EVALUATION OF CARCINOEMBRYONIC ANTIGEN AS A MONITOR MARKER IN CARCINOMA OF THE LUNG[+]

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Abstract

Evaluation of clinical value of serum tumor marker CEA in the lung cancer was carried out . This tumor marker was measured in preopoperatively and postoperatively in 130 patients of lung cancer . Data analysis showed that CEA has limited value in the screening for the early lesion , modest value in presaging a successful resection and considerable value monitoring the course of disease following resection . CEA is a clinical tool that merits further investigation and has the potential of leading to the identification of a lung tumor specific marker .

المستخلص

يتضمن البحث تحديد القيمة السريرية للمستضد السرطاني الجنيني (CEA) في مرضى سرطان الرئة. حيث تم تقدير مستوى المستضد CEA في وصول المرضى المصابين باورام الرئة الخبيثة قبل وبعد الاستئصال الجراحي فقد دلت النتائج ان القيمة التنبوئية للـــ CEA تكون محدودة لغرض التشخيص السريري في حين يمكـــن عـــد CEA كمؤشر تشخيصي وتكهني دال للاورام عند متابعة حالة المريض بعد الاستئصال الجراحي وخلال فترة المعالجة.يتطلب اجراء المزيد من الدراسات والبحوث بخصوص تقييم الـــ CEA كدالة ورمية ودورها في التشخيص او المساعدة في التشخيص .

Introduction:

Tumor markers are used in the diagnosis and monitoring the course of treatment in the malignant processes. The presence and concentration of the tumor marker antigens correlate with the persistence and dissemination of the disease. Although they are most a bundate in serum, typical marker are also observed in body cavity fluids, in the urine, on cell membranes or in the cytoplasm. An ideal tumor marker should be directly correlated with the extent of the tumor and the type of neoplasia in order to aid in the diagnosis [1,2]. Thus, the diagnostic value of the tumor markers depend upon their sensitivity and specificity.

CEA has been one of the most popular and most frequently used tumor markers for evaluating and monitoring colorectal, breast, pancreatic, and uterine cervical cancers[3].

Unfortunately, no suitable markers are available for lung cancer, the major cause of cancer death worldwide [4]Several efforts have been made to find out useful markers for this heterogeneous disease [5,6]. Among these carcinoembryonic antigen (CEA) has been most

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extensively studied[7,8] In spite of the low specificity and sensitivity, the antigen has been reported to be of some clinical value in the lung cancrinoma patients[7,8].

There are relatively few data in the literature with regard to the effect of CEA during systemic treatment for lung cancer. This study has been designed to evaluate CEA as a monitor of successful surgical extripation of lung cancer or presage the failure of surgery to totally ablate the tumor.

Material and Methods

Blood samples were drawn from 130 patients prior to surgery. Upon confirmation of a histologic diagnosis of carcinome of the lung, additional blood samples were drawn postoperatively and in 30 day intervals for 3 months and then 3 month intervals until the patient was lost to be followed up .

CEA concentration from the samples were assayed using double antibody CEA-RIA kit obtained from Diagnostic Products Corporation, U.K. The assay was performed as per the manufacturer's guidelines.

Results:

For purposes of analysis and comparison the patients were divided into four groups consisting of the following.

Group I :

Thirty- two(32) patients who had lived longer than 15 months and were currently alive without clinical evidence of progressive disease or who died at any time but were shown by a complete autopsy to be free of disease.

Most patients who were not cured by surgery would give clinical evidence of this fact with in six to 15 months after surgery. For this reason the 32 patients in this group were regarded as having been cured by surgery.

The median preoperative CEA value for this group was 0.4 ng/ml. In the initial CEA evaluation, 4 patient exceeded 5 ng/ml with one of these values reaching 14.9 ng/ml. Of importance was the fact that the interval medi-period never exceeded 1.5 ng/ml. Of all the interval sample collected in this group after the first 3 months of the follow up, 5 ng/ml was exceeded 3 time and 6.5 ng/ml only once (Fig 1).

Group II :

Of the 23 patients in this group, survival was greater than 15 months but in every instance surgery failed to control the disease. The median CEA value at the time of diagnosis was 3.7 ng/ml (Fig 1). While the post-resection median value dropped to 2 ng/ml with in six months of surgery, subsequently the median values continued to rise progressively to exceed 6 ng/ml by the 12 th month of follow- up.

Four of these patients lived longer than three years. Two of these four were surgically explored because of an unexplained increase of CEA levels. One had recurrence in the lung and the second had a second primary of the second lesion accomplished.

Group III:

All of these 39 patient died with in 15 months of surgery and where it could not be shown that other causes were responsible for death it was presumed that death was secondary to persisting lung cancer and that surgery had failed to control the disease (Fig 1). The median preoperative diagnostic value for this group was 5.6 and while CEA values generally decreased after surgical resection, within six months the values usually exceeded 6.0 ng/ml.

Group IV:

Thirty –six (36) patients were alive without evidence of disease but less than 15 months since surgery. Since these patients were not yet designated as either surgical"cures" ar "failures" they are not included in subsequent statistical evaluations.

CEA As Monitor

While it is apparent that there is a paralled between rising CEA values and progression of malignant disease, it is important to determine if there is sufficient correlation between these two factores to be able to use CEA values to detect or anticipate progressive disease before it becomes clinically evident.

A comparison is made in the median CEA values of patients cured by surgery and those who failed following surgery(Fig.2). The date of last contact is used as the endpoint in the surgically cured patients and the median CEA value characteristically remained at 1.5 ng/ml or lower at all follow up intervals.

Where clinical recurrence of disease became evident, a CEA value of 6 ng/ ml preceeded thisendpoint in 50% of the patients by 3 months with one case being followed with an elevated CEA for more than 24 months (Fig.2).

Where death is used as an endpoint a CEA value of 8.0 ng/ml preceeded death by 9 months in 50% of the patients (Fig.2)

Discussion

It was evident from the data that CEA is not sufficiently sensitive to be used to screen high risk populations for the presence of luncancer particularly for lesions that are deemed to be respectable[9]. Sixty percent of those patients who were resected in this series did not have an initial CEA value elevated above 2.5 ng/ml.

The initial CEA value, however, can be of some help in suggesting the eventual clinical prognosis. In the clinical evaluation of the lung cancer patient, 2.5 ng/ml and 6.5 ng/ml represent important levels of discrimination. A patient with evidence of pulmonary disease that has a CEA concentration of less than 2.5 ng/ml may or may not have malignant disease but should be followed. A patient with CEA between 2.5 ng/ml and 6.5 ng/ml has very suggestive evidence of the presence of malignancy.

If the CEA concentration in this patient increases or does not decrease with effective treatment of concomitant bengign conditions the diagnosis of possible malignancy must be taken seriously. In a patient with pulmonary disease and a CEA in excess of 6.5 ng/ml the clinician should be very reluctant to abandon a diagnosis of lung cancer. A CEA concentration of 15 ng/ml in a potential surgical candidate casts great doubt on the possibility of successful surgical resection.

Forty –nine percent of the patients with preoperative concentrations of 2.5 ng/ml or less remain disease free following the resection. On the other hand, 74% of patients that had CEA above 2.5 ng/ml preoperatively eventually developed disease and were regarded as treatment failures.

If CEA has any value as a monitor to reflect progression or remission of disease it will be in the event of the surgical patient where there is a sudden reduction of tumor volume with some possibility that there has been a total extirpation of the tumor. The data as here presented suggest that CEA can serve as clinical prognosticator in the surgically resected patient within certain limitations.

If during a post- operative follow -up period that has been greater than 3 months the CEA values exceed 2.5 ng/ml the surgeon should follow the patient carefully and hope for a lesser value upon the next examination. However, if the CEA rises during this period to 5 ng/ml adiagonstic evaluation of the patient is indicated with the intent of finding residual disease or a second primary. Where the CEA exceeds 6.5 ng/ml in two measurements during the postoperative period, consideration should be given to the institution of additional antineoplastic therapy.

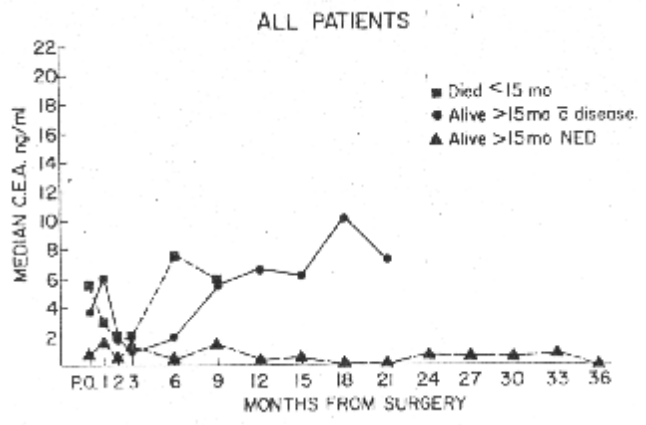

Fig.1 The serial CEA value in patients following surgical resection of lung cancer contrasting the median CEA values in the patients who are cured with values where tumor recurrence become evident

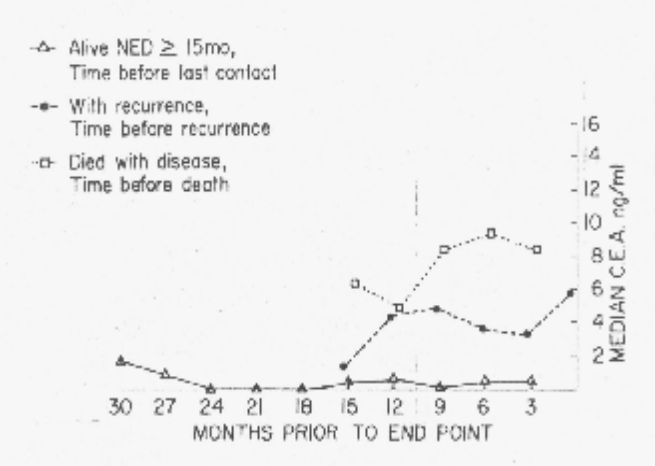

Fig.2 A comparison of median CEA values at different intervals prior to:
a-the date of last contact in the patients with a totally disease free interval.
b-the date of first evidence of recurrent disease.
c-the date of death in all patients who failed surgical resection and died of disease

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