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T LYMPHOCYTE SUBSETS IN PROSTATE CANCER SUBJECTS IN SOUTH EASTERN NIGERIA

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ABSTRACT

Humoral and cellular mechanisms play roles in immune response to foreign antigens. The present study was designed to determine the T lymphocyte subsets (CD4 + T cells, CD8 + T cells and CD4/CD8 ratio) in the prostate cancer subjects and control subjects. CD4 + T cells ($\mu\text{l}/\text{count}$) and CD8 + T cells ($\mu\text{l}/\text{count}$) were estimated using flow cytometric method by Partec while CD4/CD8 ratio was calculated from the results obtained from the CD4 + T cells and CD8 + T cells. CD4 + T cells and CD8 + T cells decreased significantly while the CD4/CD8 ratio increased significantly in the prostate cancer subjects compared to the control subjects. The suppressed CD4 + and CD8 + T cell counts in prostate cancer subjects may indicate immune instability in the prostate cancer subjects.

Key words: T lymphocyte subsets, prostate cancer, tumour

SOUS –ENSEMBLES DE LYMPHOCYTES T CHEZ LES SUJETS ATTEINTS DE CANCER DE LA PROSTATE DANS LESUD – EST DU NIGERIA.

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RESUME

Des mécanismes humoraux et cellulaires jouent un rôle dans la réponse immunitaire aux antigènes. La présente étude a été conçue pour déterminer les sous – ensembles de lymphocyte T (CD4 + cellules T, CD8 + cellules T et le rapport CD4/CD8) dans les sujets atteints de cancer de la prostate et sujets témoins. CD4 + cellules T ($\mu\text{l}/\text{count}$) et CD8 + cellules T ont été estimées en utilisant la méthode de cytométrie en flux par Partec tandis que rapport CD4 /CD8 a été calculé à partir des résultats obtenus des CD4+ cellules T et CD8+ cellules T. Lymphocytes T CD4 + et CD8 + ont diminué de manière significative tandis que le rapport CD4/CD8 a augmenté de manière significative chez les sujets atteints de cancer de la prostate par rapport aux sujets témoins. Les cellules T CD4 + et CD8+ supprimés comptent chez les sujets atteints de cancer de la prostate peut indiquer une instabilité immunitaire chez les sujets de cancer de la prostate.

Mots clés : Sous – ensembles de lymphocytes T, cancer de la prostate, tumeur.

INTRODUCTION

The incidence of prostate cancer in Nigeria is 18.2% and prostate cancer is about 9.6% of all mortality from cancer cases [1]. Both humoral and cellular mechanisms play roles in immune response to foreign antigens. Although, most humoral responses cannot prevent tumour growth, effector cells, such as T cells, macrophages, and natural killer cells have relatively effective tumouricidal abilities. Despite the activity of effector cells, host immunoreactivity may fail to control tumour occurrence and growth. Tumours

develop when this immune surveillance breaks down or is overwhelmed [2,3]. It has been stated that although many tumours are eliminated by the immune system (and thus are never detected), others continue to grow despite the presence of Tumour associated antigens [4]. Immune cells infiltrating human solid tumours have been extensively studied and found to exhibit unique phenotypic and functional characteristics [5,6]. Tumour-derived factors have been shown to induce death of immune cells at the tumour sites and in the peripheral

circulation [7]. The frequency of CD8+ T cells undergoing spontaneous apoptosis in the blood of patients with cancer was found to be significantly elevated relative to that in sex- or age-matched healthy controls [8]. CD8+ T cells were preferentially targeted for cell death compared to circulating CD4+ T cells [9]. It has long been recognized that disease progression in cancer patients is not solely determined by the characteristics of the tumour but also by the host response to foreign antigen [10].

The conversion of CD8+ T cells into suppressor cells may be one of the mechanisms by which tumours restrict the immune system's ability to control tumour growth and that activated CD4+ T cells that enter tumours may secrete factors that support the CD8+ T cell anti tumour functions, or may help other immune cells located in the tumour block the processes by which CD8+ T cells acquire their suppressive activity [11].

The study therefore aimed to determine the levels of T lymphocyte subsets (CD4+ T cells and CD8+ T cells) in prostate cancer subjects since they play active roles in immune response against tumours.

MATERIALS AND METHODS

A total of fifty prostate cancer subjects were recruited using non probability consecutive sampling. All the subjects gave their consents after they were informed of the investigations to be carried out. Ethical clearance was also obtained from the ethical committee of the Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State. The mean age of the prostate cancer subjects was 69 ± 7 . Thirteen subjects out of all the subjects were in stage 1, twenty three were in stage 2 and fourteen were in

stage 3. Twenty-nine out of all the subjects were on chemotherapy. The subjects who went through orchidectomy received Bicalutamide (Casodex) 150mg once daily while the other prostate cancer subjects who did not go through orchidectomy received Goserelin (3.6mg) every 28 days and Casodex (50mg) once daily.

A total of fifty apparently healthy males without any family history of cancer participated in the study. The mean age of the subjects was 52 ± 13 years. They were recruited after they underwent digital rectal examination and no clinical tumour was observed. The subjects were apparently healthy subjects without any other diseased condition.

Two milliliters of blood samples were collected from each subjects into Disodium ethylene diamine tetra acetic acid (EDTA) for the estimation of CD4 + and CD8 + T cells within 2 hours of collection using flow cytometric method[12].

The Mean and Standard Deviation (SD) were calculated for each parameter using Statistical package for Social Sciences (SPSS version 17.0). Differences in the means for each parameter between the two groups were compared using Student's t test and analysis of variance (ANOVA).

RESULTS

CD4 + T cells and CD8 + T cells in the prostate cancer subjects were significantly decreased ($p < 0.05$) compared to the control subjects; while the CD4/CD8 ratio in the prostate cancer subjects were significantly increased (Table 1).

There was no significance difference in CD4 + T cells, CD8 + T cells and CD4/CD8 ratio based on stages and chemotherapy (Tables 2 and 3).

TABLE 1: T LYMPHOCYTE SUBSETS IN PROSTATE CANCER

| Parameters | Prostate cancer | Control | P value |
|---|-----------------|-----------------|---------|
| CD4+ T cells ($\mu\text{l}/\text{count}$) | 696 \pm 86 | 1084 \pm 167 | 0.000* |
| CD8 +T cells ($\mu\text{l}/\text{count}$) | 391 \pm 51 | 666 \pm 100 | 0.000* |
| CD4/CD8 Ratio | 1.79 \pm 0.19 | 1.65 \pm 0.18 | 0000* |

*significant at $p < 0.05$

TABLE 2: T LYMPHOCYTE SUBSETS IN PROSTATE CANCER STAGES

| Parameters | Prostate cancer subjects in Stage 1 | Prostate cancer subjects in Stage 2 | Prostate cancer subjects in Stage 3 | F-values | P-values |
|---|-------------------------------------|-------------------------------------|-------------------------------------|----------|----------|
| | N=13 | N=23 | N=14 | | |
| CD4+ T cells ($\mu\text{l}/\text{count}$) | 728 \pm 111 | 689 \pm 91 | 703 \pm 73 | 0.353 | 0.704 |
| CD8 +T cells ($\mu\text{l}/\text{count}$) | 405 \pm 16 | 393 \pm 51 | 382 \pm 57 | 0.346 | 0.709 |
| CD4/CD8 Ratio | 1.79 \pm 0.22 | 1.76 \pm 0.17 | 1.86 \pm 0.23 | 1.391 | 0.259 |

TABLE 3: T LYMPHOCYTE SUBSETS IN PROSTATE CANCER BASED ON CHEMOTHERAPY

| Parameters | Prostate cancer subjects not on chemotherapy N=21 | Prostate cancer subjects on chemotherapy N=29 | P-values |
|-------------------------|--|--|----------|
| CD4+ T cells (µl/count) | 713 ± 90 | 683 ±83 | 0.238 |
| CD8 +T cells (µl/count) | 399 ± 49 | 385 ± 53 | 0.351 |
| CD4/CD8 Ratio | 1.80 ± 0.18471 | 1.79 ±0 .20 | 0.884 |

DISCUSSION

In this study, there was significant decrease in the levels of the T lymphocyte subsets of prostate cancer subjects compared with the male control subjects. The decrease in the mean CD4 + T cells and CD8 + T cells are as a result of their involvement in the destruction of the tumour antigens. The decrease in the T lymphocyte subsets is in line with another work which similarly observed decreases in CD4 + T cells and CD8 + T cells of prostate cancer subjects [13]. T-cell lymphocytes are important elements in the immune response and are regulated through a cascade of cellular and cytokine-based interactions. Furthermore, CD4+ lymphocytes, or T-helper cells, recognize antigens in conjunction with antigen presenting cells (APC) and produce cytokines that induce a wide response against foreign proteins on viruses or those on tumour cells [13]. The CD8 + T cells have direct tumouricidal activities that lead to the destruction of the tumour antigens [13,14,15]. These activities contribute to the significant increase recorded for the CD4/CD8 ratio in the prostate cancer subjects. However, it was reported that men with higher counts of CD4 + T cells in their prostate tumour environment have an increased risk of dying of prostate cancer [16]. The study did not observe any

significant difference in the T lymphocyte subsets based on the stages of prostate cancer as well as the use of chemotherapy.

Conclusion

Thus, the study concluded that there were significant decreases in CD4 + T cells and CD8 + T cells of prostate cancer subjects compared with the control subjects while the CD4+ T cells / CD8+ T cells ratio was significantly raised showing immune instability in the cancer subjects

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Competing interests
The authors declare that they have no competing interests.

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