CIRCULATING IMMUNE COMPLEXES AS A POSSIBLE DIAGNOSTIC AND PROGNOSTIC INDICATOR OF CANCER CERVIX UTERI

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SUMMARY

A longitudinal study of circulating immune complexes (CICs) has been undertaken in 40 women suffering from cancer cervix and in 10 healthy females. On estimation, the concentration of CIC was found to be significantly raised in cancer group as compared to that of controls. The levels ran parallel to the severity of the disease and highest values were detected in grade III. On 10th post-operative/post-radiotherapy day the values of CICs decreased significantly and were found to increase with the relapse of cancer cervix.

Introduction

Many authors have described from time to time the immunological aspects of genital cancers, yet sufficient data is not available regarding cancer cervix uteri. The discovery of immune complexes (IC) has greatly altered the concept of immunologic tolerance. ICs were found to be blocking factors in the tumour bearing individuals for the first time by Sjogren *et al* (1971), since then various investigators have worked in this field of tumour immunology yet very scant literature is available about the role of circulating immune complexes (CIC) in the cancer cervix. In the present study the quantitative estimation of CIC has been done in the cancer cervix patients in different grades of the disease, in remission and in the relapse states to justify the role of CIC in the clinical management of cancer cervix.

Accepted for publication on 9-1-89.

Material and Methods

A total number of 50 cases have been studied. Out of this, 40 females were of histopathologically proved cancer cervix and other 10 were healthy controls matched for age, parity and socio-economic status. The test group was classified according to Broder's (1926) histological grading as follows:

(a) Cancer in situ—3 patients
(b) Squamous cell carcinoma
- Grade I 5
- Grade II 21
- Grade III 11

Out of total 40 cases of cancer cervix 6 cases were studied on 10th post-operative day and other 6 subjects on 10th post-radiotherapy day also.

Estimation was done with the use of polyethylene glycol turbidity method of Riha *et al* (1979). It is based on the direct photometric measurement of turbidity due to precipitation of IC in diluted

human sera (1:30) by 3.75% polyethylene glycol. All the samples were run in duplicate and absorbance of the mixtures was determined by sP 500 double beam spectrophotometer at 450 μm wave length. The results were evaluated statistically.

Results and Discussion

We found that CIC levels were significantly raised in cancer patients. The concentration in controls was 54 ± 11.14 while that in cancer patients was 307.96 ± 234.29. With the advancement of cancer, the CIC levels increased. The mean value in cancer in situ was 100 ± 21.60 while in grade III it was 624.54 ± 258.25. The difference was found to be significant statistically (Table I) ($p < .01$).

TABLE I
Levels of CICs in Control and Different Grades of Cancer Cervix Patients
(O.D. x 10^3)

	Control (n=10)	Cancer (n=40)	CA-Situ (n=3)	Gr.-I (n=5)	Gr.-II (n=21)	Gr.-III (n=11)
Range	40-70	70-1000	70-120	130-220	230-500	300-1000
Mean	54	307.96	100	174	333.33	624.54
±S D.	11.14	234.29	21.60	34.40	80.08	258.25

Our findings run parallel to those of Theofilopoulos *et al* (1977). They studied the nature of CICs in human cancer sera, and reported significantly high levels of CICs in patients with advanced malignancy. They also reported that increase in tumour mass and metastasis were associated with high levels of CICs and low levels were found with subclinical amount of tumour. Poulton *et al* (1978) also found highest values of CICs in patients with large tumour in ovarian Mn.

These high levels of CICs in cancer cervix patients might be due to excessive formation of antibodies in response to stimulation by tumour antigen. These antibodies on inter-action with antigens form IC. Poulton *et al* (1978) suggested that tumour directed antibody present during early Mn may disappear with progressive dissemination and CIC have been implicated as the blocking factor in progressive disease.

Dodd *et al* (1982) also reported high concentration of CIC in gynaecological malignancy including cancer cervix.

After tumour ablation by surgery or by radiotherapy we estimated the CIC levels on 10th day in the cancer cervix patients and found dramatic fall in the levels. Mean pre-operative and pre-radiotherapy values were 240.06 ± 100.9 and 485 ± 33.00 respectively (Tables II and III). The difference was significant statistically also. This fall in CIC levels might be due to reduction in tumour load which decreased the antigenic stimulus for antibody production and as the ICs are formed due to interaction of antigens and antibodies the levels of ICs were low. Also probably due to radiotherapy a change is expected in the antigenicity of the tumour tissue as well as in the antibody response which may again be responsible for decreased IC formation.

TABLE II

Levels of CICs in Pre and Post Operative Cases
(O.D. x 10^3)

	Range	Mean	± S.D.
Pre--Oper. (n=6)	150-380	240.06	100.9
Post-Oper. (n=6)	70-180	100	36.96
		p .01	

TABLE III

Levels of CICs in Pre and Post Radiation Cases
(O.D. x 10^3)

	Range	Mean	±S.D.
Pre-Radio-therapy (n=6)	420-780	485	206.94
Post-Radio-therapy (n=6)	180-300	280.66	33.00
		p .05	

TABLE IV

Mean CIC Levels in Pre-operative, Remission and Relapse States
(n=2) (O.D. x 10^3)

Pre-operative	Remission	Relapse
240	100	190

Dodd *et al* (1982) estimated CIC levels in gynaecological malignancies including 56 cases of cancer cervix. They reported significantly greater levels ($p < .01$) of CICs in cancer cervix patients (mean 132.4 ugm/ml; range 86.2-203.3) than that of control females (mean 72.2 ugm/ml, range 53.7-97.1) and the concentration decreased in cancer patients in the remission state. The analysis for paired observations showed highly significant ($p < .001$) fall in CIC levels and the remission values were not significantly different to the values from the control group.

Similarly Poulton *et al* (1978) reported fall in CIC levels in patients who obtained remission from the malignancy and attributed this to little or no residual tumour to create the quantity of circulating tumour antigen necessary to maintain elevated levels of ICs.

Recently two of our cases in the follow up, about 6 to 8 months after therapy. were found to be having rise again in the levels of CICs. On further specific investigations they were found to be having recurrence of the disease. Dodd *et al* (1982) also reported a rise in the levels of CICs with the recurrence.

In contrast to our findings Clarke *et al* (1982) could not appreciate any difference in the levels of CICs in control and cancer patients and reported that measurement of ICs is of little value as a screening test or as a guide to the extent of disease, prognosis or therapy.

Conclusion

Estimation of certain immunological parameter (ICs) could be of potential significance in cancer cervix patients and may help much in its early detection, in knowing the extent of tumour load, the efficacy of therapeutic protocol and in diagnosing the recurrence of the cancer. The projected use of study in immunological parameters as screen for occult malignant disease is severily limited by the lack of specificity but there is potential for development of a screening marker for monitoring progress following diagnosis and initial therapy.

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