DEPRESSION OF CELLULAR IMMUNITY IN PATIENTS WITH MALIGNANT AND PREMALIGNANT LESIONS OF THE ORAL CAVITY

Pages with reference to book, From 201 To 203

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The cellular immunity of cases with carcinoma of the oral cavity and leukoplakia were tested by delayed cutaneous hypersensitivity reaction to DNCB, PPD and Candida extract. Overall cellular immunity was depressed in carcinoma and leukoplakia patients and more so in carcinoma patients. It was further noted that impairment of cellular immunity was more marked with advance of the disease (JPMA 30201, 1980).

Introduction

The body immune mechanisms arc responsible for expression of the biologic individuality of the organism and also hold various body organs and tissues at their proper places (Bellanti, 1971). It has been postulated that the first line of defence in preventing the development of tumours may be immunologic surveillance, which recognizes as 'nonself, the small number of malignant or premalignant cells and destroy them before a true cancer develops (Burnet, 1968).
It has further been shown that patients with carcinoma of various organs have decreased response to variety of immune stimuli (Keller et al., 1976). A reduction in immune-competence as assessed by skin responsiveness to tuberculin in advanced cases of breast carcinoma (Hughes and Mackay, 1965), bronchogenic carcinoma (Krant et al., 1968) and Hodgkin's disease (Schier et al., 1956) has been reported.
It has been suggested that carcinomatous transformation in leukoplakia might be associated with some immunological changes (Lehner, 1971). Therefore, the present study was planned so as to assess the immune status of carcinoma and leukoplakia patients in comparison to normal individuals.

Material and Methods

Seventy patients, 54 of carcinoma and 16 of leukoplakia of the oral cavity and oropharynx were included in this study. Fifty-four controls of approximately the same age, sex and socioeconomic group having no systemic disease were also included.To evaluate cell mediated immunity skin tests were done with the following antigens:
1. 2-DINITROCHLOROBENZENE (DNCB) following the method of Blueminket al (1974) with slight modification.
Patients and controls were sensitized with a dose of 2,000 ug/ml DNCB solution in acetone and then challenged after 14 days with 0.05 ml of 0.3%, 0.1% and 0.01% of DNCB solution in acetone. DNCB solution was applied on volar aspects of the left upper arm.
2. CANDIDA ALBICAN EXTRACT (locally prepared) following the method of Man-ckiewicz et al (1959).
3. PURIFIED PROTEIN DERIVATIVE (PPD) following the method of Mantoux reaction (1910, as cited by Wilson and Miles, 1964).

Results

The result of the hypersensitivity reactions to DNCB, PPD and Candida extract are summarized in Tables I-IV and Fig. I.

Table I: Skin Reactivity to DNCB, PPD and Candida Extract Antigens

Group	DNCB		PPD		Candida extract	
	No. tested	No. +ve	No. tested	No. +ve	No. tested	No. +ve
Controls	46	46 (100%)	42	42 (100%)	47	44 (93.6%)
Carcinoma patients	54	48 (88.8%)	54	36** (66.66%)	54	41* (75.92%)
Leukoplakia patients	16	16 (100%)	16	16 (100%)	17	15 (88.23%)

Figures in parenthesis indicate percentage of each group.

*P <0.05 as compared to control. **P <0.001 as compared to control.

Table II: Distribution of DNCB Contact Sensitization Score in Cases of Carcinoma of The Oral Cavity & Oropharynx, Leukoplakia and Controls

Group	DNCB SCORE													
	0	1	2	3	4	5	6	7	8	9	10	11	12	Mean score ± SE
Control (46)	—	—	—	—	1 (2.17)	1 (2.17)	6 (13.04)	7 (15.2)	11 (23.9)	8 (17.39)	8 (17.39)	—	4 (8.69)	8.3 ± .27
Carcinoma (54)	6 (11.11)	—	6 (11.11)	4 (7.4)	10 (18.5)	10 (18.5)	12 (22.22)	3 (5.5)	1 (1.8)	1 (1.8)	—	—	1 (1.8)	*4.37 ± 0.32
Leukoplakia (16)	—	1 (6.2)	2 (12.5)	1 (6.2)	4 (2.5)	2 (12.5)	12 (6.2)	1 (6.2)	2 (12.5)	2 (12.5)	—	—	—	*5.06 ± 1.03

*P <0.001 as compared to controls.

Table III: Skin Reactivity to PPD (Quantitative Distribution)

Group	PPD Score					
	0	1+	2+	3+	4+	Mean score ± SE
Control (47)	—	5 (10.6)	20 (42.55)	18 (38.29)	4 (8.51)	2.44 ± 0.112
Carcinoma (54)	18 (33.33)	16 (29.62)	16 (29.62)	4 (7.4)	—	**1.11 ± 0.131
Leukoplakia	—	7 (43.75)	7 (43.75)	1 (6.25)	1	*1.75 ± 0.214

*P <0.01 as compared to controls. **P <0.001 as compared to controls.

Table IV: Skin Reactivity to Candida Extract (Quantitative Distribution)

Group	*Candida extract skin reaction score*					
	0	1+	2+	3+	4+	*Mean Score ± SE*
Control (42)	3 (6.38)	7 (14.89)	15 (31.91)	21 (44.68)	1 (2.02)	2.21 ± 0.14
Carcinoma (54)	13 (24.0)	21 (38.8)	12 (22.2)	8 (14.8)	—	**1.27 ± 0.14
Leukoplakia (17)	2 (11.7)	7 (41.1)	5 (29.4)	3 (17.6)	—	*1.52 ± 0.23

*P < 0.02 as compared to controls. **P < 0.001 as compared to controls.

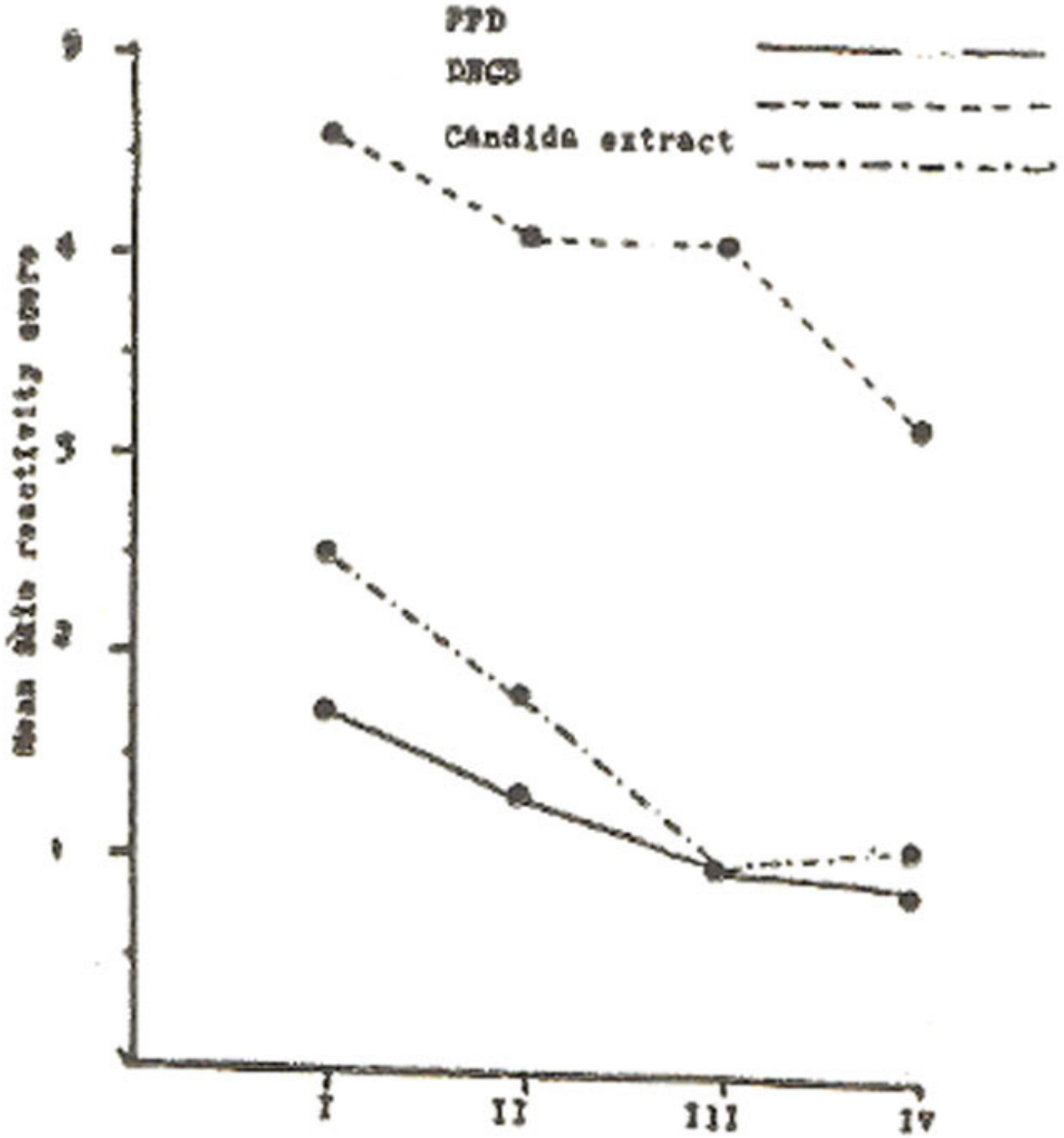

Fig : Hypersensitivity reaction to DNCB,PPD and Candida extract.

Discussion

Skin response to DNCB, PPD and Candida extract antigens was depressed in carcinoma and leukoplakia patients as compared to controls in the present study. Although statistically there was no difference (P>0.05) in number of positive cases for DNCB in carcinoma, leukoplakia and control

groups; however, the mean DNCB score was significantly lower ($P<0.001$) in carcinoma and leukoplakia patients as compared to the controls (Table I and II). These findings are in agreement with many other workers showing depressed immunity to DNCB skin reactivity in Hodgkin's disease (Aisenberg, 1962), lung cancer (Krant et al., 1968), squamous cell carcinoma of the rectum (Bone and Camplejohn, 1973), and urinary tract (Catalona et al., 1974).

Skin reactivity to PPD and Candida extract was reduced in significantly lower ($P<0.001$ and $P<0.05$, respectively) number of carcinoma patients as compared to controls. The mean PPD and Candida extract scores were also significantly lower in carcinoma ($P<0.001$) and leukoplakia ($P<0.01$ and <0.02, respectively) patients as compared to controls (Table I, II, IV). A reduction in the immunecompetence as assessed by skin responsiveness to tuberculin has also been reported in advanced cases of breast carcinoma (Hughes and Mackay, 1965), bronchogenic carcinoma (Krant et al., 1968), Hodg-kin's disease (Schier et al., 1956) and nassopharyn-geal carcinoma (Wara et al., 1975; Chan et al., 1976). A similar reduction of immune competence has also been reported with various other antigens such as candidin, mumps, etc in a variety of malignancies and autoimmune diseases (Thompson et al., 1975).

The correlation between delayed cutaneous hypersensitivity and stages of carcinoma of oral cavity and oropharynx has been demonstrated in Fig. 1. A decrease in the delayed cutaneous hypersensitivity to DNCFB, PPD and Candida extract was seen with the advance in disease, indicated by decreased percentage of positive cases and a decrease in the mean score from stage I to stage III (Fig. 1).

The impairment of cellular immunity could be an expression of failure of surveillance mechanisms which monitor the recognition and disposal of abnormal cell type arising spontaneously or induced by certain viruses and chemicals (Bellanti, 1971) though the production of circulating lymphocytes capable of destroying tumour cells on contact (Mckhann and Yarlott, 1975). But whether the impairment of cellular immune response in patients with various malignancies is an effect or cause of the malignancy is not completely settled. A 5-6% incidence of denovo cancer in organ transplant recipients receiving various forms of immunosuppressive therapy (Penn and Starzl, 1973) and simultaneous occurrence of malignancy with immunological deficiency diseases like ataxia telangiectasis (Peterson et al., 1964; Waldmann et al., 1972) show that in all probability the failure of cellular immune response is a cause rather than an effect of malignancy.

References

1. Aisenberg, A.C. (1962) Studies on delayed hypersensitivity in Hodgkin's disease. J. Clin. Invest., 41:1964.
2. Bellanti, J.A. Immunology. Philadelphia, Saunders, 1971, pp. 15, 323-38.
3. Bluemink, E., Nater, J.P., Koops, H.S. and The, T.H. (1974)A standard method for DNCB sensitization testing in patients with neoplasma. Cancer, 33:911.
4. Bone, G and Camplejohn, R. (1973) The role of cellular immunity in control of neoplasia. Br. J. Surg., 60:824.
5. Burnet, F.M. (1968) Evolution of the immune process in vertebrates. Nature, 218:426.
6. Catalona, W.J., Chretien, P.B. and Trahan, E.E. (1974) Abnormalities of cell-mediated I mmunocompetence in genitourinary cancer. J. Urol., 111:229.
7. Chan, S.H. Chew, T.S., Goh, E.H., Simons, M.J. and Shanmugaratnam, K. (1976) Impaired general cell-mediated immune functions in vivo and in vitro patients with nasopharyngeal carcinoma. Int. J. Cancer, 18:139.
8. Hughes, L.E. and Mackay, W.D. (1965) Suppression of tuberculin response in malignant disease. Br. Med. J., 2:1346.
9. Keller, S.E., Iochim, H.L., Pearse, T. and Siletti, D.M. (1976) Decreased T-lymphocytes in patients

with mammary cancer. Am. J. Clin. Pathol., 65:445.
10. Krant, M.J., Manskopft, G., Brandrup, C.F. and Madoft", MA. (1968) Immunologic alterations in bronchogenic cancer. Sequential study. Cancer, 21:623.
11. Lehner, T. (1971) Quantitative assessment of lymphocytes and plasma cells in leukoplakia, candidiasis and Lichen planus. J. Dent. Res., 50:1661.
12. Mckhann, C.G. and Yarlott, M.A. Jr. (1975) Tumour immunology. C.A., 25:187.
13. Manckiewicz, E., Stakiewicz, E. and Liivak, M. (1959) A polysaccharide isolated from Candida albicans as a growth-promoting factor for mycobacterium tuberculosis. Cand. J. Microbiol., 5:261.
14. Penn, I. and Starzl, T.E. (1973) Immunosuppression and cancer. Transplant. Proa, 5:943.
15. Peterson, R.D.A., Kelly, W.D. and Good, R.A. (1964) Ataxiatelangiectasia, its association with defective thymus, immunological-deficiency disease, and malignancy. Lancet, 1:1189.
16. Schier, W.W., Roth, A., Ostroff, G. and Schrift, M.H. (1956) Hodgkin's disease and immunity. Am. J. Med., 20:94.
17. Thompson, C.D., Whittingham, S., Mackay, I.R., Khoo, S.K., Toh, B.H. and Stagg, R.J. (1975) Quantitation of cell mediated immunity: Response to dinitrochlorobenzene and ubiquitous antigens. Can. Med. Assoc. J., 112:1078-1081.
18. Topley, W.W.C. Principles of bacteriology and immunity. 5th ed., edited by Sir Graham S. Wilson and Sir A. Ashley Miles. London, Arnold, 1964, p. 1599.
19. Waldmann, T.A., Strober, W. and Blaese, R.M. (1972) Immunodeficiency disease and malignancy. Various immunologic deficiencies of man and the role of immune processes in the control of malignant disease. Ann. Intern. Med., 77:605.
20. Wara, W.M., Wara, D.W., Phillips, T.L. and Ammann, A.J.(1975)Elevated IGA in carcinoma of the nasopharynx. Cancer, 35:1313.