 58 females ranging in age from 37 to 87 years, with a mean age ± standard deviation (SD) of 61.6 ± 9.0 years. These patients were enrolled in this study. Seventeen patients were positive for HBs antigen, 204 had anti-HCV antibody, and 16 were negative for both of virus markers. Two hundred one patients underwent ethanol injection therapy for management of HCC according to our previous reports, and 27 patients were treated by microwave coagulation therapy.[8][9]The control group consisted of 63 cirrhotic patients free of HCC, with 60 patients HCV antibody positive and 3 patients HBs antigen positive. Thirty-five patients were male and 28 female, ranging in age from 35 to 81 years, with a mean age ± SD of 60.4 ± 9.6 years.

Diagnosis of HCC

All of the patients underwent contrast-enhanced dynamic CT and ultrasound studies. Of 237 patients, 231 had a histopathologically confirmed diagnosis based on a specimen obtained by percutaneous fine-needle biopsy under ultrasonographic guidance. Specimens were independently reviewed by two pathologists on a blinded basis. We adopted a higher histologic grade when the diagnoses differed between the two pathologists. Diagnostic criteria was based on previous reports.[10] Diagnosis of the remaining six patients was made by a typical imaging pattern of HCC, such as contrast-enhanced area in the early phase and washout of contrast in the late phase on dynamic CT.

Serum AFP and Plasma DCP Determinations

The serum AFP concentration was determined by latex agglutination immunoassay (AIA-PACK AFP, Tosoh Co., Yamaguchi, Japan). Plasma concentration of DCP was tested by monoclonal antibody against DCP according to the manufacturer's instructions (EI-test mono-P-II kit E-1023, Eisai Laboratory, Tokyo, Japan)

RESULT AND DISCUSSION:

The clinical backgrounds of HCC patients in this study. The median value for AFP was 29 ng/mL, whereas that of DCP was 0.0625 arbitrary units (AU)/mL. Cutoff values determining high or low levels of AFP and DCP were set at 100 ng/mL and 0.0625 AU/mL, respectively, according to receiver operating characteristic curves. AFP levels were high in 60 of 237 patients (25.3%), and DCP levels were high in 33 patients (13.9%). The sensitivity and specificity gauged by the cutoff value for AFP were 25.3% and 90.5%, and those for DCP were 13.5% and 100%, respectively.

To evaluate clinical characteristics of HCC patients, the patients were categorized into the four following groups, according to the levels of AFP and DCP values: those with high levels of AFP and low levels of DCP ("AFP single high"), those with high levels of DCP and low levels of AFP ("DCP single high"), those with low levels of both AFP and DCP ("both low"), and those with high levels of both AFP and DCP ("both high"). The group with high levels of DCP and low levels of AFP (n = 48) was designated as the group showing high serum AFP levels and low plasma DCP. The group with high levels of DCP with low levels of AFP (n = 22) was defined to include those with elevated DCP, whereas AFP stayed under the cutoff value. Neither AFP nor DCP were elevated in the "both low" group (n = 155), whereas both AFP and DCP were high in the "both high" group (n = 12).

We focused our interest on the clinical features of HCC lesions and HCC patients. We have long been impressed the few patients we have observed who had a curious pattern of tumor markers, in which the AFP level remained below the cutoff value of 100 ng/mL but DCP exceeded 1.0 AU/mL, and in whom disease seemed highly

progressive. We have also been impressed by the observation that they tended to have only one or a few large-sized HCC nodules. As far as we know, there are no previously published reports that comment on these HCC characteristics. In this study, "DCP single high" populations were preponderantly male and characterized by a large-sized tumor with only a few nodules. For these reasons, DCP measurement is important for patients with "DCP single high" characteristics, as they would otherwise be overlooked because of low AFP levels. Finally, the significance of the markers in relation to the biologic grade of malignancy was analyzed. Based on these results, AFP and DCP tumor markers seem to aid greatly in the characterization of HCC.

CONCLUSION

Patients with high levels of DCP but low levels of AFP were predominantly male and had large lesions but few nodules. Patients with high levels of both tumor markers had the most discouraging outcome observed in this study (death within 3 years).

Conclusions of the study is a patients with high levels of DCP and low levels of AFP exhibited the unique clinical characteristic of large HCC nodules that were few in number. In addition, it was observed that measurement of both AFP and DCP can predict the survival of patients.

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