Original Article

Study of Serum Carcinoembryonic Antigen's Profile for Breast Cancer in Western Algeria: 100 cases

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Abstract

Background: Breast cancer is the most common cancer in women worldwide. Biology contributes to the early diagnosis and monitoring of breast cancer with several categories of markers such as prognostic markers (ER, PR, HER2), proliferative markers (Ki67), and tumor markers such as CEA and CA 15−3. CEA can be detected at a high concentration in serum of patients with malignant tumors.

Aim: The aim of our study was to evaluate the concentrations of CEA in serum of women with breast cancer and to verify the existence of a possible link between the average rates of CEA and SBR grade.

Methods: Serum samples from 100 patients with breast cancer and 100 controls was recovered and examined with an AxSYM analyzer (Abbott Laboratories, USA) to measure CEA using Microparticle Enzyme Immunoassay (MEIA) technology.

Results: In our clinical study, the mean age of patients and controls were 52.7 and 50.3 years respectively. The results revealed an elevation in the CEA levels from patients with an average value of 16.61 ± 0.2 ng/ml. Positive correlation was found between CEA concentrations and SBR grade, it has found with $45,7 \pm 1$ ng/ml in grade III.

Conclusion: CEA represents an excellent marker for breast cancer development. Changes in its concentration reflect the effectiveness or ineffectiveness of treatment.

Keywords: Breast cancer, tumor markers, CEA, SBR grading, prognosis

Introduction

Breast cancer is the most commonly diagnosed form of cancer in women. It figures among the leading causes of morbidity and mortality [1]. All cancer registries worldwide indicate an increase in the incidence of breast cancer during the last 20 years [2]. The biological management of breast cancers also contributes to early diagnosis and surveillance with prognostic markers such us ER (Estrogen Receptor), PR (Progesterone Receptor), HER2 (Human epidermal growth factor receptor 2), proliferative markers (Ki67), and tumor markers such as CEA (Carcinoembryonic antigen) and CA 15−3 (Cancer Antigen 15−3). On the other hand, there are studies that focus on genes susceptibility in families at risk [3]

Major blood tumor markers used in oncology are the CA15−3 (Cancer antigen 15−3), the CA19−9 (Cancer antigen 19−9), the CEA (Carcinoembryonic antigen), and αFP (alpha−fetal protein) [4]. CEA was first described in 1965 by Gold and Freedman [5]. Its upper threshold of normality is 5 ng / ml [6] and its molecular weight is 200 kDa [3]. The amount of this antigen is much lower in normal tissues than in neoplastic tissues [3]. CEA was characterized as a glycoprotein with a b−electrophoretic mobility. The very low concentrations of CEA were revealed in body fluids, and also in normal and diseased tissues [4]. The overexpression of CEA is partly responsible for resistance to chemotherapy [5,3]. CEA is very ubiquitous and an elevation of its level may be observed in various situations such as age, pregnancy and sex. Indeed, the CEA is on average higher in smokers, the commonly accepted threshold value is 10 ng / ml [5]. Besides breast cancer, elevated levels of CEA may be found in the following cancers: uterine and ovarian cancer, thyroid carcinoma and lung cancer [3].

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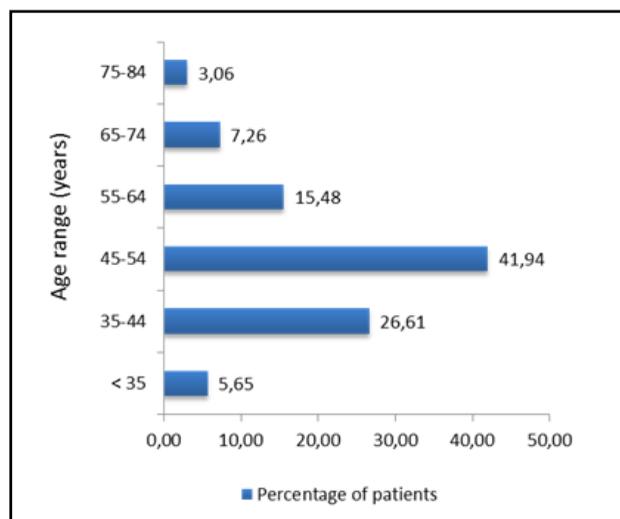
Figure 1. Distribution of patients according to age

Figure 2. Distribution of patients according to SBR grading

Materials and methods

We recruited 100 women with breast cancer and 100 alleged healthy women over two years (2011 to 2013) at Anticancer Center at the Institute Pastor of Oran for this study. Patients from both group are from the West Algerian region. Their age ranged from 25 to 85 years with a mean value of 52.7 years. A study of their medical records was conducted to gather information concerning age and histoprognosis grade of Scarff–Bloom–Richardson (SBR). Every woman is asked to give her agreement to participate in our study by signing the consent form.

Furthermore, we collected blood from heparinized tubes and the plasma is recovered to estimate the average rates of CEA using the Abbot's AxSYM analyzer which is based on Microparticle Enzyme Immunoassay (MEIA) technology.

Samples and the AxSYM CEA reagents were pipetted in the following sequence:

- All AxSYM CEA reagents and samples essentials for tests were pipetted by the sampling probe into various wells of a reaction vessel (RV). The RV was at once transferred into the processing center. Farther pipetting is done in the processing center by the Processing Probe.

The reactions occur in the subsequent steps:

- Anti–CEA Coated Microparticles and samples were pipetted to wells of RV. In the course of incubation of reaction mixture, an antibody–antigen complex was formed by binding of the CEA in samples with the Anti–CEA Coated Microparticles.
- An aliquot of the reaction mixture was transferred to the matrix cell. The bind of microparticles to the glass fiber matrix was irreversible.
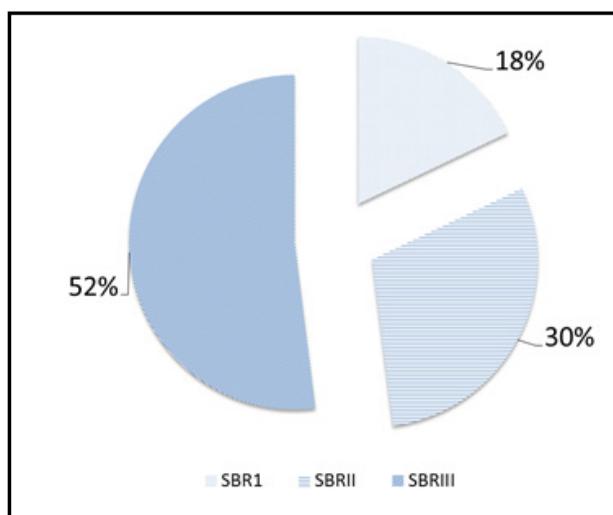
- The matrix cell was washed to eliminate unrelated materials.
- The detection of the immune complex is realized by using an alkaline phosphatase (conjugate) and 4–methylumbelliferyl phosphate (fluorogenic substrate). The fluorescent product is measured by the MEIA optical assembly.

Results

Although breast cancer can be diagnosed at any age, its frequency in our patients is low at 35 years and below and then increases steadily with age to reach a peak between 45 and 55 years at 41.94% (Figure 1). The average age of patients and controls were 52.7 and 50.3 years respectively.

The SBR grade is a crucial tool in adjuvant therapy. Over half of the cases were scored as high SBR grade (grade III) with 52% of all cases. The grades I and II represented 18% and 30% respectively (Figure 2).

The mean serum CEA concentration were 16.61 ± 0.2 and 0.8 ± 0.1 ng/ml in patients and controls, respectively. CEA levels were significantly higher in breast cancer women when compared with controls ($p < 0,0001$) (Table 1, Figure. 3).

The average rates of CEA found according to SBR histoprognosis grade were illustrated in Figure 4. CEA levels increased with the advance of SBR grade. A positive correlation was noted ($r = 0,280$, $p = 0.00006$). The average values of the CEA obtained in terms to the SBR grade were 1.5 ± 0.05 ng/ml (grade I), 2.65 ± 0.1 ng/ml (grade II) and 45.7 ± 1 ng/ml (grade III) (Table 2).
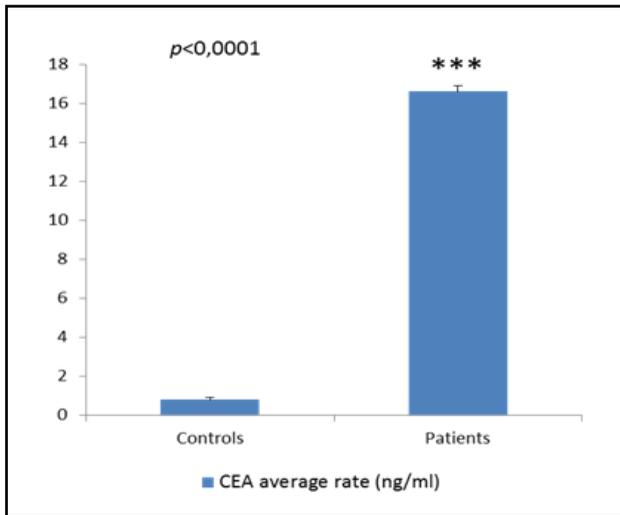
Figure 3. CEA average rate in patients with breast cancer and in controls

	Controls	Patients
Cases number	100	100
CEA average rate ± SD (ng/ml)	0.8±0.1	16.61±0.2***

Table 1. Distribution of CEA average rates in patients and in controls
SD: standard deviation, ***: p<0.0001

Discussion

The CEA is one of the earliest tumor markers with seven extracellular domains including an N–terminal domain of 108 amino acids homologous to the variable domain of the immunoglobulin (IgV–like) and the six homologous domains of the constant domain immunoglobulin (IgG–like) [7–9]. The CEA may act as an adhesion molecule. Changes in cell adhesion may be involved in metastasis. It was therefore assumed that the CEA can have a role in the metastasis process [7,10,11]. The CEA antigen is present in the intestine, liver, embryos or fetuses' pancreas's during the first two months of pregnancy and is absent in normal adult tissues. It is generally present in most adenocarcinomas such as those of the digestive tract, breast, lung but not in kidney, thyroid, prostate and ovary w12). It has been suggested that overexpression of CEA in
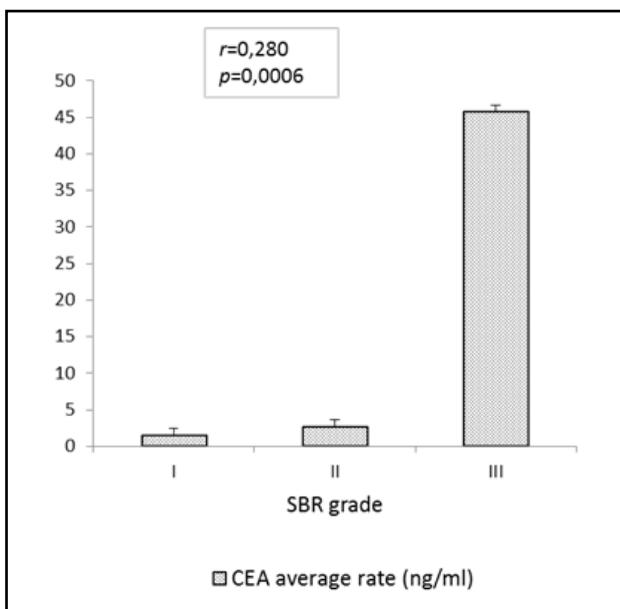
carcinoma could interfere with the of cells differentiation. Indeed, ectopic expression of CEA in rat myoblasts blocks their differentiation [13].

The analysis of the literature on the usefulness of CEA assay in colorectal cancer revealed that in 60–75% of cases, rising rates of CEA is the first sign of recurrence and precedes the radiological and clinical signs of 3 to 8 months [14]. A meta–analysis of non–randomized trials has objectified a modest benefit of a regular monitoring of CEA on survival [15]. However, four randomized trials showed no difference in five years of survival comparing between an intensive, a minimal or no surveillance. Two of them objectified an advance diagnosis that does not translate into improved prognosis [16–18]. In one of these trials, the regular dosage of CEA does not appear to provide prognostic improvement, however the low numbers in this study do not allow formal conclusion either [17]

CEA can be detected in 12% of non–metastatic breast cancer and 35–40% in metastatic cancers [19,20]. Several studies have reported elevated levels of CEA in serum of patients with breast cancer and this percentage is even higher in women with metastases [21,22]. Many authors have shown that an increase or decrease in CEA levels may reflect the state of the progression or regression of this disease [21]. The literature suggests that the CEA can be useful in post–surgical monitoring of patients with breast cancer for early diagnosis of recurrence [23,24] and monitoring response to treatment [25]. Our results corroborate perfectly those of literature.

SBR grade	I	II	III
CEA average rate ± SD (ng/ml)	1.5±0.05	2.65 ±0.1	45.7±1

Table 2. Distribution of CEA average rates according to the SBR grading

Figure 4. The mean value of CEA according to the SBR grading.

Conclusion

This study allowed the quantitative evaluation of CEA in serum of patients treated against breast cancer. The CEA represents an excellent tumor marker of breast cancer evolution and variations in its concentration reflect the effectiveness or ineffectiveness of treatment. If the rate exceeds the threshold it is probable to find metastases. The sensitivity of CEA is low so it cannot be used as an

initial diagnostic test. It must be combined with other tumor markers such as CA15–3 to get better results.

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