

CORRELATIVE ANALYSIS OF IN VITRO PARAMETERS OF CELLULAR IMMUNE PROFILE IN PATIENTS WITH DIFFERENT TYPES OF CANCER CERVIX BEFORE AND AFTER RADIOTHERAPY

by

P. K. SINGH
M. C. SHARMA
M. P. MISHRA
A. AGARWAL
P. DUBEY

and

V. S. RAJVANSHI

SUMMARY

Cellular Immune profile of 40 patients of cancer cervix was assessed before and after radiotherapy. The results were compared with 10 age, sex and socio-economic status matched control cases. The profile constituted absolute lymphocyte count, T-Cell percentage and absolute T-Cell Count. Each patient was given 4500 to 6000 rads irradiation by ^{60}Co unit at J.K. Cancer Institute, Kanpur depending upon the extent of lesion.

The present study has shown that there was gradual decrease in all these parameters from grade I squamous cell carcinoma to anaplastic carcinoma. The decrease in T-Cell percentage was significant in all groups ($P = < 0.05$) except in adenocarcinoma ($P > 0.05$).

Introduction

Tumour antigen elicits both humoral as well as cell mediated immune response. However, cellular immunity to tumour specific transplantation antigen (TSTA'S) is generally thought to have more significant role than humoral immunity as a host defence against neoplasia. Recent studies have indicated correlation between cell mediated com-

ponent of immune system and progress of patients with tumour (Marrin and Han, 1974 and Dellon *et al*, 1975).

Various workers have reported diminished T-Cell percentage in many tumours of breast, colon and lung (Wybren and Fudenberg, 1973) and cancer of head and neck (Sinha *et al*, 1985 and Singh *et al*, 1978). However, the studies are lacking on cancer of cervix uteri which constitutes the most common cancer in women in this country. Therefore, the present study was undertaken to asses the cell mediated

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immune status in these cases before and after radiotherapy, using various parameters like absolute lymphocyte count, T-cell percentage and absolute T-cell count. The results were statistically analysed.

Material and Methods

Forty cases of different histologic types of cancer cervix were studied in department of pathology and J.K. Cancer Institute, G.S.V.M. Medical College, Kanpur. Ten age and socio-economic status matched control cases were also included in the study. Control group was constituted by relatives of patients not taking any medicine known to cause immune suppression.

Five ml heparinised peripheral blood sample (25 units heparin/ml) was collected in sterile test tube from each case. Simultaneously blood was also collected in EDTA vial for routine haematological investigation. T-Lymphocytes were demonstrated by E-rosette technique (Jondal *et al*, 1972). Total and differential leucocyte count was also done and then absolute values were calculated.

Every patient was subjected to radiotherapy, 4500-6000 rads were given depending upon the lesion and its extension by ^{60}Co unit at J.K. Cancer Institute Kanpur. Haematological parameters were repeated one week after radiotherapy.

Observations

Age distribution of control and study group cases has been shown in Table I. Peak incidence of cancer cervix was in 4th decade followed by 5th and third decade. The maximum number of control cases were also in 4th decade followed by 3rd and 5th. The mean age

incidence in study group as well as in control group was almost the same viz., 44.8 (± 8.40) and 45.5 (± 9.85) respectively.

TABLE I
Age Distribution of Controls and Study Group Cases

Age range (Years)	Controls	Study group cases
21-30	1	2
31-40	2	10
41-50	4	15
51-60	2	12
61-70	1	1
Total	10	40
Mean \pm S.D.	45.5 (± 9.85)	44.8 (± 8.40)

Out of 40 cases there were 20 cases of different grades of squamous cell carcinomas; 10 were of grade II and 5 were of grades I and III each.

Absolute lymphocyte count (ALC), T-cell percentage and absolute T-cell count were done in all cases before and 1 week after radiotherapy as shown in Table II. There was gradual decrease in T-cell percentage and absolute values from control to anaplastic carcinoma except in adenocarcinoma where values were not significantly low.

On statistical analysis, the difference in T-cell percentage as compared to control was significant (P-value < 0.05) in all types except adenocarcinoma (> 0.05).

The values after radiotherapy were still less than preradiotherapy and they were significantly less (P value < 0.05).

Discussion

T-cell percentage is one of the most important criteria for assessment of cell mediated immune status. There is wide variation in normal population 5% (Bach *et al*, 1969) to 80% (Bentwich *et al*, 1973).

TABLE II
Distribution of Absolute Lymphocyte Count, T-Cell Percentage and Absolute T-Cell Count in Control and Study Group Cases Before and After Radiotherapy

Type of cases	No. of cases	Before Radiotherapy			After Radiotherapy			Pre radiotherapy VS post radiotherapy
		ALC Mean \pm SD	T-Cell %	Abs T-Cell count	LC Mean \pm SD	T-Cell %	Abs T-Cell count	
Controls	10	2473.76 \pm 914.10	64.16 \pm 4.86	1481.21 \pm 539.98	—	—	—	—
S.C.C. P-Value	20	1824 \pm 1043.26	49.3 \pm 11.70 <.05	902.41 \pm 609.1	1400.5 \pm 789.85	28.55 \pm 6.71 <.05	415.30 \pm 273.10	<0.05
Grade I P-Value	5	2102 \pm 1402.6	56.4 \pm 9.26 <.05	693.32 \pm 183.63	1925 \pm 955.65	32.2 \pm 4.62 <.05	611.86 \pm 288.23	—
Grade II P-Value	10	1829.6 \pm 1038.72	47.8 \pm 9.8 <.05	857.38 \pm 484.5	1370 \pm 701.29	31.1 \pm 4.88 <.05	430.46 \pm 244.78	—
Grade III P-Value	5	1537.5 \pm 262.36	44.5 \pm 13.89 <.05	664.36 \pm 272.87	936.2 \pm 284.9	19.8 \pm 2.85 <.05	188.51 \pm 69.9	—
Adeno Ca P-Value	10	2217.1 \pm 337.41	63.66 \pm 3.38 >.05	1376.8 \pm 227.83	1956.5 \pm 246.74	48.4 \pm 5.48 <.05	955.55 \pm 203.34	<0.05
Anaplastic Ca P-Value	10	1740.31 \pm 324.26	38.3 \pm 8.54 <.05	698.6 \pm 227.44	1200.5 \pm 303.36	21.6 \pm 2.8 <.05	260.13 \pm 73.71	<0.05

Significant <0.05

Not significant >0.05.

There are various factors which affect T-cell percentage in normal human peripheral blood like source of sheep erythrocyte (Evans and Alexander, 1970), incubation period (Wybran and Fundenberg, 1973) and difference in populations from place to place (Mendes *et al*, 1973). Therefore, to minimise these, fresh samples were used and tests were carried out at 4° to 8°C.

Diminished immune status of patients suffering from carcinoma of uterine cervix as well as other malignancies has been reported (Olsson *et al*, 1972; Lauder and Bone 1973; Khoo and Mackay 1974). Almost similar findings have been observed in the present study. The absolute lymphocyte count, T-cell percentage and absolute T-cell count were found to be significantly lowered than normal controls. Similar were the findings of Ishiguro *et al* (1981) and Sinha *et al* (1985)

Immune deficiency was related to grade of malignancy. The minimum deficiency in grade I squamous cell carcinoma and gradual decrease was observed in grades II, III and anaplastic carcinoma. However, the cases of adenocarcinoma showed decrease in all parameters but it was not statistically significant. The findings were in accordance with Marrin *et al* (1974), though not with Cohen *et al* (1975). Dellon *et al* (1975) had investigated 112 patients with various types of bronchogenic carcinoma and they had found T-cells were significantly lowered than control values. They had also noticed progressive decrease in T-cells with advancing stage. Our findings are similar as maximum decrease was in anaplastic carcinoma.

Haemopoetic tissue is most radio sensitive organ complex of the body. Lymphocytes decrease more rapidly and granulocytes little more slowly; later on

platelets diminish in number and much later circulating red blood cells decrease (Reynieors *et al*, 1975). These factors would be responsible for decrease in count after radiotherapy as we have assessed these values one week after radiotherapy and the decrease in values were statistically significant as compared to pre-radiotherapy. However, partial recovery has been reported by Chee *et al* (1974) after 6 months. Jenkins *et al* (1976) who have also reported that extent of depression depends on the area of irradiation.

Thus it is concluded from the present study that immunological behaviour of cancer cervix is almost same as the cancer of other parts of the body. The extent of depression of CMI status is directly proportional to the grade of tumour and its metastasis. As the follow up could not be done in the present study because most of the cases were from rural area and did not turn up for follow up, further studies are in process to assess the status and then to follow up to see the prognosis.

References

1. Bach, J. F., Dormont, J., Dardenne, M. and Balner, M.: *Transplantation*. 8: 265, 1969.
2. Bentwich, Z., Douglas, S. D., Skutelsky, E. and Kinkel, H. G.: *J. Exp. Med.* 137: 1532, 1973.
3. Chee, C. A., Ilberty, P. L. T. and Rickingson, A. B.: *Brit. J. Radiol.* 47: 37, 1974.
4. Cohen, C. J., Gusberg, S. B. and Chen Sy. Yanno Poulos, G.: *Am. J. Obstet. Gynec.* 121: 91, 1975.
5. Dellon, A. L., Potivin, C. and Chretein, P. B.: *Cancer*. 35: 687, 1975.
6. Evan and Alexander, P.: *Nature*. 228: 620, 1970.
7. Ishiguro, T., Sugitachi, I. and Katon, K.: *Gynec. Oncol.* 9: 80, 1981.
8. Jenkins, V. K., Ray, P., Ellis, H. N., Griffiths, C. M., Perry, D. R. and Oslon,

M. H.: Arch. Otolaryngol. 102: 596, 1976.

9. Jondal, M., Holm, G. and Wigzell, H.: J. Exp. Med. 236: 207, 1972.
10. Khoo, S. K. and Mackay, F. V.: Brit. J. Obstet. Gynec. 81: 229, 1974.
11. Lauder, J. and Bone, G.: Brit. J. Cancer. 27: 409, 1973.
12. Marrin, C. and Hand, T.: J. Urol. 111: 170, 1974.
13. Mendes, N. F., Tolrai, M. E. A., Sylveira, N. P. A., Gilbertsen, R. B. and Metzgar, R. S.: J. Immunol. 118: 860, 1973.
14. Olsson, C. A., Rao, C. N., Men Zoian, J. O. and Byrd, E. W.: J. Urol. 107: 607, 1972.
15. Merrin, C. and Hand, T.: J. Urol. 11: 170, 1974.
16. Reyniers, J. A., Trexler, P. C., Scruggs, W., Wagner, M. and Gordon, H.: Radiation Research. 5: 591, 1956.
17. Singh, S. N., Agrawal, B. M. D., Shankar, C. and Rajvanshi, V. S.: A study of T-Lymphocyte and delayed cutaneous hypersensitivity reaction in patients with squamous cell carcinoma head and neck region. Ind. J. Cancer. 16: 53, 1978.
18. Sinha, R., Gupta, S. C. and Naithani, Y. P.: Indian J. Cancer. 22: 8, 1985.
19. Wybran, J. and Fudenberg, H. H.: New Engl. J. Med. 228: 1071, 1973.

Plasma is the liquid part of blood which is important in maintaining the normal function of cells. Low levels of serum transferrin has been observed during pregnancy and further lowering levels were seen in those with iron deficiency anemia. The role in enzymatic activity of cells in relation to well established (Lindner 1977) but its role in relation to abortion is obscure.

The present study was undertaken with the aim to find out serum transferrin levels in various types of abortion which may provide an insight into the role of iron in the pathogenesis of this clinical condition responsible for cessation of abortion and effective management.

The study was undertaken in the women attending Antenatal Clinic at Hospital S.P. Medical College, Bikaner. They were studied in following groups:

Group No.	Type
1	Normal non-pregnant women
2	Normal pregnant women
3	Threatened abortion
4	Incomplete abortion
5	Missed abortion
6	Hydatid mole

Plasma is important in maintaining the normal function of cells. In present study serum transferrin was studied in 60 women of various type of abortions. Twenty non-pregnant normal women and 50 normal pregnant women were included in the control. Serum transferrin study was done using method of Lindner (1977). In normal pregnancy serum transferrin was lower than non-pregnant women (Lindner 1977). In cases of various types of abortion further lower levels were seen. In cases of missed abortion and hydatid mole serum transferrin was lower than normal pregnancy. Low level of serum transferrin was observed in cases of hydatid mole.