The Clinical Value of Serum CA15-3 Assay Postoperatively in Breast Cancer Patients

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ABSTRACT: Serum carbohydrate antigen (CA15-3) values were examined in 300 normal subjects in order to determine the standard value of this antigen. The clinical relevance of repeatedly assaying this marker in patients with or without recurrent breast cancer postoperatively was compared with assaying the serum carcinoembryonic antigen (CEA) values. The upper limit of CA15-3 was calculated as being 25.3 U/ml in the normal subjects and the distributions of CA15-3 values were not markedly different among the normal subjects, even if they had been selected according to sex or age. Moreover, no differences were observed among normal women who had been randomly selected according to the age distribution of the breast cancer patients. Thirty samples taken from the breast cancer patients postoperatively revealed values of higher than 25 U/ml and 73 samples showed lower levels. The serum CEA values were positive in 16 samples and negative in 85 samples. Although the accuracy of the CEA assay was about 10 per cent higher than that of the CA15-3 assay, its low positive rate was unsatisfactory for effective use in the breast clinic. The results of this study suggest that serum CA15-3 is not detectable unless there is a relatively large number of tumor cells. The higher false positive rate of the CA15-3 assay should therefore be considered as suggesting recurrence.

KEY WORDS: breast cancer, tumor marker, CA15-3, CEA

INTRODUCTION

Although a specific serum tumor marker for human breast cancer is necessary, not only for diagnosing the disease but also to assess the effects of treatments, such suitable markers have not been found until recently.

A serum carbohydrate antigen (CA15-3) detected by two monoclonal antibodies was revealed to have a relatively high specificity for human breast cancer patients. The assay kit for this tumor marker has therefore been introduced into various breast clinics, however, a difference in the upper limits of this antigen in the sera of normal subjects has been reported by many laboratories. The specificity and accuracy of this tumor marker during the follow up of the clinical course of breast cancer patients also remain to be clarified. The authors examined serum CA15-3 values in a large number of normal subjects in order to determine the standard value of this antigen. The clinical relevance...
of repeatedly assaying this marker in patients with or without recurrent breast cancer postoperatively, was then compared with assaying serum carcinoembryonic antigen (CEA) values.

**MATERIALS AND METHODS**

One hundred and fifty men and 150 women, without any evidence of disease were selected as the normal subjects. There were 30 men and women in each decade, from the twenties to sixties. The sera were prepared from blood samples obtained in the morning before breakfast and stored at -20°C until the assay. The serum CA15-3 values were determined using a radioimmunoassay kit from Centocor Inc., (Malvern, PA, USA). The frequency of values was analyzed as normal, root normal, cubic root normal and logarithmic normal distributions, respectively. The most suitable patterns of histogram obtained after these distribution analyses were selected from the calculated mean values and standard deviations. After the rejection test, carried out according to the method of Smirnov-Grubs, the upper limit of the normal subjects was determined as the converted value of the mean value plus twice the standard deviation (M + 2SD).\(^6\)

The correlation between serum CA15-3 value and recurrence or effects of treatment in 31 postoperative breast cancer patients was studied by means of repeated serum CA15-3 assays and a clinical evaluation using physical, radiological and ultrasoniological examinations.

The serum CEA values were also assayed in 101 samples from the same patients using the sandwich method. The upper limit of the normal value was 5 ng/ml.

**RESULTS**

Both the standard curve and the dilution diagram of the kits showed good straight lines. The coefficients of variation in the intra and inter assay procedures were under 10 per cent in both low and high concentrations of CA15-3.

The values of serum CA15-3 in the normal subjects ranged from 3.0 U/ml to 30 U/ml and the distribution profile of the total number of normal subjects showed a logarithmic normal distribution (Fig. 1). The upper limit of CA15-3 was calculated as 25.3 U/ml after the conversion of M + 2SD.

The distributions of CA15-3 values did not differ greatly even when the subjects had been selected according to sex or age (Table 1). A similar result was observed in the analyses of data after the selection of normal subjects who were in their fifth and sixth decades. Moreover, no difference was observed among the subjects who had been randomly selected according to the age distribution of the breast cancer patients.

The serum CA15-3 assay was performed on the 31 postoperative breast cancer patients, 13 of whom had recurrence, a total of 103 times. Thirty samples revealed values of higher than 25 U/ml and 73 samples showed lower levels (Fig. 2). Of these samples, 63 per cent (19/30) and 26 per cent (19/73), respectively, were taken from those patients with recurrence. The true positive, true negative, false positive and false negative rates were 63 per cent, 74 per cent, 36 per cent and 26 per cent, respectively. Thus, the accuracy of the assay was 70.9 per cent (Table 2). The serum