DELAYED CUTANEOUS HYPERSENSITIVITY RESPONSES IN PATIENTS WITH WARTS

BHUSHAN KUMAR,* SURRINDER KAUR † AND ANIL NARANG ‡

Summary

Twenty five patients of viral warts were tested with various antigens of Secondary (recall antigens), primary delayed (DNCB) and inflammatory (Croton oil) type. Significantly depressed responses were elicited with various antigens in patients with warts as compared to controls.

Warts, a common viral infection of the skin occur most frequently in patients with diseases that are associated with deficiency of cell mediated immunity, marked[1] or subtle[2]. Humoral antibody is thought to have little role in acquisition, regression or recurrence of warts, although rapid resolution during treatment has been predicted by the presence of complement fixing anti-wart antibodies (IgG), that appear before or during the course of therapy[8]. Patients with Hodgkin's disease, lymphoma and chronic lymphocytic leukaemia have an increased incidence of warts compared with multiple myeloma where immunologic deficit is humoral[1]. The possession of a competent cell mediated immune system would thus be a prerequisite for the successful resolution of warts. The patients who have difficulty in eradicating their warts are perhaps, different from the normal population either in respect of cell mediated immune functions in general or as it applies specifically to wart antigen.

* Lecturer in Dermatology
† Asstt. Professor of Dermatology
‡ Lecturer in Pediatrics
Departments of Dermatology & Pediatrics
Post-graduate Institute of Medical Education and Research, Chandigarh, India
Received for publication on 18—9—1978

We studied the cell mediated immunity (CMI) in 25 patients with warts by their response to various antigens. The study was designed to evaluate the CMI n these patients with skin test response to secondary (recall antigens), primary delayed (DNCB) and inflammatory (Croton oil) type.

Material and Methods:

Twenty five patients suffering from Papova virus infection (fifteen having verruca vulgaris and ten having condylomata acuminata) were the subjects of study. They were chosen from the Dermatology Department of the Nehru Hospital of Post Graduate Institute of Medical Education & Research, Chandigarh. Duration of the desease varied from two months to more than seven years. All the patients had multiple lesions on various parts of the body. The age of the patients varied from nine to sixty nine years. There were nineteen males and six females (Table-1). Most of the patients had taken various topical and systemic therapies in the past. None of the patients was taking immunosuppressive therapy. The patients were screened to exclude any other accompanying systemic disorder.

TABLE 1

Depicts the response of individual patients to various irritants and sensitizing antigens.

No.	Age	Sex	Diagnosis	Duration	PPD	Mumps	Candidin	Cocci-diodin	C.Oil.	DN CB.
1.	19	M	VV	1 year	—	—	1×1 cm	—	+	—
2.	23	M	VV	1 year	+ ve	—	—	—	—	2 +
3.	9	F	VV	6 months	—	—	1×1 cm	—	+	—
4.	26	M	VV	6 months	+ ve	—	—	—	+	—
5.	52	F	VV	2 years	+ ve	—	—	—	+	2 +
6.	14	F	VV	7 years	—	—	—	—	+	—
7.	20	F	VV	6 months	—	—	—	—	—	2 +
8.	25	M	VV	6 months	—	—	1×1 cm	—	+	4 +
9.	30	M	VV	1 year	—	—	—	—	+	2 +
10.	23	M	VV	6 months	—	—	—	—	+	1 +
11.	25	M	VV	1 year	—	—	—	—	—	1 +
12.	27	M	VV	2 years	—	—	—	—	—	—
13.	16	M	VV	2 years	—	—	—	—	—	3 +
14.	25	M	VV	1 year	+	—	—	—	—	1 +
15.	53	M	VV	3 years	+	—	—	—	+	2 +
16.	23	M	CA	2 months	—	—	—	—	+	—
17.	20	M	CA	6 months	—	—	—	—	++	2 +
18.	13	F	CA	4 months	—	—	1×1 cm	—	—	—
19.	20	F	CA	3 months	—	—	—	—	+	2 +
20.	23	M	CA	3 years	—	—	8×8 cm	—	+	1 +
21.	30	M	CA	5 months	—	—	—	—	+	4 +
22.	28	M	CA	2 months	—	—	—	—	+	—
23.	30	M	CA	4 months	—	—	—	—	+	—
24.	27	M	CA	2 years	—	—	—	—	+	—
25.	20	M	CA	6 months	—	—	—	—	+	2 +
Percentage positivity					20	0	20	0	72	60

V. V. –Verruca Vulgaris C. A. –Condylomata acuminata.

The patients and 50 normal controls were tested with the following antigens and irritants :

(*1*) *Purified Protein Derivative* (*PPD*) (Serum Institute, Copenhagen, Denmark). 1 TU and 5 TU in individuals with negative response to 1 TU.

(*2*) *Mumps Antigen* (2 complement fixing units/ml). (Eli Lilly and Co. Indianapolis, Indiana, USA).

(*3*) *Candida Albicans* (100 protein nitrogen units (PNU)/ml) (Hollister-Stein labs., Burbank and San-Leandro, California, USA).

(*4*) *Coccidiodin*, (1 : 100 of Standardised mycelial coccidiodin) (Pasteur Institute, Paris).

0.1 ml of each antigen was injected intradermally into the forearm at one sitting. An induration of 5 mm or more after 24 hours was taken as positive for all antigens, except PPD where 10 mm or more induration after 72 hours was considered as positive. Patients or controls giving positive response to only one antigen were considered as negative.

(*5*) *Croton Oil* (10%) was applied to the forearm in the dose of 0.1 ml. It

TABLE 2

The comparative figures for patients and controls to irritants and antigens.

Group	No.	PPD	Mumps	Candidin	Coccidiodin	Croton oil	DNCB
Patients	25	5 (20)	0 (0)	5 (20)	0 (0)	18 (72)	15 (60)
Normal Controls	50	33 (66)	0 (0)	18 (36)	0 (0)	44 (88)	46 (92)

Figures in parenthesis show the percentage.

was allowed to dry and covered with a non-porous patch kept in position for 24 hours with a pad and adhesive tape. The development of only erythema at the site after 24 hours was labelled as negative, but marked erythema with small vesicles was considered a positive reaction.

(6) DNCB (Dinitro Chloro Benzene) 0.1 ml was applied to the forearm in the concentrations of 200 ug/ml and 50 ug/ml. If the response was negative after 14 days—a challenge form 50 ug/ml solution was applied and read again after seven days. The technique of DNCB testing used was that of Catalona et al, 1972(4).

Mumps and Coccidiodin antigens gave uniformly negative results in all patients and controls. Candidin and PPD gave positive results in five patients (20%) each respectively, whereas 66% and 36% of the normal controls reacted to PPD and candidin. Positive response to croton oil was obtained in 72% of the patients and 88% of the controls. Sensitization with DNCB could be achieved in 60% of the patients, versus 92% of the controls who gave positive response.

Discussion

Warts are very common viral infections and it would seem probable that in general, they develop not because of any significant immune deficiency state but, rather as a result of exposure and chance. However, there is marked variation in patients ability to control and eradicate the infection and some patients have what appear to be resistant warts. The existence of defective CMI in otherwise healthy subjects who have difficulty in eradicating the warts has been demonstrated[1,2,5]. The degree of defect correlated with the duration of the warts. An association of immunologic abnormalities and warts has also been suggested by a study on school children vaccinated with BCG. Those in whom warts develop were more likely to be anergic to PPD[6]. The evaluation of the delayed cutaneous hypersensitivity response has been shown to be a useful indicator of host immune competence[7]. Though the ability of an individual to respond to recall antigens depends on previous exposure, age, prior testing, other diseases and nutritional status[8,9], still these tests serve as best in viv parameters to indicate host's immune responses.

In the present study positive PPD responses with 1 TU or 5 TU were seen in only 20% patients whereas the controls showed such responses in 66%. The differences are statistically significant ($P < 0.001$). Since the tuberculin reactions are known to wane with time[10], the controls selected were age matched. None of the patients and controls had been tested with PPD during the three previous years, as it has been shown that repeated tuberculin testing may boost the tuberculin reaction[11,12].

The positive response to candidin was very low both in patients (20%) and controls (36%). The expected figures were high, especially for controls. Even

when the antigen is considered to be of low antigenicity the differences, though not very marked are statistically significant ($P < .05$). The low reactivity rate of normal age matched controls is difficult to explain.

Croton oil being an irritant, produced inflammatory changes almost to the same extent in patients (72%) and controls (88%). The differences though apparent, are not statistically significant.

Skin testing with DNCB gives more consistent and reliable results[4,7,13]. The response by sensitization is significantly less ($P < 0.001$) in patients (60%) as compared to controls (92%). The DNCB response seems to be the best in vivo measure of host CMI, as humoral antibodies are not significantly involved[15] and most people have had no prior exposure to the antigen. The age and medication also do not affect sensitivity response. A temporary depression to tuberculin[16,17,18] and sensitivity to other antigens during and after acute viral infections is well documented [19,20,21].

An increase in the incidence of viral diseases in patients with CMI defects, congenital, or due to therapeutic immunosuppression have been reported[22,23,24]. Decreased percentage and total T-lymphocytes in patients with warts and in those, whose warts had cleared in the immediate past have been reported[25]. Curiously the T-cell counts returned to normal after one year. An indirect evidence for involvement of CMI has been provided by the restoration of delayed hypersensitivity in anergic patients with warts by the anthelmintic agent levamisole[26]. Levamisole has been used for regression of warts in very resistant cases[27,28].

The present study shows significantly decreased responses to PPD and DNCB in patients with warts as compared to normals, indicating a definite depression of CMI. It is impossible to say whether the depression is the result of viral infection (warts) or the neoplastic disease (the wart) induced by the virus is a result of defective cellular immunity[6].

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