

Immune Status in Prostatic Benign Hypertrophy and Cancer

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Present knowledge of immune status in urologic patients is in its infancy. However, clinical immunology has made remarkable achievements in the last ten years (Banch 1978). Recently a new technique for monitoring the immune system was introduced. It was discovered that in patients with variety of urologic disorders many immunologic parameters such as recall, delayed-type hypersensitivity, lymphocyte blastogenesis and percentage of E-rosettes (an indication of the percentage of thymus dependent lymphocytes) were decreased below normal (Catalona, Chretien, Trahan 1974). Such patients were termed immunodepressed or immunoincompetent.

Benign prostatic hyperplasia (BPH) is the most frequent urologic disease seen in old male. At the same time carcinoma of the prostate (CP) is one of the most common malignancy in older age (Lopatkin 1982). Moreover old age itself is believed as a cause of immune deficiency (Makindon, Yunis 1977). All these facts make clear the importance of study on immune status in this group of patients.

In the present study, immune status in 20 controls (Group I), 50 patients with BPH (Group II) and 36 patients with CP (Group III) were evaluated and compared.

Materials and Methods:

Fifty patients with a histologic diagnosis of benign prostatic hypertrophy and thirty six with adenocarcinoma of the prostate were admitted and followed by the Faculty of Urology, First City Hospital, Moscow, were evaluated and compared with 20 controls.

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Immunological evaluation:

Immunologic studies were carried out in peripheral blood sample; peripheral blood lymphocytes were obtained by centrifugation on ficellurographin gradient. Lymphocytes were washed in medium 199. Lymphocyte reactivity to phytohem agglutinin (PHA) was determined (WHO / IARC work shop 1974) after 4 hours labeling with Tritiated Thymidine (^3H Tdr) before terminating 72 hours incubation. The incorporation of ^3H Tdr by the lymphocytes was quantitated and absolute activity was expressed in counts per minute (cmp). The result is expressed as stimulation index (SI) which is a ratio of mean counts per minute PHA stimulated culture to mean counts per minute unstimulated cell culture.

A part of the washed lymphocytes was used for rosette assay. E-rosette assay for T-lymphocytes was performed according to the method of Wybran & Fudenberg (1973); and EM-rosette assay for B-lymphocytes according to Gupta, Greco (1975).

lymphocytes unable to form E-rosettes were taken as "Null".

Presentation of Results – the results have been expressed as arithmetic means together with standard errors of the mean (See table). The significance of the results have been assessed by the Student's t-test.

Results

The total number of peripheral blood lymphocyte count was 1818.85 ± 102.9 , 1387.12 ± 80.09 and 1332.37 ± 105.68 for controls, BHP and CP respectively. The value for P was less than 0,001 in comparison to controls. There was no difference between the total number of circulating lymphocytes in peripheral blood in BPH and CP ($P > 0,05$).

There was marked difference in the percentage of lymphocytes which formed E-rosettes in three groups. The percentage of E-rosettes were 56.13 ± 1.75 ; 36.74 ± 9.56 and 49.8 ± 1.43 respectively for group I, II and III. These differences also remained significant. P less than 0,001 & 0,01 respectively. Except that, the difference between BPH and CP was also significant ($P < 0,001$).

The absolute number of T lymphocyte was calculated for each group. It was 1024.69 ± 70.04 , 499.14 ± 28.49 and 691.63 ± 68.63 for group I, II and III respectively. P was less than 0,001 and 0,02 for group II and III in comparison to controls. The difference between the absolute number of T lymphocytes in BPH and CP was also significant ($P < 0,02$).

Comparison of Immunologic parameters in controls
and urologic patients.

Lymphocytes donors	Controls (20)	Benign Pros- tatic hyperplasia	Prostatic carci- noma (36)	P** in comparision to group		
Parameters	group I	(50) group II	group III	I	II	III
Absolute Lymphocyte count per cu mm. ± S.E.M.	1818.85 ± 202.9	1387.12 ± 80.09	1332.37 ± 105.68	<0.001	<0.001	> 0.05
E-Rosette (%) ± S.E.M.	56.13 ± 1.75	36.74 ± 0.56	49.8 ± 1.43	<0.001	<0.001	<0.001
Total T - lymphocyte count per cu mm. ± S.E.M.	1024.69 ± 70.04	499.14 ± 28.49	691.63 ± 68.63	<0.001	<0.001	<0.02
EM - Rosette (%) ± S.E.M.	14.86 ± 0.35	24.67 ± 0.51	17.51 ± 0.84	<0.001	<0.01	<0.001
Total B - Lymphocyte count per cu mm ± S.E.M.	270.56 ± 16.92	371.97 ± 28.11	246.57 ± 30.63	<0.01	<0.05	<0.01
"Null cells" (%) ± S.E.M.	29.01 ± 1.76	39.36 ± 0.70	32.69 ± 1.72	<0.002	<0.05	<0.002
Total "Null cells" per cu mm. ± S.E.M.	523.59 ± 40.08	561.39 ± 36.94	401.03 ± 26.87	> 0.05	<0.02	<0.002
Lym phocyte stimula- tion index ± S.E.M.	19.39 ± 2.65	13.32 ± 0.98	5.7 ± 0.31	> 0.001	<0.001	<0.001

*S.E.M. — Standard error of mean

**Differs by P less than by the Student's "t".
Numbers of cases examined in parentheses.

The percentage of lymphocytes, which formed rosettes with mouse erythrocytes, was 14.86 ± 0.35 ; 24.67 ± 0.51 and 17.51 ± 0.84 respectively for group I, II and III. P was significant.

Absolute number of EM-rosette-forming lymphocytes was 270.56 ± 16.92 ; 374.97 ± 29.11 and 246.57 ± 30.63 for group I, II and III. The statistical difference between group I and II was significant ($P < 0.01$). But the value for P between group I and II was more than 0.05. However, the value between BPH and CP groups was significantly different ($P < 0.01$).

The percentage of the "Null" lymphocytes and their absolute number was calculated. It was 29.10 ± 1.76 ; 39.36 ± 0.70 ; 32.69 ± 1.72 and 523.59 ± 40.08 ; 561.39 ± 36.94 ; 401.03 ± 26.87 respectively for group I, II and III. All data regarding "Null" lymphocytes, was significantly different between BPH groups and CP groups ($P < 0.992$).

The stimulation index was 19.39 ± 3.65 for control, 13.32 ± 0.98 and 5.7 ± 0.31 for BPH and CP patients group. These data for prostatic cancer patients significantly differed from the control ($P < 0.001$), but does not differ from BPH group ($P < 0.05$). Moreover, there was significant difference between BPH and CP groups ($P < 0.001$).

Discussion:

The results described in this paper show that absolute count of circulating lymphocyte in BPH and CP is significantly low ($P < 0.001$).

It is believed that level of circulating lymphocytes has prognostic value. A decreased number of lymphocytes has always bad prognosis in cancer patients (Franks, Williams 1976; Papatestas et al. 1976). Moreover, host defence (as measured by outcome in children with measles) appeared to be better correlated with the absolute lymphocyte level than with any other parameters of immunity, including enumeration of T- and B-lymphocytes, PHA-Stimulation, and others (Coodavia et al. 1977).

Further we have found that the percentage of T-lymphocytes in BPH (36.74 ± 0.56) and CP (49.8 ± 1.43) was significantly low in comparison to controls (56.13 ± 1.75). P was less than 0.001 and 0.01 respectively. Moreover, there is significant difference between the percentage of the T- lymphocytes in BPH and CP ($P < 0.001$). It showed that though the absolute number of the circulating lymphocytes does not differ ($P < 0.05$) there was clear difference between

the T-lymphocytes in BPH and CP. The percentage of T-lymphocytes in BPH is lower than in CP.

The principal cell in immunologic surveillance against cancer was thought to be the T-lymphocyte; a decrease in lymphocytes would therefore be anticipated to increase new primary cancer. But our results regarding T-lymphocytes in CP show that low total count of T-lymphocytes is not the primary cause for the development of CP. Moreover, a number of observations have failed to confirm a major role for the T-lymphocytes in immunologic surveillance (Prehn, 1975).

The percentage of B cells, measured by EM-rosette in the peripheral blood from patients with BPH and CP, was high. The absolute number of cells measured by this technique was significantly high in BPH but not in CP. But the difference between the BPH and CP was high. P less than 0.001. These findings suggest that B cells may not play the dominant role in immunologic surveillance against cancer or in determining prognosis. The author believes that the disbalance observed in B cells is mainly due to secondary bacterial infection which is often seen in BPH and CP as a result of residual urine, that promotes bacterial proliferation and pyelonephritis.

In CP group patients the absolute number of "Null cells" (lymphocytes which do not form rosettes with sheep and mouse erythrocytes and were taken as "Null cells") is reduced in comparison with controls and BPH group patients. It shows that the role of other potential effector cells such as Natural Killer (NK) cells, K cells and macrophages warrant more intensive investigation in prostate cancer.

In prostate cancer patients group there is significant deficiency of T-lymphocyte function ($P < 0.001$). Our results agree with others (Robinson, Nakhla, Whitaker 1971; Mc Laughlin et al 1974) who reported that lymphocyte responsiveness to PHA was impaired. The impaired function of T-cell in prostate carcinoma with metastasis is suspected as a result of serum blocking factor but it was demonstrated only in 29 percent of patients (Catalona et al 1974).

Summary:

In 106 cases immunologic parameters were studied. Out of them 20 were controls (group I), 50 had benign prostatic hyperplasia (group II) and 36 were suffering from prostate carcinoma (group III).

In peripheral blood, number of total lymphocyte; percentage and total number of circulating T-, B- and "Null" lymphocyte and lymphocyte reactivity in response to PHA were measured and compared to levels found in controls. Except that these parameters were compared between group II and III.

It was observed that the number of circulating lymphocyte in peripheral blood was significantly low in group II and III in comparison to group I. But the statistical difference between group II and III for this parameter was not significant. The percentage and total number of T-lymphocyte was significantly reduced in group II and III in comparison to group I. Though the percentage of B-lymphocyte was high in group II and III (P less than 0,001 and 0,01 respectively), the total number of T-lymphocyte was significantly high only in group II.

It was found that the percentage of "Null cells" was significantly decreased only in group II but their total number was low only for group II ($P < 0,02$).

The lymphocyte reactivity in response to mitogen PHA was significantly low only in group III.

It was noted that, though there was no significant difference in total lymphocyte count between group II and III, the rest parameters differed significantly.

It became obvious that impaired immune response in benign prostatic hyperplasia and prostate cancer is related with low level of circulating peripheral blood lymphocytes, reduced number of E-rosette forming cells and with their decreased blast transformation capacity.

The total number of B-lymphocytes is increased in benign prostatic hyperplasia, whereas in prostate cancer group the number of "Null cell" is reduced.

In conclusion, the immunologic study may provide useful information of the patients' condition both in benign prostatic hyperplasia and prostate cancer. Suppression of cell mediated immunity, alteration of humoral mediated immunity and potential effector cells appear to be of value in the differential diagnosis of benign prostatic hyperplasia and prostate cancer. The role of immunity in the pathogenesis of benign prostatic hyperplasia and prostate cancer remains to be established.

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