A CORRELATIVE STUDY OF IMMUNE STATUS AND SEVERITY OF CANCER CERVIX

by

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SUMMARY

Immune status (cell mediated immunity and humoral im munity) of 51 patients of cancer cervix in various clinical stages and 33 control cases were studied by absolute lymphocyte count, E-rosette forming cells, skin sensitivity to PPD and estimation of serum immunoglobulins. Both cellular and humoral immunity were depressed in patients of cancer cervix. There was a good correlation between depressed cell mediated immunity and severity of the disease.

Cancer has been known since time immemorial. Development of malignant cells is a frequent event and under normal condition these cells are destroyed by immunological control or surveillance mechanism (Good, 1970; Burnet, 1969). A few of these abnormal cells escape recognition by immune system, the mechanism of which is not well understood. The abnormal cells when given a chance for favourable growth form cancer.

The present work has been undertaken to study the immunological status in patients of carcinoma of the cervix uteri and an attempt has been made to correlate it with clinical severity of the disease.

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Material and Methods

Fifty-one patients of biopsy-proved cancer cervix were selected from gynaecological and radiotherapy departments of S.S. Hospital, Varanasi, Thirty-three age matched healythy volunteers served as controls. Detailed clinical history was taken and physical examination was done in every case with special reference to clinical staging of the disease. Necessary laboratory investigation were done.

Following investigations were carried out to assess the immunological status of the subjects:

Cell Mediated Immunity

(a) Delayed cutaneous hypersensitivity reaction to recall antigen i.e. puri-

fied protein derivative (PPD) by the method of Nalick *et al* (1974).

(b) T-lymphocyte estimation was done by E-rosette assay by the method of Jondal *et al* (1972).

(c) Absolute lymphocyte count.

Humoral Immunity

Serum level of major immunoglobulins i.e. IgG, IgA and IgM were estimated by radial immunodiffusion technique (Fahey and Mckelvey, 1965).

Observations

Out of 51 patients of cancer cervix, 4 were of stage I, 14 of stage II, 22 of stage III and 11 of stage IV.

Cell Mediated Immunity

Absolute lymphocyte count showed no significant variation in stage I as compared to healthy controls. However, absolute lymphocyte count decreased significantly in stage II ($P < 0.001$), stage III ($P < 0.001$) and stage IV ($P < 0.001$) (Table I).

The mean area of skin sensitivity to PPD in healthy controls was 5.92 ± 0.1 mm. It was significantly decreased in all the stage of cancer cervix as compared to controls (Stage I—$P < 0.005$; Stage II—$P < 0.001$; Stage III—$P > 0.001$ and II—$P > 0.001$; Stage III —$P < 0.001$ and Stage IV—$P < 0.001$) (Table II).

The T-lymphocyte measured in terms of E-Rosette forming Cells (E-RFC), was 53.78 ± 1.84 in healthy controls. There was a marked reduction in the percentage E-RFC in cancer cervix, which went on reducing with increasing severity of the disease (control vs. stage I—$P < 0.002$; vs. stage II, III and IV—$P < 0.001$) (Table III).

TABLE I

Absolute Lymphocyte Count in Different Stages of Carcinoma Cervix

Group	No. of cases	Mean (cell/cu. mm)	S.E.	Range (Cell/cu.mm)	P value
Controls	33	3646.90	40.55	3327-9375	—
Carcinoma cervix					
Stage I	4	3458.25	25.16	3393-3515	N.S.
Stage II	14	3269.21	26.92	3100-3375	<0.001
Stage III	22	3002.75	39.73	2354-3225	<0.001
Stage IV	11	2705.80	26.91	1500-3115	<0.001

N.S. = Not significant.

TABLE II

Purified Protein Derivation (PPD) in Carcinoma Cervix

Group	No. of cases	mean (mm)	S.E.	Range (mm)	P value
Control	33	5.92	0.10	5.00-6.75	—
Carcinoma cervix					
Stage I	4	5.18	0.32	4.25-5.75	<0.005
Stage II	14	3.88	0.13	2.95-5.75	<0.001
Stage III	22	2.96	0.09	2.25-3.75	<0.001
Stage IV	11	2.02	0.07	1.17-3.10	<0.001

TABLE III
Percentage of E-rosette Forming Cells in Different Stages of Carcinoma Cervix

Group	No. of cases	Mean	S.E.	Range	P value
Control	33	53.78	1.84	49.0-57.0	—
Carcinoma cervix					
Stage I	4	48.00	1.08	45.0-50.0	<0.002
Stage II	14	42.07	1.09	30.0-47.0	<0.001
Stage III	22	26.68	0.63	21.0-32.0	<0.001
Stage IV	11	16.82	0.42	11.0-23.0	<0.001

Humoral Immunity

It was seen that serum IgG decreased significantly in all clinical stages of cancer cervix in comparison to controls (Table IV). IgA was found to be increased in all the four clinical stages. The rise was highly significant in stage II, III and IV ($P < 0.001$) (Table V). IgM was found to be decreased in carcinoma cervix, but the change was not so significant as in IgG and IgA (Table VI).

Discussion

Great deal of information is now available on cell mediated and humoral immunologic responses of patients with neoplasms of the female genital tract (Khoo and Mackay, 1974). However, only scanty literature is available regarding

TABLE IV
Serum IgG Level in Carcinoma Cervix

Group	No. of cases	Mean (mg%)	S.E.	Range (mg%)	P value
Control	33	1932.00	15.35	1045-2075	—
Carcinoma cervix					
Stage I	4	1636.50	60.99	1510-1775	<0.001
Stage II	14	1449.57	24.49	1299-1595	<0.001
Stage III	22	1336.50	13.59	1232-1482	<0.001
Stage IV	11	1284.40	17.27	1197-1404	<0.001

TABLE V
Serum IgA Level in Different Stages of Carcinoma Cervix

Group	No. of cases	Mean (mg%)	S.E.	Range (mg%)	P value
Control	33	194.98	2.88	155.25-223.12	—
Carcinoma cervix					
Stage I	4	208.00	11.88	181.50-232.50	N.S.
Stage II	14	285.05	12.18	212.00-345.00	<0.001
Stage III	22	295.95	4.21	267.00-325.00	<0.001
Stage IV	11	312.06	7.62	305.00-342.00	<0.001

N.S. = Not significant.

TABLE VI*

Serum IgM Level in Different Stages of Carcinoma Cervix

Group	No. of cases	Mean (mg%)	S.E.	Range (mg%)	P value
Control	33	184.93	2.74	150.00-205.15	—
Carcinoma cervix					
Stage I	4	163.50	2.21	159.00-169.00	N.S.
Stage II	14	176.35	1.96	159.00-189.50	N.S.
Stage III	22	171.27	2.30	149.00-192.00	<0.001
Stage IV	11	152..28	1.80	139.75-168.00	<0.001

N.S. = Not significant.

the immunological studies on cancer cervix. According to Khoo and Mackay, 1974 anergy to recall antigens and contact allergens increased with increase in clinical severity of the disease.

T-lymphocytes are attributed to be a carrier of cell mediated immunity and seen as to be an index of cellular immune competence (Burnet, 1969). Absolute lymphocyte count is one of the sensitive parameters for immunity which is supressed with the onset of the disease and it becomes more marked with the increase in the clinical stage of the disease as seen in the present series. These findings are consistent with the observation of Whitaker *et al* 1971 and Papatestas *et al* 1976.

A study of recall antigen sensitivity in cancer cervix showed reduction in skin sensitivity. Similar results have been observed by Lamb *et al* 1962.

The value of E-RFC in cancer cervix declined from 48.0 ± 1.05 in stage I to 42.07 ± 1.09, 26.86 ± 0.63 and 16.82 ± 0.42 in stage II, III and IV respectively. These observations suggest that E-RFC% is directly related with immune status of the patients and immune surveillance decreases with increasing severity of the disease. Similar observations have been reported by Jondal *et al* 1972.

There was statistically significant reduction of IgG in cancer cervix which further decreases with increasing severity of the disease. IgM was also found to decrease in cancer cervix. It is known that globulin level constitutes circulating antibodies and reduction of these results in increased tendency for infection (Lee *et al* 1970). IgA level increases linearly with increasing severity of cancer cervix. This is in confirmity with the observations of Brown *et al* 1975. From the immunoglobulin studies it appears that cancer may result from an alteration in response to prolonged autoimmune stimulation of the epithelium. The mechanism of depression of immune response in malignancy is poorly understood. Whitaker *et al* (1971) explained it as due to deficiency and abnormality of lymphocytes which makes the patient hyporesponsive.

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