SHORT REPORTS

Peripheral Blood Lymphocyte Subpopulations in Patients with Viral Warts

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Peripheral blood T-cell subpopulations were evaluated in 32 patients affected by viral warts and in 32 unaffected individuals belonging to a control group. A significant decrease was found in total lymphocytes as well as OKT3 and OKT4 subsets among affected patients. A significant negative correlation was also found between OKT3 and OKT4 numbers as well as OKT4/OKT8 ratio and duration and extent of lesions. A significant positive correlation was found between the duration and the extent of lesions and the percentage of OKT8 subsets, but not the total number of OKT8. These data confirm that a cell-mediated immune deficiency is present in patients with viral warts. We then discuss whether the decrease of cellular immunity in these patients is a primary event or, rather, the result of persistent verrucosis. *Key words: T-cell subpopulations; Cellular immunodeficiency.* (Received August 7, 1985.)

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It is believed that the immune system plays an important role in the control of wart-virus infections. These infections indeed occur more frequently in diseases with a deficiency of CMI, cell-mediated immunity, (1, 2).

Several studies have shown that in patients with viral warts there was an impairment in cellular immunity as measured in vitro with response to PHA and PPD (1), and a decreased T-cell level with the rosette assay (3). In order to further investigate the relationship between viral warts and the functional status of the immune system, we have studied peripheral blood T lymphocyte subsets using monoclonal antibodies specific for surface markers of human T lymphocytes.

PATIENTS AND METHODS

Thirty-two patients, aged 12–70 years (mean 31.15±13.02), affected by viral warts were studied. All patients were evaluated by standardized clinical and laboratory tests: complete blood count, urinalysis, ESR, protein electrophoresis and immunoglobulins. No patient had ever received immunosuppressive or immunomodulating therapy. Thirty-two healthy, sex matched subjects were tested at the same time.

The duration of illness (in months) and the extent of lesions (number of warts) was measured in all patients. Monoclonal antibodies (Ortho Pharmaceutical Corp., Raritan, N. J., USA) directed against various human T cell antigens were produced as previously described (4). Three monoclonal antibodies named OKT3, OKT4, OKT8 were employed. As stated, OKT3 reacts with all peripheral T cells, OKT4 with T cells having helper-inducer function, OKT8 identifies cells with suppressor-cytotoxic activity. The absolute number of T cell subsets was calculated using the peripheral blood lymphocyte count. Results were analyzed by the Mann-Whitney U test and the Student's *t*-test.

RESULTS

All results are summarized in Tables I and II. Patients with viral warts show a significant decrease in total lymphocyte count and in OKT3, OKT4 and OKT8 subpopulations as

Table I. *Lymphocyte number and T-lymphocyte subsets in 32 patients with viral warts (number and percentage)*

	Lymphocyte counts/mm³	OKT3		OKT4		OKT8		OKT4/ OKT8
		Number	%	Number	%	Number	%	
Patients (mean±SE)	1 943.75± 66.89	1 241.84± 48.14	62.94± 1.73	743.21± 43.91	37.77± 1.87	502.90± 15.04	25.34± 1.27	1.53± 0.11
Control group (mean±SE)	2 405.88± 217.17	1 645.17± 176.07	66.06± 1.97	1067.47± 147.09	43.23± 1.58	633.29± 64.99	26.35± 1.13	1.66 0.09
Significance	$p<0.05$	$p<0.05$	NS	$p<0.05$	$p<0.05$	$p<0.05$	NS	NS

compared to the control group. On the other hand, only the OKT4 subpopulation exhibits significantly reduced percentages compared to the control group. In our patients, the duration of the lesions varied from 1 to 36 months (mean 10.38±2.64), while the number of lesions varied from 1 to 25 (mean 8.27±1.57). We have observed a significant negative correlation between the extent and the duration of lesions and the total number of OKT3 and OKT4 subpopulations. The total number of OKT8 lymphocytes did not reveal any significant correlation with the above mentioned parameters. The total count of lymphocytes showed a negative correlation only with the extent of the lesions. With regard to T-subset percentages, we have found a significant negative correlation only between OKT4 and the extent and duration of lesions and a positive correlation between OKT8 cells and these parameters. The OKT4/OKT8 ratio was negatively correlated with the duration and the extent.

DISCUSSION

It is well established that cellular immunity plays an important role in the control of viral infection. Various studies have demonstrated a cell-medited immune deficiency, especially in patients with recurrent or chronic viral warts (5, 6). The use of monoclonal antibodies now available against distinct blood T-lymphocyte subsets gives us a better understanding

Table II. *Statistical correlation between clinical parameters and T-cell subsets (total number and percentage) in patients with viral warts*

r=coefficient of correlation

	Lymphocyte counts/mm³	OKT3		OKT4		OKT8		OKT4/ OKT8
		Number	%	Number	%	Number	%	
Duration of the lesions (in months)	$r=-0.32$	$r=-0.49$	$r=0.32$	$r=-0.60$	$r=-0.60$	$r=-0.15$	$r=0.58$	$r=-0.79$
Significance	NS	$p<0.01$	NS	$p<0.01$	$p<0.01$	NS	$p<0.05$	$p<0.01$
Extent of the lesions (number)	$r=-0.51$	$r=-0.61$	$r=0.41$	$r=-0.73$	$r=-0.69$	$r=-0.14$	$r=0.75$	$r=-0.70$
Significance	$p<0.01$	$p<0.01$	NS	$p<0.01$	$p<0.01$	NS	$p<0.01$	$p<0.01$

of some immunological facts regarding the immunity of viral warts. Our data show a significant reduction in the total count of lymphocytes, OKT3, OKT4 and OKT8 subsets.

A reduction in the lymphocyte total count has already been observed in association with viral infection (7, 8), but this is the first report, to our knowledge, of an imbalance of T-lymphocyte subsets in patients affected by viral warts. We can only speculate about the significance of this lymphocytic depletion and OKT^+ subsets re-distribution. According to the hypothesis of Roujeau (9), the lowering of OKT3 and OKT4 lymphocytes may only be the marker of a viral infection. In any case, our data support and more precisely define the concept previously suggested by Mohanty of "dyslymphocytosis" to explain the development of viral warts (8), as a re-distribution of activated T-lymphocyte subsets with a reduction of the OKT4 subpopulation. Various studies have shown that the immune response to wart virus was weaker in patients whose warts were cured in a relatively short period (5). Persistent viral infection (more than one year) might contribute to depression of T cells (3) during the life span of warts and particularly of the OKT4 subset, which represents the central point in the control of cellular immunity. Our finding of a negative correlation between the lymphocyte total count, the number of $OKT3^+$, $OKT4^+$ lymphocytes and the duration and the extent of the lesions add new data about the behaviour of the cell-mediated immunity in patients suffering from viral warts. In vitro assay of CMI (cell-mediated immunity) to human wart antigen has shown defective response in patients with a long history of wart infection (5) stating that duration of viral infection may be an important factor in CMI. On the basis of our results we infer that the extent of the lesions (and consequently the number of viral particles) take some part in the changes of CMI in these patients, resulting in an altered distribution of lymphocyte subsets. It is very hard, however, to determine whether the decrease in CMI is a primary event leading to the development of warts or the result of persistent verrucosis. We can only draw the conclusion that these conditions, though seemingly not serious, could be the evidence of other underlying cell-mediated immunodeficiencies.

REFERENCES

1. Morrison WL. Viral warts, herpes simplex and herpes zoster in patients with secondary immune deficiencies and neoplasms. Br J Dermatol 1975; 92: 625–630.
2. Thivolet J, Viac J, Staquet MJ. Cell-mediated immunity in wart infection. Int J Dermatol 1982; 21: 94–98.
3. Chretien JH, Esswein JG, Garagusi VF. Decreased T-cell levels in patients with warts. Arch Dermatol 1978; 114: 213–215.
4. Reinherz EL, Kung PC, Goldstein G, Schlossman SF. Separation of functional subsets of human T cells by a monoclonal antibody. Proc Natl Acad Sci USA 1979; 76: 4061–4065.
5. Lee AKY, Esinger M. Cell mediated immunity (CMI) to human wart virus and wart associated tissue antigens. Clin Exp Immunol 1976; 26: 419-424.
6. Morrison WL. Cell mediated immune responses in patients with warts. Br J Dermatol 1975; 93: 553–556.
7. Carney WP, Rubin RH, Hoffman RA, Hansen WP, Healey K, Hirsh MS. Analysis of T lymphocyte subsets in cytomegalovirus mononucleosis. J Immunol 1981; 126: 2114–2116.
8. Mohanty KC, Roy RB. Thymus derived lymphocytes (T cells) in patients with genital warts. Br J Vener Dis 1984; 60: 186–188.
9. Roujeau JC, Moritz S, Guillaume JC, Bombal C, Revuz G, Weil B, Touraine R. Lymphopenia and abnormal balance of T-lymphocyte subpopulations in toxic epidermal necrolysis. Arch Dermatol Res 1985; 227: 24–27.