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Diagnostic Significance of CEA and CA 19-9 for the Early Diagnosis of Cancer

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Abstract

The purpose of this review is to give a brief diagnostic significance to enable the judicious use of widely performed serum cancer markers. The markers usually proteins could be product of cancerous cell or as response to cancer, which are mainly found in blood or urine. Sometimes, some tumor markers also increase in non-cancerous conditions. CEA (carcino embryonic antigen) and Ca 19-9 (Carbohydrate antigen 19-9) are two blood tests commonly used to follow patients with known cancers. CEA is a glycoprotein (sugar protein) present in embryonic tissues and in extracts from normal colonic washings. CA 19-9 is a modified blood group antigen (Lewis (a)). Neither test should be used as a cancer screening test of asymptomatic individuals. Although CEA and/or levels are often elevated in patients with gastrointestinal malignancies (colon, pancreas, etc), patients with confirmed cancers frequently have normal levels (in the range of healthy individuals). Elevations in CEA and CA 19-9 levels may occur in patients without cancer. For example, elevated CEA levels may be observed in smokers as well as patients with a variety of non-malignant diseases. Therefore, levels, regardless of their values cannot be used as a diagnostic test for cancer. The greatest value of these tests is in detecting recurrence of malignancy (cancer) after treatment of the tumor.

Keywords: CEA; CA-19.9; Cancer

Introduction

Tumor markers are not the primary modalities for cancer diagnosis rather they can be used as laboratory test to support the diagnosis[1]. Serum or tissue tumor markers have been proposed for use in clinical practice in order to predict prognosis, monitor response to treatment, and help detect recurrence Some markers may be elevated in more than one type of cancer, thereby decreasing the diagnostic accuracy e.g. elevated CEA levels are found in multiple malignancies of gastrointestinal origin. Also many markers share cross-reacting epitopes with products of normal tissues, which leads to errors in their quantitative estimation.

Among such markers, carbohydrate antigen 19-9 (CA 19-9) is the most widely investigated tumor-associated antigen that was first described in the early 1980s[2]. However, some of them are not sufficiently sensitive and/or specific to distinguish between the benign and malignant forms of the disease. Huang and Liu conducted a meta-analysis and concluded that serum CA 19-9 plays an important role in the diagnosis of pancreatic cancer[3]. A large literature review of 24 pancreatic cancer studies in 1990 by Steinberg and associates showed that when using 37 kU / L as a cutoff point, CA 19-9 was reported to have a median sensitivity of 81% and specificity of 90%, whereas increasing the cutoff point to 100 kU / L improved specificity to 98% but reduced sensitivity to 68%[4].

However, because CA 19-9 may be an imprecise or insufficient indicator of disease progression, treatment decisions should not be based solely on an increase of CA 19-9 levels. CA19-9 is the carbohydrate determinant that functions as an adhesion molecule and plays a role in the process of tumor progression[5].

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CEA is a complex oncofetal tumor marker glycoprotein produced by embryonic tissue of gut, pancreas, and liver discovered in 1965 by Gold and Freedman. It plays an important role as an inter-cellular adhesion molecule[6].

Carcino embryonic antigen (CEA)-The serum level is positive has been reported in different carcinoma are as follows

- 60–90% - Colorectal carcinoma
- 50–80% - Pancreatic carcinoma
- 25–50% - Gastric and breast carcinoma.

CEA is elevated in many benign disorders: Alcoholic cirrhosis; Hepatitis; Ulcerative colitis; CEA assays lack both sensitivity and specificity required for detection of early cancers.

The aim of this review is to identify the diagnostic significance of tumor marker CEA and CA19.9 which has high complexity and consists of several components that converge to articulate the development of cancer.

Discussion

Cancer embryonic antigen (CEA) and carbohydrate antigen (CA19-9) are well-known tumor markers that are used in the diagnosis of colorectal cancer. CEA and CA19-9 are used in clinical practice, but we have to accept the reality that they are not specific for early detection of colon cancer, meaning they cannot be used in the diagnosis of carcinoma in situ[7]. These tumor markers have been used for diagnostic and surveillance purposes[8-10]. Furthermore, in some previous reports, the significance of these tumor markers as prognostic factors was reported[11-13].

Physicians must be careful when using CA 19-9 as a diagnostic aid for pancreatic cancer. CA 19-9 exists as an epitope of salivated Lewis A blood group antigen and it is not expressed in subjects with Lewis α-β- genotype, which accounts for approximately 5–10% of the Caucasian population[14,15]. CA 19-9 is increased in multiple gastrointestinal cancers, but elevated levels are also found in benign diseases, including peptic ulcers, chronic and acute pancreatitis, cirrhosis, cholangitis, and obstructive jaundice[16-18]. In patients with cholangitis and obstructive jaundice, it is recommended to recheck CA 19-9 levels after treatment, as levels usually decline after biliary decompression[19]. CA 19-9 lacks the sensitivity for detecting early pancreatic cancer and is elevated in only 50% of pancreatic adeno carcinomas less than 3 cm in size.

CA 19-9 levels were assessed for potential use in determining the antitumor activity of treatment. In a study by Micke and colleagues that sought to determine the predictive value of CA 19-9 in locally advanced pancreatic cancer patients treated with the combination of radiation and 5-FU, CA 19-9 was measured before and during therapy[20]. Patients who had a treatment-related decline in CA 19-9 levels exhibited prolonged median survival. Okusaka and coworkers found that in patients receiving chemotherapy and radiotherapy for locally advanced pancreatic cancer, the CA 19-9 responders had a longer median survival of 10.6 months compared to 4.1 months in non responders[21,22].

Conclusions

CA 19-9 has been the most widely used tumor marker in pancreatic cancer. Certain limitations of CA 19-9, such as elevated levels in benign jaundice, pancreatitis, ovarian cancer, or other gastrointestinal malignancies, have made it unfavorable as a screening test. The rising CA 19-9 levels in patients under observation or in those receiving active therapy could be an indicator of disease recurrence, progression, and ineffectiveness of the current regimen, and may be correlated with shorter survival time. However, the value of initiating therapy based on rising CA 19-9 levels remains to be demonstrated. Decisions to initiate or change chemotherapy should not be made before seeking additional confirmative tests.

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