Original Research Paper Social Science

Study on the Levels of CRP Among the Cancer Patients Before and After Chemotherapy Treatment

Arpita Chatterjee Barasat College, 1, Kalyani Road, PO- Nabapally, Barasat, Kolkata – 700 126, India

Sudip Kumar Sinha Victoria Institution (College), 78B, APC Road, Kolkata – 700 009, India

Gopeswar Mukherjee Department of Research and Development, Barasat Cancer Research and Welfare centre, Banamalipur, Barasat, Kolkata – 700 124, India

ABSTRACT

The C-reactive protein (CRP), an acute phase protein produced by liver or adipocytes. It is regarded as a positive acute-phase protein because it characteristically rises directly with increased disease activity. The present investigation is aimed to evaluate the correlation between the change of serum CRP levels response to before and after chemotherapy treatment with various cancer patients. The results revealed that the CRP levels of cancer patients were significantly higher than those of the healthy subjects. Further, in all the cases this the CRP levels increased after chemotherapy treatment. Since chemotherapy is not specific it kills cancerous cell along with few normal healthy cells and thus at times it leads to massive tissue damage depending on the dose and course of therapy. Thus, CRP can be used as a marker for activation of the immune system.

KEYWORDS Acute phase protein, cancer marker, immune response

Introduction:

Chemotherapy is a drug treatment that destroys cancer cells. To achieve maximum results, a mixture of several drugs (combination chemotherapy) is often used. But the side effect of chemotherapy is that it can also damage the healthy cells that grow and divide rapidly. Since chemotherapy is not specific it kills cancerous cell along with few normal healthy cells and thus at times it leads to massive tissue damage depending on the dose and course of therapy which leads to many complications. The extent of tissue damage can be determined by measuring the C-reactive protein (CRP) level, an acute phase protein produced by liver or adipocytes, in the patient's serum[1]. CRP seems to assist in complement binding to foreign and damaged cells, enhances phagocytosis by macrophages and play important role in innate immunity as an early defense system against infections[2].

The CRP gene is located on chromosome one (1q21-q23) which encodes the CRP monomeric 224 residue protein[3], but naturally secreted CRP comprises two pentameric discs. CRP can be used as a marker for activation of the immune system. CRP is regarded as a positive acute-phase protein because it characteristically rises directly with increased disease activity. In healthy individuals, CRP is naturally very low and difficult to detect in the blood. CRP did not show any significant seasonal heterogeneity[4,5]. When inflammation occurs there is a rapid rise in CRP levels, usually proportional to the degree of immunological stimulation. When inflammation resolves the CRP rapidly falls. Collectively, these properties make CRP potentially useful as a marker of active inflammation in certain situations.

The present investigation is aimed to evaluate the correlation between the change of serum CRP levels response to before and after chemotherapy treatment with various cancer patients.

Materials and Methods:

A total of 20 cases were enrolled for each investigation in the study. The malignancy was diagnosed by various investigations like radio-imaging, cytology and histo-pathological examinations by physicians of Barasat Cancer Research & Welfare Centre, a prime hospital in West Bengal. Controls (n = 20) were randomly selected patients admitted to the same hospitals as the cases during the same time period. They were frequency matched to cases by age, sex, and selected from hospital admission lists. Blood samples were collected from cases and controls both before and after the commencement of chemo treatment. Then blood samples (1ml) were centrifuged at 3000 rpm for 15 minutes and clear serum was collected. Written informed consent was obtained from all participants in accordance with the guidelines from hospital center review board.

The CRP level in the serum samples was assayed using turbidimetric immunoassay, based on the principle of agglutination reaction, as per manufacturer instruction (Tulip Diagnostics, India). Activation buffer (500µl) and latex reagent (50µl) were mixed properly, incubated at 37^0C for 10 minutes and used as working solution. The serum sample (3µl) was added to the working solution and the CRP concentration was estimated by spectrophotometric reading at 546 nm.

Result:

In the present study CRP test were performed from blood samples of the cancer patients before chemotherapy, and then 1-2 weeks after the chemotherapy. The result revealed that in all the cases this chemotherapy treatment increased the CRP levels in their body (Table 1). These means that chemotherapy treatment caused tissue damage in normal as well as in oncogenic cells and it indirectly increased the CRP level. It also indicated that the cancer treatment was in the positive direction. The concentration of CRP was greater in cancer patients as compared with healthy one (0.6 mg/dl). The study revealed even more increase in serum CRP level in every patient after chemotherapy (Table 1).

Discussion:

The study was aimed to evaluate the CRP protein as a good

marker to detect the cancer progression and its normalization prior to its elevated increased value. Any inflammation or tissue damage or necrosis cause increased value of CRP. CRP is used mainly as a marker of inflammation. Measuring the CRP value is useful in determining disease progression or the effectiveness of treatment. The results revealed that the CRP levels of cancer patients were significantly higher than those of the healthy subjects as reported in early studies[2,8,9]. Recent evidence has associated CRP elevation using static measurements with pregression of melanoma, ovarian, colorectal and lung cancer, and CRP has been used to detect recurrence of cancer after chemotherapy in certain situations[6,2]. Persistent elevation of CRP has also been reported to detect colorectal cancer in men[7] and overall cancer risk.

CRP is a member of the class of acute phase reactants as its level rise dramatically during inflammatory processes occurring in the body[2]. This increment is due to a rise in the plasma concentration of IL-6, which is produced predominantly by macrophages as well as adipocytes[1]. The present investigation revealed that chemotherapy, despite being a successful treatment for cancer, causes massive tissue damage which is evident from the elevated level of CRP in the serum of the patients after radiation. This may lead to great suffering of patients from many short term and long term side effects. This observation puts a question mark on the efficiency of chemo treatment when the health of the patient is in stake.

The search for a suitable biomarker which indicates immune system responses in cancer patients has long and arduous, but a widely known biomarker has emerged as a potential candidate for this purpose. CRP is an acute-phase plasma protein that can be used as a marker for activation of the immune system. The short plasma half-life and relatively robust and reliable response to inflammation make CRP an ideal candidate marker for inflammation[6]. The high-sensitivity test for CRP, termed Low-Reactive Protein (LRP, L-CRP or hs-CRP), measures very low levels of CRP more accurately, and is even more reliable than standard CRP for this purpose. Usually, static sampling of CRP has been used for clinical studies and these can predict disease presence or recurrence, notably for a number of cancers. Here we have used CRP Turbid and Latex methods to measurements across the clinical laboratories and for different advanced cancers, and have demonstrated similar, repeatable observations of a cyclical variation in CRP levels in these patients. We hypothesis that these L-CRP oscillations are part of a homeostatic immune response to advanced malignancy and have some preliminary data linking the timing of therapy to treatment success. This knowledge might also open the way for improved timing of treatments for improved clinical efficacy.

Table 1: Level of CRP before and after chemotherapy.

Case No.	Age (yr.)	Sex	Types of cancer	CRP level (mg/dl)	
				Before Chemo-therapy	After Chemo-therapy
1	15	F	Lung cancer	48	210
2	42	M	Ovarian cancer	62	190
3	40	F	Tongue cancer	24	96
4	15	F	Breast cancer	48	210
5	47	F	Breast cancer	7	150
6	57	F	Ovarian cancer	14	169
7	47	F	Uterine cancer	19	115
8	50	F	Throat cancer	6	56
9	29	F	Lung cancer	1	86
10	32	M	Tongue cancer	11	169
11	15	F	Endometrial cancer	48	145
12	52	F	Breast cancer	12	190
13	40	M	Bladder cancer	6	80
14	61	M	Squamous cell carcinoma	18	186
15	74	M	Lung cancer	22	148
16	56	M	Prostrate cancer	35	196
17	49	F	Breast cancer	5.5	89
18	55	F	Ovarian cancer	7.9	59
19	50	M	Lung cancer	16	96
20	80	M	Prostrate cancer	5.7	89

REFERENCES

1. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. J Clin Invest 2003; 111(12): 1805–1812.
2. Erlinger TP, Platz EA, Rifai N, Helzlsouer KJ. C-reactive protein and the risk of incident colorectal cancer. JAMA 2004; 291(4): 585–590.
3. Szalai AJ, Agrawal A, Greenhough TJ, Volanakis JE. C-reactive protein: structural biology, gene expression, and host defense function. Immunol Res 1997; 16(2): 127-136.
4. Rudnicka AR, Rumley A, Lowe GDO, Strachan DP. Diurnal, seasonal, and blood-processing patterns in levels of circulating fibrinogen, fibrin D-dimer, C-reactive protein, tissue plasminogen activator, and von willebrand factoe in a 45-year-old population. Circulation 2007; 115: 996-1003.
5. Meier-Ewert HK, Ridker PM, Rifai N, Price N, Dinges DF, Mullington JM. Absence of diurnal variation of C-reactive protein concentration in healthy human subjects. Clin Chem 2001; 47: 426-430.
6. Mahmoud FA, Rivera NI. The role of C-reactive protein as a prognostic indicator in advanced cancer. Curr Oncol Rep 2002; 4(3): 250-255.
7. Chiu HM, Lin JT, Chen TH, Lee YC, Chiu YH, Liang JT, Shun CT, Wu MS. Elevation of C-reactive protein level is associated with synchronous and advanced colorectal neoplasms in men. Am J Gastroenterol 2008: 103(9): 2317-2325.
8. Bjorge L, Hakulinen J, Vintermyr OK, Jarva H, Jensen TS, Iversen OE, Meri S. Ascitic complement system in ovarian cancer. BJC 2005; 92: 895–905.
9. Rhaegen H, Ock WE, Decree J, Vekbruccen F. Increase of serum complement levels in cancer patients with progressing tumors. Cancer 1976; 38: 1608-1613.