

Cellular immunity in urologic cancer patients.

Dr. A.D. Bhatta *

"The host - Tumor relationship" consist of at least two parts, the aggressiveness of the tumor and the resistance of the host. Tumor immunology believes growth as a foreign tissue graft the body is unable to reject because of a deficiency in it's immune mechanisms. Several lines of evidence suggest that cellmediated immunity function plays a crucial role in the development and control of neoplasia (Mathe' 1980). New technique for monitoring the immune system was applied in last ten years. It was discovered that in patients with a variety of neoplasms many immunological parameters such as renal delayed-type hypersensitivity, lymphocyte blastogenesis and percentage of E-rosettes were decreased below normal (Hersh, Mavligit, Gutterman 1976). It is demonstrated that the degree of immunodepression had, in some circumstances, prognostic significance. Depressed immune reactivity was a harbinger of the relapse (Eilber, Morton 1970).

The evaluation of immune status in urologic cancer patients is in it's infancy.

The results reported are somewhat conflicting (Mc Laughlin et al. 1974: Robinson, Nakhla, Whitker 1971). Here we present cellular immunity in 118 urologic cancer patients.

Materials and Methods

Peripheral blood sample from 118 urologic cancer patients and 20 controls were tested for immunologic parameters. Of the 118 patients with proved malignancies 36 had prostatic carcinoma, 52 had bladder carcinoma and 30 had hypernephroma.

* D. Sc. level research worker. Faculty of urology. Second Moscow Medical Institue.

Lymphocyte reactivity to phytohemagglutinin (PHA) was determined from radiolabeled tritiated thymidine (3HTdr) uptake following 72 hours of lymphocyte culture in the presence of the PHA. The results are expressed as lymphocyte stimulation index (LSI). Where, $LSI = \text{Mean counts per minute PHA stimulated culture} / \text{Mean counts per minute unstimulated cell cultures}$.

T cells were determined by making use of their ability to form rosettes with sheep red blood cells at 0-4°C. When three or more cells were attached to an individual lymphocyte it was counted as a rosette.

The data presented here are preoperative. None of the patients had received immunotherapy. The differences observed were evaluated by Student's "t" test.

Results

CONTROLS. The mean peripheral blood lymphocyte count for this group was 1818.85 lymphocytes per cu mm. The mean percentage of lymphocytes which formed E-rosettes was 56.13 per cent and the mean absolute lymphocyte count was 1024.69 cells cu mm. The mean lymphocyte stimulation index was 19.39. Standard errors of mean are presented in table.

PROSTATIC CARCINOMA. The mean total lymphocyte count for this group was 1332.12 lymphocytes per cu mm, a mean percentage of E-rosette forming cells was 49.8 and a mean absolute T lymphocyte count of 691.63 T cells per cu mm. The prostatic cancer patients differed significantly from controls with respect to T cell percentages and absolute T lymphocyte counts ($P < 0.01$ and < 0.002 respectively). The mean stimulation index for this group was 5.7 ($P < 0.001$).

BLADDER CARCINOMA. In bladder carcinoma the mean total lymphocyte count was 1621.94 lymphocytes per cu mm ($P < 0.05$); the mean percentage of T lymphocytes was 40.26 ($P < 0.001$), and the mean absolute T lymphocyte count was 630 T cells per cu mm ($P < 0.001$). The mean stimulation index was 8.48. This data significantly differed from the controls. Pless than 0.001.

HYPERNEPHROMA. In hypernephroma patients the mean total lymphocyte count was 1423.47 ($P < 0.02$). The mean percentage of E-rosette forming lymphocytes in peripheral blood was 42.9 ($P < 0.001$). The absolute count of T lymphocytes was 635.04 cells per cu mm ($P < 0.001$). In this group the mean stimulation index was 9.13. P was less than 0.002.

Discussion

It is believed that cellular immunity is impaired in different diseases as well as in urologic cancer patients (Akaza et al. 1979). The impaired cellular immunity has nonspecific character and its mechanism is not always clearly understood. Many factors may act as immune suppressive in cancer patients (Castro 1976). The knowledge of immune status specially cellular has definite therapeutic and prognostic value in urologic cancer patients. Wybran, Fundenberg 1973 Showed that T cell level was low in patients with malignant neoplasms. They found that T cell levels were significantly lower in patients with metastases.

Our results suggested that cellular immunity, measured by peripheral blood absolute lymphocyte count, E-rosette forming lymphocytes and lymphocyte stimulation by PHA, in urologic patients with bladder and prostatic carcinomas and hypernephroma is impaired. It is expressed by decreased number of peripheral blood absolute lymphocyte count in prostatic carcinoma and in hypernephroma. Pless than 0.001 and 0.02 respectively by the Student's "t" test. But in bladder carcinoma total number of lymphocyte count in peripheral blood is not significantly altered ($P > 0.05$).

The percentage of the E-rosette forming lymphocytes is significantly low in hypernephroma, bladder carcinoma ($P < 0.001$) and in prostatic carcinoma ($P < 0.01$). The total number of the E-rosette forming lymphocyte is also significantly low in comparison with controls. In bladder carcinoma, though the number of the peripheral blood lymphocyte dose not differ significantly, the total number of the T lymphocytes is low (630 ± 39.64) in comparison with controls (1024.69 ± 70.04). This difference is significant by Pless than 0.001. It shows that, though total number of the periferal blood lymphocyte in bladder carcinoma does not differ from controls ($P > 0.05$), there is marked

Comparison of peripheral blood lymphocyte counts, percentages of E-rosette-forming lymphocytes, absolute T lymphocyte counts and PHA - induced lymphocyte stimulation index in controls and urologic cancer patients.

Lymphocytes donors	Absolute lymphocyte Count per cu.mm	T lymphocytes (%) + S.E.M.	Absolute T lymphocytes per cu.mm + S.E.M.	Lymphocyte stimulation index + S.E.M.
Controls (20)	1818.85 + 102.9	56.13 + 1.75	1024.69 + 70.04	19.39 + 2.65
Prostatic carcinoma (36)	1332.37 + 105.68 p** < 0.001	49.8 + 1.43 p < 0.1	691.63 + 68.63 p < 0.002	5.7 + 0.31 p < 0.001
Bladder carcinoma (52)	1609.94 + 118.40 p > 0.05	40.26 + 0.8 p < 0.001	630 + 39.64 p < 0.001	8.48 + 0.48 p < 0.001
Hypernephroma (30)	1423.47 + 114.83 p < 0.02	42.9 + 1.30 p < 0.001	635.04 + 65.62 p < 0.001	9.13 × 1.24 p < 0.002

* S.E.M. - standard error of the mean.

** Differs from controls by Pless than... by the Student's "t" test. Number of cases examined in parentheses.

lack of E-rosette forming lymphocytes as in other urologic cancer groups. Comparative high level of absolute peripheral lymphocyte in bladder carcinoma is mainly due to B "null" lymphocytes (author's unpublished data reported in scientific joint conference of faculty of urology under Second Moscow Medical Institute, Research Institute of Urology in Moscow and First City hospital urology department Moscow held in 24th December 1981).

The lymphocyte reactivity in response to PHA is significantly decreased in all groups. But the lymphocyte stimulation index is most low in prostatic carcinoma (5.7 ± 0.31 ; $P < 0.001$). However, it is significant low in hypernephroma (9.13 ± 1.24 ; $P < 0.002$) and in bladder carcinoma (8.48 ± 0.40 ; $P < 0.001$). As others (Robinson, Nakhla, Whitker 1971; Catalona, Potvin, Chretien 1974) the author is unable to demonstrate a correlation between PHA responsiveness and tumor stage. Though the impaired function of T cell in urologic cancer patients is suspected as a result of serum blocking factor (Akoza et al. 1979) it was demonstrated (Catalona et al. 1974) only among patients with metastastasis in prostate and kidney carcinomas (29 and 33 per cent respectively).

Summary

In 118 urologic cancer patients in peripheral blood number of total lymphocyte, percentage of circulating E-rosette forming lymphocytes, their absolute number and lymphocyte reactivity in response to PHA were measured and compared to levels found in 20 controls.

It was found that in all patient groups the 4 parameters of lymphocyte levels studied were significantly decreased except total lymphocyte count in bladder carcinoma.

It becomes obvious that impaired cellular immune response in urologic cancer patient is related with low level of peripheral blood lymphocytes which is always accompanied by significantly reduced number of T lymphocytes and their mitogenic response to PHA.

For routine clinical use simple lymphocyte count and measurement of E-rosette forming lymphocytes are preferable before the poshisticated and time-consuming lymphocyte blast transformation study.

REFERENCES

1. Akaza H. et al (1979) Restoration by levamisole of E-rosette formation and it's abrogation by autochthonous serum from patients with bladder cancer. Cancer, 43, 71.
2. Castro J.E. (1976) Immunology for surgeons. University Park Press, Baltimore.
3. Catalona W.J., Potvin C. and Chretien P.B. (1974) T lymphocytes in bladder and ptostatic cancer patients. J. Urol. 112,378.
4. Catalona W.J. et al (1974) Lymphocyte stimulation in urologic cancer patients. J. Urol. 112, 373.
5. Eilber F.R., Morton D.L. (6970) Impaired immunologic reactivity and recurrence following cancer surgery. Cancer 25, 362.
6. Hersh E.M., Marligit G.M. and Gutterman J.U. (6976) Immunodeficiency in cancer and the importance of immune evaluation of the cancer patients. Med. clin. North Am. 60, 623.
7. Mathe' G. (1980) Active immunotherapy of cancer. Russian translation from French, Moscow.
8. McLaughlin A.P. et al (6974) Immunologic competence in patients with urologic cancer. U. 666, 233.
9. Robiason M.R.G., Nakhla L.S. & Whitker R. (5976) Lymphocyte transformation in carcinoma of the prostate. Brit. J. Urol, 43, 480
10. Wybran J, and Fundenberg H, H, (6973) Thymus derived rosette forming cells in various human disease states: cancer, lymphoma, bacterial and viral infection and other diseases, J, Clin, Invest, 52, 6026